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MARIA LUIZA VEIGA DA FONSECA

ELETROESTIMULAÇÃO TRANSCUTÂNEA PARASSACRAL PARA BEXIGA HIPERATIVA ISOLADA EM CRIANÇAS E ADOLESCENTES. O PAPEL DA CONSTIPAÇÃO.

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Tese apresentada ao curso de Pós-graduação em Medicina e Saúde Humana da Escola Bahiana de Medicina e Saúde Pública para obtenção do título de Doutora em Medicina e Saúde Humana.

Orientador: Prof. Dr. Ubirajara de Oliveira Barroso Júnior

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EBMSP - Escola Bahiana de Medicina e Saúde Pública

ADAB – Ambulatório Docente Assistencial da Bahiana

CEDIMI – Centro de Distúrbios Miccionais na Infância

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Aos meus queridos e amados avós, Venceslau e Valda Veiga,
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RESUMO

Introdução: A Estimulação Elétrica Nervosa Transcutânea (TENS) parassacral é um método eficaz para o tratamento da Bexiga Hiperativa (BH), além de melhorar os sintomas da constipação. Entretanto, ainda não é conhecido se a constipação *per si* é um fator de risco de falha para a resolução dos sintomas de BH após a TENS. Além disso é possível que a ação do TENS em relação à BH seja diretamente associada com a melhora da constipação. **Objetivos**: Avaliar a presença da constipação como fator prognóstico na resolução dos sintomas de Bexiga Hiperativa Isolada (BHI) em escolares tratados com TENS parassacral. Testar a hipótese de que o efeito da TENS parassacral na BHI seria devido ao fato de que a constipação é melhorada com este método. **Materiais e Métodos**: Estudo prospectivo de escolares com BHI, constipadas ou não, que foram submetidas a TENS parassacral. A melhora dos sintomas miccionais foi avaliada pela Escala Visual Analógica e o Critério Roma III foi usado para diagnosticar a constipação antes e após o tratamento. Os sintomas de urgência, urge-incontinência, Infecção do Trato Urinário (ITU), polaciúria, noctúria, manobras de contenção, enurese e constipação foram avaliados. Todos os pacientes foram orientados quanto à uroterapia padrão, exceto em relação ao tratamento da constipação. Além disso, nenhuma criança fez uso de medicamento anticolinérgico. **Resultados**: 51 crianças com BHI foram incluídas no estudo, tendo resolução completa dos sintomas em 25 (49%). Vinte e cinco crianças eram constipadas antes do tratamento e obtiveram resolução dos sintomas em 15 casos (60%). Não houve diferença estatisticamente significativa entre idade, sexo e os sintomas urinários entre as crianças constipadas e não constipadas. Houve uma melhora na urgência, urge-incontinência e na realização de manobras de contenção nos dois grupos, porém não houve melhora significativa da enurese. Não houve diferença significante na resolução da BHI nas crianças constipadas ou não. A resolução da BHI não foi associada com a resolução da constipação e vice-versa. **Conclusão**: A presença de constipação antes do tratamento não foi associada a um pior prognóstico para a resolução de sintomas de BHI. A melhora da BHI não está associada a melhora da constipação com a TENS parassacral.

Palavras chave: Bexiga Hiperativa Isolada, Criança e Eletroestimulação Transcutânea

ABSTRACT

Introduction: Parasacral transcutaneous electrical nerve stimulation (TENS) is an effective method for the treatment of overactive bladder (OAB) and improve the symptoms of constipation. However, it is not yet known if constipation itself is a risk of failure factor for the resolution of the symptoms of OAB after TENS. Furthermore it is possible that the action of TENS compared to OAB is directly associated with the improvement of constipation. **Objective**:To assess the presence of constipation as a prognostic factor in resolving symptoms of isolated OAB in children treated with parassacral TENS. To test the hypothesis that the effect of parasacral TENS in isolated OAB would be due to the fact that the constipation is improved with this method. **Material and Methods:** This is a prospective study children of with isolated OAB who were submitted to parasacral TENS. The Rome III criteria were used to diagnose constipation. Symptoms of urgency, urge incontinency, UTI, frequency, nocturia, holding maneuvers, enuresis and constipation were evaluated by visual analog scale. All patients were informed about the standard uyotherapy, except for the treatment of constipation. In addition, no child made use of anticholinergic medication. **Results**: 51 children with isolated OAB were included in the study, with complete resolution of symptoms in 25 (49%). Twenty-five children were constipated before treatment and achieved resolution of symptoms in 15 cases (60%). There was no statistically significant difference between age, sex, and urinary symptoms among the constipated children and not constipated. There was an improvement in urgency, urge incontinence and carrying out holding maneuvers in both groups, but no significant improvement in bedwetting. There was no significant difference in the resolution of isolated OAB in constipated children or not. The resolution of isolated OAB was not associated with resolution of constipation and vice versa. **Conclusion**: The presence of constipation before treatment was not associated with a worse prognosis for resolving symptoms of isolated OAB. Improved isolated OAB is not associated with improvement in constipation with parasacral TENS.

Keywords: Overactive Bladder Isolated, Child and Transcutaneous electrical stimulation

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ABREVIAÇÕES

BBD - Bladder Bowel Dysfunction

ITU - Infecção do Trato Urinário

RVU - Refluxo Vesicoureteral

DTUI - Disfunção do Trato Urinário Inferior

BH - Bexiga Hiperativa

TENS - Transcutaneous Electrical Nerve Stimulation

ICCS - International Children's Continence Society

BHI - Bexiga Hiperativa Isolada

IU - Incontinência Urinária

EUA - Estados Unidos da América

CEDIMI - Centro de Distúrbios Miccionais na Infância

ADAB - Ambulatório Docente Assistencial de Brotas

DVSS - Dysfunction Voiding Scoring System

Hz - Hertz

µs - milisegundos

S2 e S4 - 2ª e 4ª vértebras sacrais

EVA - Escala Visual Analógica

SPSS - Statistical Package for the Social Sciences

EBMSP - Escola Bahiana de Medicina e Saúde Pública

DP - Desvio Padrão

IC – Intervalo de Confiança

SUMÁRIO

1 INTRODUÇÃO

A Bexiga Hiperativa (BH) é o distúrbio miccional mais comum na infância e está presente em, aproximadamente, 6% das meninas e 3,8% dos meninos com 7 anos de idade.[1] Seu início pode ser lento, com o aumento gradual na piora da urgência, ou ocorrer repentinamente com episódios importantes de incontinência urinária, podendo persistir com o tempo, com impacto na função da bexiga e mais casos de infecção do trato urinário (ITU) na idade adulta.[2] Além de consequências físicas, crianças com urgeincontinência podem apresentar alterações comportamentais, como maior agressividade, isolamento social e déficits de atenção.[3] A BH pode ter associação com alguma alteração na fase de esvaziamento vesical, porém quando apresenta fluxo em sino e ausência de resíduo pós miccional, pode ser denominada de Bexiga Hiperativa Isolada.

A constipação, queixa frequente na infância, é considerada um problema de saúde pública devido à sua alta prevalência em toda a população, representando um significativo impacto nos serviços de saúde com um custo de 3,9 bilhões por ano, nos EUA.[4] Definida como um conjunto de sinais e sintomas relacionados à eliminação das fezes, o que inclui diminuição da frequência evacuatória, fezes grandes, duras ou em pequenos pedaços, dor abdominal, fezes retidas no reto e escape fecal.[5,6]

A relação entre a constipação e os sintomas do trato urinário inferior, em crianças, é bem conhecida, sendo chamada de *bladder bowel dysfunction* (BBD). A BBD está associada a um maior risco de ITU e refluxo vesicoureteral (RVU).[7,8] A constipação pode associar-se à disfunção do trato urinário inferior (DTUI) por algumas razões: 1) fezes endurecidas e retidas no reto podem comprimir a bexiga e o colo vesical, contribuindo para um pior esvaziamento vesical; 2) A contração da musculatura perianal, usada na retenção de fezes, pode contrair o esfíncter uretral externo, predispondo a uma maior retenção de urina; 3) Uma hiperatividade do assoalho pélvico pode dificultar o esvaziamento vesical; 4) Contrações do esfíncter uretral externo, para evitar a incontinência urinária, podem, por conseguinte, contrair a musculatura perianal predispondo à inibição do reflexo defecatório; 5) Elas podem vir associadas pela imaturidade neurofisiológica e sem relação de causa e efeito; 6) Pela mesma origem embriológica, alterações aferentes ou eferentes espinhais e supraespinhais podem estar envolvidas em ambas as condições.[9,10]

Recentemente, Veiga et al demonstraram que não somente a micção disfuncional, mas também a Bexiga Hiperativa (BH) com micção coordenada estão associadas à constipação.[11] Crianças com BH Isolada apresentaram uma chance quase três vezes maior de apresentar constipação do que as assintomáticas. Sendo assim, é primordial que, na abordagem da criança, ambas as disfunções sejam tratadas.

Antimuscarínicos podem ser usados para o tratamento da BH, mas uma desvantagem importante é a sua ação negativa sobre a função defecatória.[12] TENS (*Transcutaneous Electrical Nerve Stimulation*) parassacral tem se mostrado eficaz no tratamento da BH em crianças.[13] Do mesmo modo, a TENS tem mostrado resultados favoráveis para a constipação,[14] portanto, uma vantagem adicional da TENS parassacral é que, além da melhora dos sintomas miccionais, há também resolução da constipação em um número significativo de crianças.[15,16] Entretanto, ainda não é conhecido se a constipação *per si* é um fator de risco de falha para a resolução dos sintomas de BHI após a TENS.

Além disso, alguns autores têm demonstrado que o tratamento da constipação por si só faz os sintomas do trato urinário inferior melhorarem.[8,17] No estudo de Loening-Baucke et al, a melhora da constipação levou à correção da incontinência em 89% dos casos.[18] Como a TENS tem efeito positivo na resolução dos sintomas miccionais e de retenção fecal, poder-se-ia teorizar que a ação desse método na BH poderia estar diretamente relacionada à melhora da constipação. Em outras palavras, que a ação da TENS parassacral na BH seria, basicamente, devido à resolução da constipação.

2 OBJETIVO

2.1 Objetivo Geral

- Avaliar a presença da constipação como fator prognóstico na resolução dos sintomas de BHI em escolares tratados com TENS parassacral.

2.2 Objetivo Específico

- Testar a hipótese de que o efeito da TENS parassacral na BHI seria devido ao fato de que a constipação é melhorada com este método.

3 HIPÓTESE CIENTÍFICA

- A presença da constipação prévia ao tratamento com TENS é fator de risco para falha da resolução de sintomas de BHI após o procedimento.

- O efeito da TENS parassacral na Bexiga Hiperativa Isolada associa-se a melhora da constipação com este método.

4 REVISÃO DA LITERATURA

4.1 Bexiga Hiperativa

A BH é um tipo de distúrbio do trato urinário inferior e é definida, pela *International Children's Continence Society* (ICCS), como a presença de urgência miccional com ou sem incontinência urinária, geralmente acompanhada de aumento da frequência urinária e da enurese. É uma alteração da fase de enchimento vesical, na ausência de ITU ou de outra patologia associada,[19] podendo apresentar, de forma associada, alguma alteração no esvaziamento vesical, como fluxo em staccato ou resíduo significativo. Para as crianças que não apresentam nenhuma alteração no esvaziamento da bexiga, como a urofluxometria em formato de sino ou torre e resíduo pós miccional desprezível, o distúrbio urinário pode ser denominado de Bexiga Hiperativa Isolada (BHI).

O controle para a micção pode ser adquirido entre os 3 e 5 anos e envolve centros corticais superiores no cérebro, medula espinhal, sistema autonômico e somático, receptores aferentes sensoriais, além de componentes anatômicos do trato urinário inferior. O centro miccional do cérebro tem um papel relevante na percepção sensorial de plenitude da bexiga e controle motor da micção, como diversas outras áreas cerebrais (centro pontino da micção, substância cinzenta periaquedutal, tálamo, ínsula, giro cíngulo anterior e córtex pré-frontal).[20]

Uma possível teoria para a BH na infância seria um atraso da aquisição da inibição cortical nas contrações involuntárias do detrusor, no decurso da maturação do padrão miccional, que pode ser nas vias reticuloespinhais da medula ou no centro inibitório do córtex. Além disso, um retardo na sincronia entre coordenação esfincteriana durante a micção pode causar contrações do detrusor no enchimento.[21]

A BH pode estar associada a sintomas urinários como urgeincontinência, enurese, ITU de repetição, refluxo vesicoureteral e hidronefrose. Crianças com urgência miccional tendem a realizar manobras, como cruzar as pernas ou agachar para anulação do desejo e postergação da micção durante uma contração involuntária da bexiga ou momento de grande urgência miccional, proporcionando, momentaneamente, um relaxamento reflexo do detrusor. A persistência isométrica do esfíncter contra o detrusor e o seu incompleto relaxamento pode

ocasionar a hipertrofia da musculatura vesical.[22] Essa hipertrofia favorece a diminuição progressiva da capacidade funcional vesical e persistência ou aumento da hiperatividade. Além disso, a contração dos músculos do assoalho pélvico pode propiciar o retorno da urina para a bexiga nas meninas, muitas vezes infectada.[7] Essa é uma possível explicação para o quadro clínico de crianças que não têm resíduo pós miccional, porém apresentam histórico de ITU de repetição.

Em adição a esse evento, a dificuldade imposta pela criança para a saída da urina durante as contrações da bexiga pode possibilitar o retorno da urina pelos ureteres, em graus variados, podendo levar à hipertrofia da bexiga e ao aparecimento de divertículos. O aumento da pressão vesical e o refluxo vesicoureteral podem, também, levar à hidronefrose.[23] Além disso, a enurese está comumente associada à BH. Este fato pode ser explicado por uma fisiopatologia comum, pois a incapacidade neurofisiológica de controlar a bexiga durante o dia também persiste pela noite.[24]

Com a cronicidade dos sintomas relacionados ao distúrbio miccional, a criança tende a uma inibição sucessiva do ato, resultando em consequências emocionais, com um maior grau de ansiedade, autoimagem negativa e afastamento do convívio social.[25] Da mesma forma, IU está associada a alterações de internalização e externalização.[3] A associação das consequências físicas e emocionais decorrentes da BH deve ser de grande importância no manejo das crianças, sendo necessária uma equipe multidisciplinar para a sua abordagem.

Um dos tratamentos utilizados para BH é o uso de medicamentos anticolinérgicos que agem nos receptores muscarínicos, reduzindo o estímulo aferente da parede vesical ou inibindo a contração involuntária da bexiga. Esse tratamento, devido à ação generalizada em todo o sistema nervoso parassimpático, pode acarretar diversos efeitos colaterais, que inclui uma maior propensão à constipação, boca seca e intolerância ao calor.[12] Além dos efeitos adversos, a necessidade de uso diário da medicação dificulta a sua utilização na população pediátrica.

4.2 Constipação

A constipação é definida como um conjunto de sinais e sintomas relacionados à eliminação das fezes que inclui diminuição da frequência evacuatória, fezes grandes, duras, ou

em pequenos pedaços, dor abdominal, fezes retidas no reto e escape.[5,6] Outros sintomas desagradáveis e bastante angustiantes podem estar associados, como hiporexia, anorexia, náuseas e vômitos.[26]

A constipação corresponde de 3 a 5% das visitas ao pediatra[27] e 25% aos consultórios de gastroenterologistas.[28] O seu diagnóstico é basicamente clínico, sendo realizado através do Critério Roma III.[10]

A constipação pode ser classificada em orgânica (etiologia neurológica ou endócrina) e funcional. Neste caso, o fator causal é desconhecido e sua apresentação clínica varia de acordo com o período de vida da criança, correspondendo a 95% das causas da constipação infantil.[27] Pode ser desenvolvida em três momentos a partir de uma experiência defecatória desagradável: com a introdução de cereais e alimentos sólidos na vida do lactente, no período do treino defecatório e no início da vida escolar.[29]

Diversas causas podem levar à inibição do desejo de defecar, como stress, trauma, mudança na rotina, tentativa de chamar atenção dos pais ou irmãos, falta de atenção, alterações psicológicas e até abuso sexual. Um início de treino defecatório precoce e sob pressão dos pais, postura inadequada (sem tocar os pés no chão), insegurança de usar o *toilet* e pouca ingestão de fibras causando fezes endurecidas também podem levar à constipação.[26,30] Na escola, as crianças são pressionadas a não abandonarem a sala de aula e, muitas vezes, recusam-se a usar um toalete sem a devida higiene; isso pode propiciar a retenção fecal. Independente do fator precipitante, a associação da memória ou expectativa da dor durante a defecação, que pode ser consequência desses outros fatores, leva a um ciclo vicioso com defecações dolorosas e supressão de ida ao toalete.[27,31,32]

A inibição da defecação com posturas retentoras empurram as fezes de volta ao canal retal, reduzindo a urgência defecatória. Com a reabsorção de água e eletrólitos há um acúmulo de fezes endurecidas e de grande diâmetro, ocasionando evacuações com mais dor e possível fissura anal. A impactação fecal e a distensão retal prejudicam os estímulos sensoriais provocados pela chegada das fezes, a força propulsiva do reto, assim como o desejo de defecar,[27,33] podendo levar à diminuição do tônus, contribuindo ainda mais para o retardo da defecação.[34]

A constipação, muitas vezes, é subdiagnosticada pelos pais, o que dificulta seu tratamento pela demora da identificação e da intervenção terapêutica. Um estudo encontrou uma elevada frequência de constipação em crianças enuréticas, quando avaliadas por questionário, porém com baixa correlação, quando comparada com a opinião dos pais sobre o diagnóstico da constipação (36,1% *versus* 14,1%; Kappa=0,155, p=0,003).[35]

Comorbidades comportamentais são frequentemente encontradas em crianças constipadas, principalmente quando relatam incontinência fecal associada. Essas alterações psicológicas podem ser, ainda, mais agravadas quando associadas à incontinência urinária, sendo 3 a 6 vezes maior quando comparadas com crianças sem alguma incontinência.[36]

4.3 Relação entre Bexiga Hiperativa e Constipação

O trato urinário e gastrointestinal são sistemas anatomicamente e fisiologicamente interdependentes. Isso inclui a mesma origem embriológica da bexiga e reto, músculos do assoalho pélvico com a mesma função para enchimento e esvaziamento da urina e das fezes e inervação sacral e supraespinhal.[6,17] Em indivíduos saudáveis, esses sistemas devem funcionar em sincronia.

A constipação e os sintomas urinários são frequentemente encontrados na população pediátrica. Essa proximidade entre esses dois sistemas designou o termo de *Dysfunction Elimination Syndromes*,[7] porém engloba apenas alteração na fase de evacuação de urina e fezes. Entretanto, crianças com sintomas de BHI (alteração apenas no enchimento da bexiga) têm uma chance quase três vezes maior de apresentar constipação quando comparadas às crianças que não têm queixas miccionais, com uma frequência de quase 60%.[11] Dessa forma, o termo melhor empregado para designar a relação dos sintomas é a *Bladder and Bowel Dysfunction* (BBD),[19] independente se ocorrem na fase de enchimento ou esvaziamento vesical.

É provável que a associação entre BH e constipação seja multifatorial. A principal hipótese é a de que, como os centros espinhais e supraespinhais envolvidos na defecação e função do trato urinário inferior são comuns, parece provável que uma alteração neurofisiológica (ainda completamente desconhecida) desses centros pudesse levar a essas

condições. Estudos de ressonância magnética funcional têm demonstrado que o córtex pré-frontal e córtex cingulado, além de outros centros, como ínsula e porção anterior do mesencéfalo apresentam-se alterados em indivíduos com urgência miccional e constipação.[21] Outros fatores comportamentais podem, também, predispor a essas duas condições. Muitas crianças com BH evitam tomar líquidos durante o dia para não passarem pelo inconveniente de perderem urina, principalmente no período escolar. Essa baixa ingestão de líquidos pode causar retenção fecal ou piorar uma constipação leve. Além disso, sabe-se que crianças com BH contraem o assoalho pélvico quando fazem manobras de retenção para evitar a perda urinária. A contração da musculatura esfincteriana anal causa *feedback* negativo, inibindo a contração retal e, portanto, estimulando a retenção fecal. A presença dessa manobra, várias vezes ao dia, pode, então, causar a constipação em muitas dessas crianças.

Por outro lado, em alguns casos, também é possível que a constipação predisponha a BH. Estudos têm demonstrado que o reto repleto pode piorar a função vesical. Um estudo em que um balão foi insuflado no reto, simulando plenitude retal, em dois grupos (crianças com DTUI associado à constipação e sem sintomas fecais), os autores evidenciaram que a distensão retal aguda afeta a função da bexiga em crianças com DTUI, independente da existência de constipação crônica, através de uma resposta excitatória vesical à distensão retal.[9]

4.4 Eletroestimulação Transcutânea Parassacral

A Estimulação Elétrica Nervosa Transcutânea ou *Transcutaneous Electrical Nerve Stimulation* (TENS) tem emergido como uma opção terapêutica eficaz para o tratamento da BH em crianças. Em 2001, Hoebeke et al. e Bower et al descreveram, pela primeira vez, os resultados da utilização da TENS no tratamento de sintomas do trato urinário inferior.[37,38] Embora tenha relatado sucesso com essa técnica, o tratamento foi realizado, através de sessões diárias e prolongadas, ao longo de meses.

Em seguida, um estudo mostrou os resultados do tratamento de estimulação elétrica feita em nível ambulatorial (20 sessões, 3 vezes por semana) com resolução completa dos sintomas da BH em 62% dos pacientes.[39] O acompanhamento dessas crinças, a longo prazo,

mostrou que pacientes com urgência ou incontinência urinária, antes do tratamento (84% e 74%, respectivamente), permaneceram assintomáticos durante um mínimo de 2 anos após o tratamento de TENS parassacral.[40]

Estudos randomizados também demonstraram que a TENS parassacral pode ser mais eficaz do que o tratamento placebo.[41,42] Por ser um método de fácil uso e sem efeitos adversos aparentes, a TENS parassacral tem emergido como um tratamento de primeira linha da BH em crianças.

A TENS, também, parece melhorar a constipação na infância, demonstrada em ensaios clínicos randomizados.[14,43] Exame de ressonância magnética funcional após distensão retal não dolorosa demonstrou ativação do tálamo, ínsula, giro cíngulo anterior e córtex pré-frontal;[44] regiões semelhantes no controle vesical[20] são ativadas na eletroestimulação sacral, o que pode justificar a sua ação em ambos os problemas. Veiga, et al em um estudo piloto, que utilizou TENS parassacral em crianças constipadas com BHI, encontrou uma melhora dos sintomas da constipação em 86% e 93% da urgeincontinência.[15] Apesar dos resultados promissores, trata-se de um estudo com pequena amostra e sem grupo controle.

5 PACIENTES E MÉTODO

5.1 Tipo de Estudo

Trata-se de um ensaio clínico não controlado, cuja coleta de dados ocorreu no período de julho de 2013 a julho de 2015.

5.2 Local do Estudo

O estudo foi realizado no Centro de Distúrbios Miccionais na Infância (CEDIMI), serviço do ADAB (Ambulatório Docente Assistencial de Brotas), localizados na Unidade Acadêmica da Escola Bahiana de Medicina e Saúde Pública, que se encontram no bairro de Brotas, na cidade de Salvador – Bahia.

O CEDIMI é um centro especializado e multidisciplinar em Distúrbios Miccionais na Infância que possui médicos, fisioterapeuta, enfermeira e psicóloga. Todos os exames necessários para o diagnóstico das crianças e material para o tratamento são de propriedade do ADAB ou financiados pelas pesquisas que ocorrem no centro.

5.3 População do Estudo

A população-alvo selecionada para este estudo foi composta de escolares de ambos os sexos, com idade de 4 a 14 anos. A população acessível foi de crianças com diagnóstico de BHI, com constipação ou não, que compareceram para o atendimento no CEDIMI.

5.3.1 Critérios de Inclusão

Os critérios de inclusão foram escolares com BHI, definida como queixa de urgência ou urge-incontinência, urofluxometria com curva em sino ou em torre, resíduo pós-miccional menor do que 20 ml ou menor que 10% da capacidade esperada para a idade [(idade + 1) x 30],[19] avaliados através da ultrassonografia.

5.3.2 Critérios de Exclusão

Os critérios de exclusão foram questionários incompletos de ambos os grupos, pacientes com alterações neurológicas, cognitivas e anatômicas do trato urinário inferior ou que não pudessem realizar o tratamento 3 vezes por semana.

5.2 Coleta de dados

Todas os pacientes foram avaliados previamente por um urologista para afastar casos de alterações anatômicas do trato urinário (ex: válvula de uretra posterior, ureterocele ou ureter ectópico), bexiga neurogênica e distúrbios cognitivos, os quais foram excluídos do estudo. Em seguida, essas crianças foram encaminhadas para avaliação da história miccional e fecal. Todas as perguntas foram direcionadas para as crianças, com auxílio dos responsáveis.

Para avaliação da história miccional, utilizou-se um questionário estruturado sobre sintomas de DTUI (Apêndice A). Perguntas sobre presença de urgência, urgeincontinência, ITU, polaciúria, noctúria, manobras de contenção (a menina sentar sobre o calcanhar, o menino apertar a glande ou ambos cruzarem as pernas para evitar a miccção) e enurese foram analisadas.

Foi aplicado o questionário *Dysfunction Voiding Scoring System* (DVSS)[45] (Anexo A), traduzido na língua portuguesa, para quantificar os sintomas como urgência miccional, incontinência urinária, manobras de contenção, ITU e constipação. O ponto de corte para sintomas de DTUI é de 6 para meninas e 9 para meninos.

Para o diagnóstico da constipação, utilizou-se o Critério Roma III infantil para crianças de 4 a 18 anos[10] (Anexo B), questionário usado como referência, com resposta positiva na presença de, pelo menos, dois ou mais itens entre os seis, presentes por mais de dois meses.

Os resultados de melhora dos sintomas do trato urinário inferior foram avaliados através da escala visual analógica (EVA – ANEXO C). Foi solicitado, a cada sessão, que os responsáveis e a criança referissem uma nota de 0 a 10 de melhora (10 sem queixa miccional

diurna) sendo essa nota transformada em porcentagem. Foi considerada resolução completa, uma melhora de 100% na EVA, durante a reavaliação feita após a 20ª sessão de TENS. Além disso, todas as crianças foram reavaliadas com o questionário DVSS para quantificar a diminuição dos sintomas, além do diário mcional de 3 dias, antes e após o tratamento. A constipação foi reavaliada pelo Critério Roma III após o tratamento.

5.3 Procedimento

A TENS parassacral foi administrada por uma única fisioterapeuta (pesquisadora). Todas as crianças foram tratadas com 20 sessões de eletroestimulação transcutânea parassacral, através de um gerador de corrente (Dualpex Uro 961, Quark, Piracicaba) aplicadas 3 vezes por semana, alternadamente, com duração de 20 minutos. A frequência utilizada foi 10Hz, largura de pulso de 700 µs. Foram colocados dois eletrodos autoadesivos Axelgaard (Valutrode) 5X5cm na região de S2 e S4 e intensidade variável, a depender do paciente, sem atingir o ponto motor.

Todas as crianças foram orientadas a urinar a cada 3 horas, não ingerir alimentos que possam ser irritativos à bexiga, como chocolate, frutas cítricas e refrigerantes, urinar antes de dormir, aumentar a ingestão de líquidos durante o dia e não realizar manobras de contenção para postergar o desejo miccional. Entretanto, nenhum criança recebeu orientação quanto ao tratamento da constipação ou uso de medicamento anticolinérgico.

5.4 Hipótese Estatística

Hipótese nula: não há diferença estatisticamente significante entre a resposta clínica da TENS parassacral na resolução da Bexiga Hiperativa Isolada nos escolares com e sem constipação antes do tratamento.

Hipótese alternativa: há diferença estatisticamente significante entre a resposta clínica da TENS parassacral na resolução da Bexiga Hiperativa Isolada nos escolares com e sem constipação antes do tratamento.

5.5 Análise Estatística

O cálculo amostral foi realizado pela calculadora WinPepi. Foi considerada a proporção de crianças com BHI sem constipação do artigo de Lordêlo et al 2009 [40], cuja melhora dos sintomas urinários de BH, a longo prazo, foi de 78%. Considerando a constipação um fator preditor negativo para a resolução da BHI, considerou-se a melhora dos sintomas miccionais em 39%, sendo necessárias 26 crianças em cada grupo para se obter um poder estatístico de 80% com erro tipo alfa de 5%.

Para a análise dos dados, os pacientes foram divididos nos grupos constipação e não constipação. Para testar a normalidade das variáveis foi utilizado o teste de Kolgomgorov-Smirnov. Para os resultados descritivos normais foram utilizados média e desvio padrão; dados categóricos, teste qui-quadrado e para os dados numéricos teste t *student*. Para a avaliação de antes e depois do tratamento com a TENS parassacral, em ambos os grupos foi usado o teste *Mc Nemar* e o teste de *Wilcoxon* para avaliar a diferença das médias do escore do DVSS. Foi utilizado o programa *Statistical Package for the Social Sciences* (SPSS) *for windows* versão 14.0.

5.6 Aspectos éticos

O estudo está de acordo com as diretrizes e normas da Resolução n 466/12, que regulamentam a pesquisa envolvendo seres humanos e foi aprovado pelo Comitê de Ética em Pesquisa da Escola Bahiana de Medicina e Saúde Pública sob CAAE 51086715.4.0000.5544 (Anexo D).

Os responsáveis pela criança foram informados dos métodos e objetivos da pesquisa, a qual oferece riscos mínimos, e da liberdade de se recusarem a participar da entrevista ou retirar o consentimento sem nenhum dano. Todos os responsáveis assinaram o termo de consentimento livre e esclarecido (Apêndice B).

6 RESULTADOS

Antes da TENS parassacral, 25 crianças eram constipadas e 26 não eram constipadas, perfazendo uma amostra de 51 pacientes. Não houve diferença estatisticamente significante entre os grupos, com relação a gênero e idade (tabela 1). Quando se compararam os aspectos clínicos entre crianças constipadas e não constipadas, observou-se que não houve diferença estatisticamente significante entre os grupos com relação à presença de urgeincontinência, polaciúria, noctúria, enurese, manobras de contenção e ITU (Tabela 1).

Tabela 1 – Comparação dos dados sócio demográficos e clínicos das crianças constipadas e não constipadas, avaliadas pela ficha de DTUI e Critério Roma III

Variável	Constipadas n=25	Não constipadas n=26	p
Sexo feminino (%)	15(60%)	17(65,4%)	0,69
Idade (média ± DP* - anos)	7,72(±2,9)	6,73(±2,44)	0,19
Urge incontinência	23(92%)	20(76%)	0,13
Polaciúria	15(60%)	16(61,5%)	0,91
Enurese	16(64%)	16(61,5%)	0,85
Manobras de contenção	19(76%)	23(88,5%)	0,24
ITU	17(68%)	15(57,7%)	0,44
Noctúria	11(44%)	9(37,5%)	0,64

*DP = Desvio Padrão

A resolução completa dos sintomas de BHI foi encontrada em 25(49%) dos 51 pacientes, e a constipação foi resolvida em 15(60%) das 25 crianças constipadas antes do tratamento.

A resposta clínica da BHI após tratamento com a TENS parassacral, distribuída em porcentagem de melhora segundo a recomendação da ICCS está na tabela 2.

Tabela 2 – Resolução dos sintomas urinários de acordo com a recomendação da ICCS, após tratamento com TENS nos grupos constipados e não constipados

Resolução dos sintomas urinários	Constipados n=25	Não constipados n=10	p
Sem resposta (<50%)	1(4%)	1(3.8%)	
Resposta parcial (50-99%)	12(48%)	12(46.2%)	0.99
Resposta completa (100%)	12(48%)	13(50%)	

A tabela 3 mostra os sintomas miccionais que foram reavaliados após o tratamento com a TENS. Houve melhora da urgência, urgeincontinência e das manobras de contenção em crianças constipadas e não constipadas, mas não da enurese de forma significante.

Tabela 3 - Comparação dos sintomas miccionais nos grupos de crianças constipadas e não constipadas antes e após o tratamento da BHI, avaliadas através da EVA e Critério Roma III

Variável	Constipados n=25			Não constipados n=26		
	Antes	Depois	p	Antes	Depois	p
Urgência	25	6		26	11	
Urgeincontinência	23	6	0,000	20	10	0,002
Enurese	16	9	0,07	16	13	0,62
Manobras de contenção	18	8	0,002	23	7	0,000

Na avaliação do DVSS, houve diferença estatística antes do tratamento com TENS nos grupos constipados e não constipados e após o tratamento não houve diferença. Na avaliação intra grupo houve diferença estatisticamente siginificante após o tratamento nos dois grupos como pode ser visto na tabela 4. A comparação dos resultados de frequência urinária média, volume urinado média e máximo após avaliados pelo diário miccional, antes e após o tratamento, podem ser vistos na tabela 5.

Tabela 4 – Avaliação dos sintomas miccionais através do DVSS nas crianças constipadas e não constipadas, antes e após tratamento com TENS parassacral

	Constipadas	Não constipadas	p
DVSS Antes	13,08±4,71*	8,91±4,25$^{\alpha}$	0,003
DVSS Depois	2,76±2,77*	3,46±3,61 $^{\alpha}$	0,44

* e $^{\alpha}$: p<0,01, teste Wilcoxon

Tabela 5: Dados do diário miccional antes e após o tratamento no grupo constipado e não constipado

	Grupo constipado		p	Grupo não constipado		p
	Antes tratamento	Depois tratamento		Antes tratamento	Depois tratamento	
Frequência urinária média	7.95±7.54	7.29±3.22	0.43	9.56±3.16	7.57±2.88	0.15
Volume urinado médio (ml)	88.83±46.22	228.18±536.94	0.33	118.91±84.56	117.82±82.74	0.91
Volume urinário máximo (ml)	222.84±183.8	195.76±100.7	0.41	258.66±178.97	295.33±226.83	0.36

As tabelas 6 e 7 evidenciam, respectivamente, que a resolução da BHI após a presença da constipação não influenciou na eficácia da TENS parassacral. Além disso, a resolução da constipação após o tratamento não se associou à melhora da BHI.

Tabela 6 - Resolução da BHI após tratamento com TENS nos grupos de crianças constipadas e não constipadas, através da EVA e Critério Roma III

	Grupo		
	Constipadas n=25	Não constipadas n=26	p
Resolução completa BHI	12(48%)	13(50%)	0,88
Resolução incompleta BHI	13(52%)	13(50%)	

Tabela 7 - Comparação da resolução da constipação após tratamento com TENS e resolução da BHI, através do Critério Roma III e da EVA

	Grupo		
	Resolução da constipado n=15	Não resolução da constipado n=10	p
Resolução completa BHI	8(53,3%)	4(40%)	0,51
Resolução incompleta BHI	7(46,7%)	6(60%)	

7 DISCUSSÃO

Os resultados demonstraram que a TENS foi eficaz no tratamento da BHI e da constipação. Porém esse efeito positivo na BHI não esteve relacionado à presença ou não da constipação antes do tratamento. Além disso, a TENS parassacral resolveu a BHI independentemente do seu efeito positivo na constipação. Da mesma maneira, a melhora da constipação não esteve relacionada à melhora da BHI.

Crianças que referem sintomas miccionais de BHI têm uma chance 3 vezes maior de apresentarem constipação quando comparadas com crianças que não têm queixas urinárias (54.9% vs. 29.7%, p<0,005; OR 2,87, 95% IC: 1.3-6.0).[15] Outro estudo mostra a inter-relação entre esses dois sistemas. Após a avaliação urodinâmica em crianças com DTUI constipadas e não constipadas, os autores concluíram que a distensão retal aguda afeta a função da bexiga em crianças com DTUI, independente de existir constipação crônica.[9]

A TENS melhorou a constipação em dois estudos randomizados. Um estudo controlado e outro duplo cego avaliaram o efeito agudo da TENS sobre a motilidade retal em 20 crianças com BH. Após a aplicação da TENS parassacral durante a manhã até a noite e com acompanhamento da urodinâmica e manometria foi verificado aumento agudo das contrações intestinais.[43] Outro estudo realizou 12 sessões de 20 minutos de eletroestimulação transcutânea com corrente interferencial. Foi realizado estudo do tempo de trânsito antes e após a eletroestimulação e encontrado um aumento significativo do trânsito colônico quando comparado ao grupo controle.[14]

Uma vantagem da TENS sobre os antimuscarínicos no tratamento da BH em crianças é que a neuromodulação pode melhorar não somente os sintomas vesicais, mas também a constipação que, frequentemente, está presente nesses casos. Em um estudo recente, evidenciamos que após o TENS parassacral houve melhora significativa dos sintomas de urgeincontinência, manobras de contenção, enurese e constipação (em 86% dos casos), bem como baixa taxa de ITU.[15] Em um outro estudo, o nosso grupo, em um ensaio clinico randomizado, demonstrou que a oxibutinina e a TENS parassacral se equivalem nos resultados de melhora das queixas miccionais, mas a TENS tem a vantagem do efeito positivo na constipação.[16]

Alguns estudos têm evidenciado que a melhora da constipação pode melhorar as queixas urinárias[8,18], porém os nossos resultados contestam esses dados, pelo menos para os pacientes com BHI que se submetem à TENS. Um estudo avaliou a frequência de incontinência urinária e infecção do trato urinário em crianças constipadas crônicas e a resolução dos sintomas após o tratamento da constipação. Os resultados foram favoráveis para a melhora da IU diurna em 89%, enurese em 63% e ITU em todos os pacientes. Entretanto, ao contrário do nosso estudo, os autores não incluíram grupo controle sendo uma limitação dos seus resultados.[18] Outro estudo prospectivo e controlado avaliou, através da ultrassonografia, alterações do trato urinário em 29 crianças constipadas e 451 sem história de constipação. Resíduo pós miccional e dilatação renal foram mais frequentes nas crianças constipadas, porém houve melhora após o tratamento com laxante.[8] Entretanto os autores consideram apenas a frequência defecatória inferior a três vezes por semana como diagnóstico de constipação, o que exclui possíveis casos mais graves quando avaliados pelo Critério Roma, sendo, provavelmente, uma amostra diferente deste estudo.

Como os pacientes com BBD são normalmente tratados para ambos com medidas cognitivo-comportamentais é difícil relacionar o efeito de, por exemplo, laxativos como um preditor independente na resolução da disfunção vesical. O fato de não termos encontrado uma dependência da melhora da constipação para o tratamento da BHI, não significa que não tenhamos que lidar com a retenção fecal. Esse é um sintoma extremamente desconfortável e que deve ser tratado. Além disso, há evidências de que a distensão da ampola retal piora a função vesical,[9] e isso poderia não ser traduzido em recorrência dos sintomas. Além disso, a constipação associa-se a maior resíduo pós-miccional e ITU.[18,46-48]

Este estudo demonstrou que a TENS atua no trato urinário inferior e na motilidade intestinal conjuntamente, mas de forma independente. Ainda não se conhece como a neuromodulação atua. Entretanto cada vez mais se evidencia a importância da ação supraespinhal da neuromodulação na região sacral[49-51] o que poderia, por neuroplasticidade, justificar o seu efeito a longo prazo no trato urinário inferior. Essa ação inicia-se por estímulo das fibras sensoriais e não motoras, aumentando a percepção ao enchimento vesical e retal.[52] O giro cingulado, o cortex sensoriomotor e o mesencéfalo atuariam nessa sensação progressiva de plenitude, a qual, por sua vez, modularia os impulsos eferentes e reflexos miccionais e defecatórios.[53,54]

Em um estudo australiano, há evidência de aumento da motilidade colônica com o TENS.[14] Como a estimulação simpática reduz o trânsito do colon, é improvável que a estimulação direta desse sistema seja o principal mecanismo de ação da neuromodulação. Além disso, há indícios de que o nervo vago seja uma via importante de estimulação.[55]

O número de pacientes, apesar de compatível com o publicado por outros autores, pode ter sido ainda pequeno para demonstrar diferenças estatisticamente significantes. Entretanto, essa é a maior série da literatura que avalia os efeitos da TENS parassacral em crianças com BHI.

A constipação e os sintomas miccionais foram avaliados por questionários, portanto, de forma subjetiva. Porém sintomas são inerentemente de natureza subjetiva e não há outra forma de avaliação. O critério Roma III para constipação em crianças é o método mais utilizado entre os diversos estudos. Não foi utilizado exames para diagnóstico da constipação ou estudo urodinâmico para confirmação da BHI. Um estudo que avaliou o diâmetro retal de crianças constipadas através da ultrassonografia mostrou que não existe correlação entre diâmetro retal e o diagnóstico dessa queixa fecal.[56] O critério Roma III é o método mais utilizado entre diversas pesquisas, sendo o escolhido para este estudo. O estudo urodinâmico é útil para diagnosticar casos de hiperatividade detrusora, porém não existe necessidade clínica para avaliar a BHI, cujo diagnóstico é realizado através da avaliação dos sintomas característicos dessa disfunção.

Alguém pode argumentar que a melhora dos sintomas vesicais e constipação seja apenas devido à utilização da uroterapia padrão ou por efeito placebo. Apesar de não termos como descartar a presença dessa interferência, há estudos randomizados mostrando que o TENS é mais eficaz que o grupo sham para a resolução da BH e constipação em crianças.[41,43]

Neste estudo, a avaliação foi realizada em curto prazo pós tratamento. Um estudo do nosso grupo mostrou que pode ocorrer uma recidiva de 10% nos sintomas miccionais,[41] entretanto ainda não há estudos que mostrem o resultado da TENS parassacral para constipação a longo prazo.

Como perspectivas futuras, faz-se necessário estudar os efeitos da TENS na constipação em longo prazo, avaliando-se a taxa de recorrência e fatores preditores de sucesso.

Também avaliar a TENS no tratamento da constipação funcional e o seu papel na prevenção de surgimento de distúrbios miccionais nesses pacientes. Além disso, incluir dados objetivos na análise como o diâmetro retal na ultrassonografia.

8 CONCLUSÃO

- A presença de constipação antes do tratamento não foi associada a um pior prognóstico para a resolução de sintomas de BHI.

- A melhora da BHI não está associada a melhora da constipação com a TENS parassacral.

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APÊNDICES

APÊNDICE A – Ficha de avaliação de BH

CEDIMI — Centro de Distúrbios Miccionais na Infância

BAHIANA — ESCOLA BAHIANA DE MEDICINA E SAÚDE PÚBLICA

ADAB

AVALIAÇÃO 1ª CONSULTA

Data: ___/___/_____

Entrevistador: _____

A) Identificação:

Nome: _____ _____

Responsável: _____

Endereço: _____ _____

_____ _____

Telefone/Celular: _____ _____

Data de Nascimento: ___/___/_____ Raça: _____

B) Anamnese:

1. Com que idade largou a fralda durante o dia?
( ) Com menos de 2 anos
( ) Entre 2 e 3 anos
( ) Após os 3 anos
( ) Ainda usa fralda

2. Antecedentes de ITU:
( ) Não
( ) Sim – Data 1° episódio: ___/___/____ Data último episódio: ___/___/____

2.1 ITU afebril (cistite):	2.2 ITU febril (pielonefrite):
( ) Não	( ) Não
( ) Sim – Quantos episódios: _____ (1, 2, 3 ou +)	( ) Sim – Quantos episódios: _____ (1, 2, 3 ou +)

3. Febre Indeterminada:
( ) Não
( ) Sim – Quantos episódios: _____ (1,2,3 ou +)

4. Urgência:
( ) Não
( ) Sim – Frequência: ( ) Diária – ____ x dia ( ) > 10 episódios no mês ( ) Entre 3 e 10 episódios no mês ( ) < 3 episódios no mês

5. Urge-incontinência:
( ) Não
( ) Sim

6. Perda sem urgência (incontinência diurna):
( ) Não
( ) Sim – Frequência: ( ) Diária – ____ x dia ( ) > 10 episódios no mês ( ) Entre 3 e 10 episódios no mês ( ) < 3 episódios no mês

7. Polaciúria: (≥ 8 vezes ao dia)	8. Micção Infrequente: (até 3 vezes ao dia)
( ) Não	( ) Não
( ) Sim	( ) Sim

9. "Giggle" (sorriso) Incontinência:	10. Incontinência aos Esforços:
( ) Não	( ) Não
( ) Sim	( ) Sim

11. Dificuldades Miccional:	12. Noctúria (acorda a noite para urinar):
( ) Não	( ) Não
( ) Sim	( ) Sim

13. Manobra de Vincent:	14. "Dança do Xixi":
( ) NA ( ) Não	( ) Não
( ) Sim	( ) Sim
15. **Se há manobras , qual a frequência:** ( ) Diária – ____ x dia ( ) > 10 episódios no mês ( ) Entre 3 e 10 episódios no mês ( ) < 3 episódios no mês	

16. Jato Miccional:
( ) Contínuo
( ) Intermitente

17. Corrimento Vaginal:	18. Irritação Vaginal:
( ) NA	( ) NA
( ) Não	( ) Não
( ) Sim	( ) Sim

19. Dor em Região Hipogástrica:
( ) Não
( ) Sim

20. Enurese Noturna:
( ) Não
( ) Sim **20.1. Tipo:** ( ) Primária ( ) Secundária **20.2. Quantas vezes por semana:** ( ) Todos os dias ( ) Em torno de 3 x por semana ( ) < 3 x por semana ( ) Ocasionalmente **20.3. Usou medicação:** ( ) Não ( ) Sim – **Qual:** ( ) Anticolinérgica ( ) Alfa-bloqueador **Resposta ao tratamento:** ( ) Falha ( ) Pouca melhora ( ) Melhora significativa ( ) Cura com recidiva

Crianças de 04 a 18 anos
No mínimo 02 dos 06 seguintes critérios por pelo menos 02 meses:
22. 02 ou + evacuações no vaso sanitário por semana: ( ) Não ( ) Sim
23. Pelo menos 01 episódio de incontinência fecal por semana: ( ) Não ( ) Sim
24. História de postura retentiva ou retenção voluntária: ( ) Não ( ) Sim
25. Evacuações com dor ou esforço intenso para a eliminação das fezes: ( ) Não ( ) Sim
26. Presença de grande massa fecal no reto: ( ) Não ( ) Sim
27. História de fezes grandes que obstruem o vaso sanitário: ( ) Não ( ) Sim
28. Tipo de fezes (utilizar figura): ( ) Tipo 1 ( ) Tipo 2 ( ) Tipo 3 ( ) Tipo 4 ( ) Tipo 5 ( ) Tipo 6 ( ) Tipo 7
29. Classificação da dor: ( ) 1 ( ) 2 ( ) 3 ( ) 4 ( ) 5 ( ) 6

EXAME FÍSICO
30. Peso:
31. Altura:
32. Impactação Fecal: ( ) Não ( ) Sim
33. Reflexo Anal: ( ) Presente ( ) Diminuído ( ) Ausente
34. Reflexo Bulbocavernoso: ( ) Presente ( ) Diminuído ( ) Ausente
35. Reflexo Cremastérico: ( ) NA ( ) Presente ( ) Diminuído ( ) Ausente
36. Coordenação Perineal: ( ) Presente ( ) Alterada
OBS:

37. ULTRASSONOGRAFIA *(todos os pacientes)*
Data: ___/___/_____
37.1. Há dilatação renal direita: ( ) Não ( ) Sim – **Grau:** ( ) I ( ) II ( ) III ( ) IV
37.2. Há dilatação renal esquerda: ( ) Não ( ) Sim – **Grau:** ( ) I ( ) II ( ) III ( ) IV
37.3. Espessamento vesical: ( ) Não ( ) Sim
37.4. Parênquima diminuído: ( ) Não ( ) Sim – **Local:** ( ) Direita ( ) Esquerda
37.5. Aumento de ecogenicidade do parênquima: ( ) Não ( ) Sim – **Local:** ( ) Direita ( ) Esquerda
37.8. Resíduo pós-miccional: ( ) Desprezível – _____ mL ( ) Significativo – _____ mL
OBS:

38. RADIOGRAFIA DA COLUNA LOMBO-SACRA
(todos os pacientes)

Data: ___/___/____

38.1. Presença de espinha bífid: ( ) Não
( ) Sim

OBS:

39. SUMÁRIO DE URINA E UROCULTURA
(todos os pacientes)

Data: ___/___/____

39.1. Alterações no sumário de urina: ( ) Não
( ) Sim – **Qual?** _____
_____

39.2. Urocultura: ( ) Negativa
( ) Positiva – **Qual o patógeno?** _____

OBS:

40. CISTOURETROGRAFIA MICCIONAL (CUM)
(realizar se ITU febril)

Data: ___/___/____

40.1. CUM: ( ) Normal
( ) Alterada – Quais achados estão presentes?

40.2. Alargamento do colo: ( ) Não
( ) Sim

40.3. Uretra em Pião: ( ) Não
( ) Sim

40.4. Trabeculação vesical: ( ) Não
( ) Sim

40.5. Divertículos: ( ) Não
( ) Sim

40.6. Presença de refluxo vesico-ureteral: ( ) Não
( ) Sim – **Grau de refluxo a direita:** ( ) I
( ) II
( ) III
( ) IV
( ) V

Grau de refluxo a esquerda: ( ) I
( ) II
( ) III
( ) IV
( ) V

OBS:

41. UROFLUXOMETRIA *(todos os pacientes)*
Data: ___/___/____
41.1. Volume urinado: _____x___ mL
41.2. Uroflu ometria: _____mL/seg
41.3. Curva da fluxometria: ( ) Forma de sino ( ) Achatada ( ) Fracionada
OBS:

42. ELETROMIOGRAFIA
Data: ___/___/____
42.1. Tipo de atividade perineal: ( ) Constante ( ) Intermitente ( ) Ausente
OBS:

43. DIÁRIO MICCIONAL *(todos os pacientes)*
Período: De ___/___/____ a ___/___/____
43.1. Número mínimo de micções por dia: _____
43.2. Número médio de micções por dia: _____
43.3. Capacidade máxima da bexiga: _____
43.4. Capacidade média da bexiga: _____
43.5. Episódios de enurese noturna: _____
43.6. Número de episódios de incontinência : _____
OBS:

APENDICE B – Termo de Consentimento Livre e Esclarecido

BAHIANA
ESCOLA BAHIANA DE MEDICINA E SAÚDE PÚBLICA

CEDIMI
Centro de Distúrbios Miccionais na Infância

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO DA PESQUISA

Eu, _____, responsável pela criança _____, permito que esta participe como voluntário(a) do estudo, cujo objetivo é conhecer a papel da constipação no tratamento de crianças com bexiga hiperativa. Fui informado(a) que esse estudo é baseado no tratamento da bexiga hiperativa com a utilização da eletroestimulação transcutânea parassacral, por 20 sessões, 3 vezes por semana, 20 minutos em cada sessão.

Estou ciente que o nome da criança será mantido em sigilo e que posso recusar a participar desta pesquisa, sem qualquer restrição ao atendimento. Fui informado que existe uma seriço de Psicologia para dar apoio emocional, caso seja necessário.

Os responsáveis pelo estudo, a fisioterapeuta Maria Luiza Veiga e o médico Dr. Ubirajara Barroso Júnior, da Escola Bahiana de Medicina e Saúde Pública estão à disposição para esclarecimento ou intercorrências pelo telefone 9984 4610.

O projeto foi submetido à avaliação do Comitê de Ética em Pesquisa da Fundação Bahiana para Desenvolvimento das Ciências (FBDC) e, portanto se surgirem dúvidas ou considerações sobre a ética da pesquisa, entrem em contato com este Comitê, (situado na própria Fundação - Av. Dom João VI, 275, Brotas - 3276-8200).

Declaro que estou ciente dos objetivos desta pesquisa citados neste documento e da decisão de participar deste estudo.

_____
Assinatura do participante

Declaro que obtive de forma apropriada e voluntária o Consentimento Livre e Esclarecido deste paciente / representante legal para a participação neste estudo.

_____
Pesquisador

Salvador, _____ de _____ de 2013

ANEXOS

ANEXO A – DVSS

Nome: _____

___ / ___ / ____ Inicial: ✕ Total: _____
___ / ___ / ____ Final: ○ Total: _____

Durante os últimos 30 dias	**Nunca ou quase nunca**	**Menos que a metade do tempo**	**A metade do tempo**	**Quase todo o tempo**
1. Seu(a) filho(a) tem molhado de xixi a roupa durante o dia?	0	1	2	3
2. Quando seu(a) filho(a) se molha de xixi, a cueca ou calcinha fica ensopada?	0	1	2	3
3. Com que freqüência seu(a) filho(a) não faz cocô todos os dias?	0	1	2	3
4. Seu(a) filho(a) tem que fazer força para fazer cocô?	0	1	2	3
5. Com que freqüência seu(a) filho(a) só vai ao banheiro fazer xixi uma ou duas vezes por dia?	0	1	2	3
6. Seu(a) filho(a) segura o xixi cruzando as pernas, agachando ou dançando?	0	1	2	3
7. Quando seu(a) filho(a) precisa fazer xixi tem que ir rápido ao banheiro? (não consegue esperar)	0	1	2	3
8. Seu(a) filho(a) tem que fazer força para fazer xixi?	0	1	2	3
9. Seu(a) filho(a) disse que sente dor quando faz xixi ?	0	1	2	3
10.Seu(a) filho(a) passou por alguma situação estressante como as dos exemplos abaixo nos últimos 30 dias? Marque ao lado sim ou não. - Bebê novo em casa - Mudança de casa - Mudança de escola - Problemas escolares - Abuso (sexual/físico) - Problemas em casa (divórcio/morte) - Eventos especiais (aniversário) - Acidente / ferimento - Outros	Não		Sim (3)	

ANEXO B – Critério Roma III Infantil

Presença de dois ou mais sintomas por no mínimo dois meses

Duas ou menos evacuações no vaso sanitário por semana **“a criança faz cocô duas ou menos vezes por semana”**
Pelo menos um episódio de incontinência fecal por semana **“a calcinha ou cueca fica suja de cocô pelo menos 1 vez por semana”**
História de postura retentiva ou retenção voluntária **“prende as pernas ou aperta o bumbum para evitar de ir ao banheiro fazer cocô”**
Evacuações com dor ou esforço intenso para eliminação das fezes **“sente dor ou faz força para fazer cocô”**
Presença de grande massa fecal no reto **“a criança sente, ou se queixa, que tem fezes guardadas no bumbum”**
História de fezes grandes que obstruem o vaso sanitário **“o cocô é grande que entope o vaso sanitário”**

ANEXO C – Escala visual Analógica

BAHIANA
ESCOLA BAHIANA DE MEDICINA E SAÚDE PÚBLICA - EBMSP

CEDIMI

Nome: _____

Diagnóstico: _____

Uso de medicamento: sim ( ) não ( ) Qual: _____

1) Data: _____

Seguindo orientações: sim( ) não ( ) _____

Perdas durante o dia: sim ( ) não ( )_____

Enurese: sim ( ) não ( )_____

Melhora: _____% Sem alteração: ( ) Intensidade final: _____mA

Ass._____

ANEXO D – Aprovação do Comitê de Ética

ESCOLA BAHIANA DE MEDICINA E SAÚDE PUBLICA / FUNDAÇÃO BAHIANA

Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Efeito do Tratamento Fisioterapêutico em Crianças Constipadas com Disfunção do Trato Urinário Inferior

Pesquisador: Ubirajara de Oliveira Barroso Júnior

Área Temática:

Versão: 1

CAAE: 51086715.4.0000.5544

Instituição Proponente: Fundação Bahiana para Desenvolvimento das Ciências

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.328.133

Apresentação do Projeto:

Projeto e adendo aprovados em submissão antes da Plataforma Brasil , em 2008 e 2010 respectivamente.

Cronograma finalizado em 2009.

Objetivo da Pesquisa:

Mantido de acordo com o protocolo de pesquisa.

Avaliação dos Riscos e Benefícios:

Mantidos de acordo com o protocolo de pesquisa.

Comentários e Considerações sobre a Pesquisa:

Pesquisa e adendo aprovados em submissão antes da Plataforma Brasil

Considerações sobre os Termos de apresentação obrigatória:

Pesquisa aprovada em submissão antes da Plataforma Brasil.

O Pesquisador Responsável anexou o relatório final da pesquisa.

Recomendações:

Endereço: AVENIDA DOM JOÃO VI, 275
Bairro: BROTAS **CEP:** 40.290-000
UF: BA **Município:** SALVADOR
Telefone: (71)3276-8225 **E-mail:** cep@bahiana.edu.br

ESCOLA BAHIANA DE MEDICINA E SAÚDE PUBLICA / FUNDAÇÃO BAHIANA

Plataforma Brasil

Continuação do Parecer: 1.328.133

Conclusões ou Pendências e Lista de Inadequações:

Após análise dos documentos anexados foi considerado aprovado.

Considerações Finais a critério do CEP:

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_572956.pdf	12/11/2015 18:23:01		Aceito
Outros	cep1.jpg	12/11/2015 18:22:29	Ubirajara de Oliveira Barroso Júnior	Aceito
Declaração de Pesquisadores	relatorio.pdf	12/11/2015 18:19:28	Ubirajara de Oliveira Barroso Júnior	Aceito
Outros	CEP.docx	07/11/2015 16:44:04	Ubirajara de Oliveira Barroso Júnior	Aceito
Folha de Rosto	plataforma.pdf	16/10/2015 11:38:29	Ubirajara de Oliveira Barroso Júnior	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE.docx	08/09/2015 21:29:43	Ubirajara de Oliveira Barroso Júnior	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_Ubirajara.doc	01/09/2015 16:14:54	Ubirajara de Oliveira Barroso Júnior	Aceito
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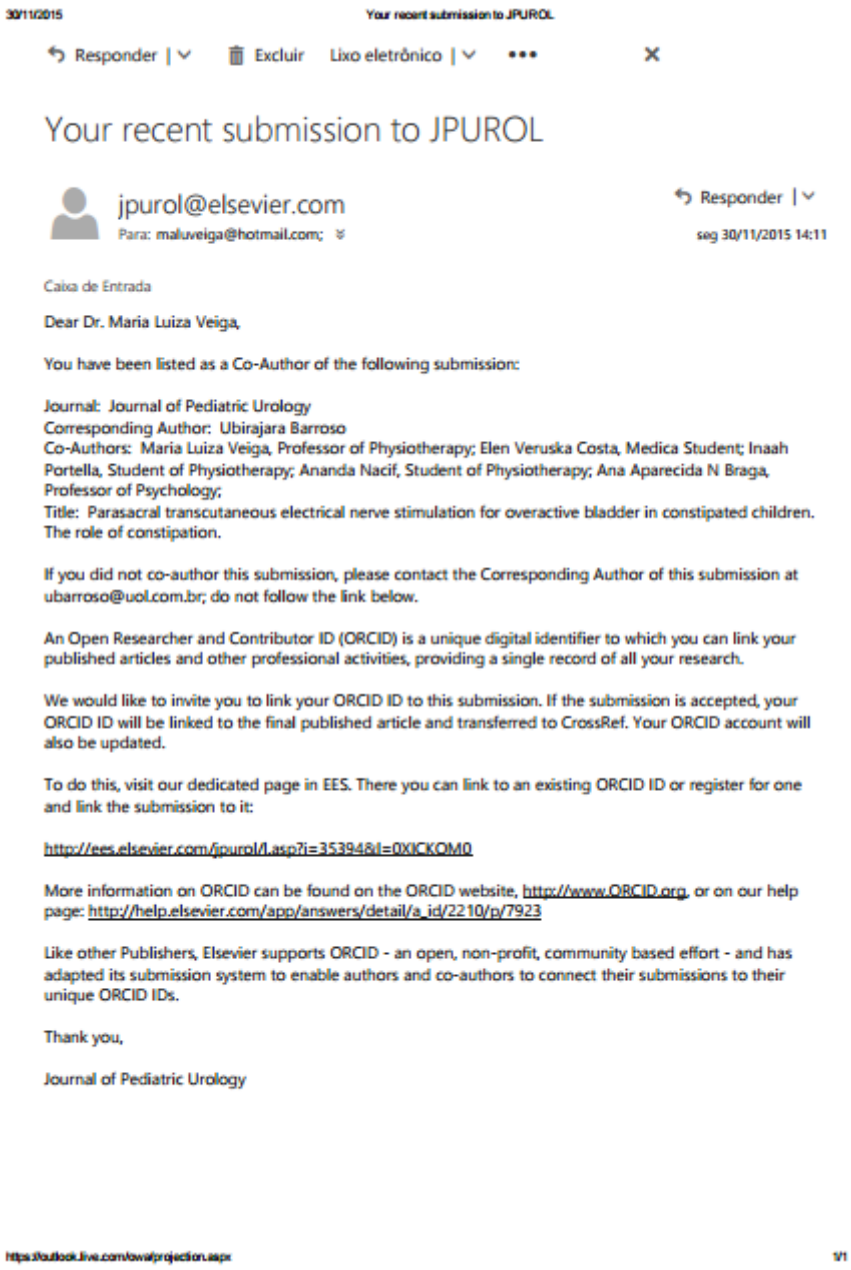
ANEXO E - Comprovante de submissão do artigo "Parasacral transcutaneous electrical nerve stimulation for overactive bladder in constipated children. The role of constipation"



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Journal: Journal of Pediatric Urology
Corresponding Author: Ubirajara Barroso
Co-Authors: Maria Luiza Veiga, Professor of Physiotherapy; Elen Veruska Costa, Medica Student; Inaah Portella, Student of Physiotherapy; Ananda Nacif, Student of Physiotherapy; Ana Aparecida N Braga, Professor of Psychology;
Title: Parasacral transcutaneous electrical nerve stimulation for overactive bladder in constipated children. The role of constipation.

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ANEXO F – Artigo "Parasacral transcutaneous electrical nerve stimulation for overactive bladder in constipated children. The role of constipation."

Parasacral transcutaneous electrical nerve stimulation for overactive bladder in constipated children. The role of constipation.

Maria Luiza Veiga, Elen Veruska Costa, Inaah Portella, Ananda Nacif, Ana Aparecida Martinelli Braga, Ubirajara Barroso Jr

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Abstract

Introduction: Parasacral transcutaneous electrical nerve stimulation (TENS) is an effective method for the treatment of OAB, and additionally, it accelerates bowel transit time. Therefore, not only does parasacral TENS improve LUTS, but it also resolves the problem of constipation in a significant number of children. Since TENS has a positive effect on LUTS and on the symptoms of fecal retention, it is possible that its action regarding OAB could be directly associated with the improvement in constipation. In other words, the positive effect of parasacral TENS in OAB would be basically due to the fact that the constipation was resolved.

Objective: To test the hypothesis that the positive effect of parasacral TENS in OAB would be due to the fact that the constipation is improved with this method.

Material and Methods: This is a prospective study children of with pure OAB who were submitted to parasacral TENS. The Rome III criteria were used to diagnose constipation. Symptoms of urgency, urge incontinency, UTI, frequency, nocturia, holding maneuvers, enuresis and constipation were evaluated. No instructions were given to the participants with respect to constipation treatment. None of the patients used anticholinergics. Standard urotherapy was also prescribed.

Results: 51 children were included in the study, 25 of whom were constipated prior to treatment. There was no statistically significant difference in urinary symptoms between the constipated and non-constipated children. There was an improvement in urgency, urge incontinency and in holding maneuvers in both the constipated and non-constipated

children; however, there was no significant improvement in enuresis. Complete resolution of the symptoms of OAB was registered in 25 children (49%). Constipation was resolved in 15 cases (60%). The resolution of OAB was not associated with the resolution of constipation

Conclusion: Parasacral TENS improves OAB and constipation. The presence of constipation prior to treatment was not associated with a poorer prognosis insofar as the resolution of the symptoms of OAB was concerned. Likewise, there was no association between the resolution of constipation with parasacral TENS and the resolution of OAB.

Abbreviations and Acronyms

OAB = overactive bladder
TENS = transcutaneous electrical nerve stimulation
LUTS = lower urinary tract symptoms
SPSS = Statistical Package for the Social Sciences
BBD = bladder bowel dysfunction
UTI = urinary tract infection

Introduction

The association between constipation and lower urinary tract symptoms (LUTS) in children is well known and referred to as bladder bowel dysfunction (BBD). BBD is associated with a higher risk of urinary tract infection (UTI) and vesicoureteral reflux [1,2]. Constipation may be associated with LUTS for several reasons: (1) hardened feces retained in the rectum may compress the bladder and bladder neck, contributing to dysfunction of the lower urinary tract; (2) contraction of the perianal muscles used to retain feces may contract the external urethral sphincter, predisposing the individual to increased urinary retention; (3) hypertonic pelvic floor dysfunction may hamper the individual's ability to empty the bladder; (4) contractions of the external urethral sphincter to avoid urinary incontinence may result in contraction of the perianal muscles, predisposing individuals to inhibition of the defecation reflex; (5) finally, symptoms may be associated with neurophysiological immaturity with no cause-effect relationship [3,4].

With the chronicity of the symptoms related to constipation, the child consequently tends to inhibit defecation, resulting in emotional repercussions that include a greater degree of anxiety, negative self-image and withdrawal from social life. Likewise, LUTS is associated with alterations in the internalization and externalization processes [5].

In addition to urinary dysfunction, overactive bladder (OAB) with coordinated micturition has also recently been shown to be associated with constipation [6]. Children with OAB are approximately three-fold more likely to have constipation compared to their asymptomatic peers. Therefore, it is essential that both dysfunctions be treated.

Antimuscarinics can be used to treat OAB; however, these drugs have a negative effect on defecation. Our

group, as well as other investigators, has demonstrated that parasacral transcutaneous electrical nerve stimulation (TENS) is effective for the treatment of OAB [7,8], and additionally, it accelerates bowel transit time [9]. Therefore, not only does parasacral TENS improve LUTS, but it also resolves the problem of constipation in a significant number of children [10,11].

Since TENS has a positive effect on LUTS and on the symptoms of fecal retention, it is possible that its action regarding OAB could be directly associated with the improvement in constipation. In other words, the positive effect of parasacral TENS in OAB would be basically due to the fact that the constipation was resolved. The objective of this study is to test that hypothesis.

Materials and Methods

In this prospective study, children with OAB alone were submitted to parasacral TENS. The inclusion criteria consisted of 4-14 year old children with OAB alone, defined as a complaint of urgency or urge incontinency, and a bell-shaped or tower-shaped uroflowmetry curve. In addition, post-void residual urine volume should be insignificant at ultrasonography (i.e. less than 10% of the expected bladder capacity for age in milliliters, estimated as [age + 1] x 30 ml, and less than 20 ml) [12]. Children with neurological or anatomical abnormalities of the lower urinary tract and those with insufficient data for analysis were excluded from the study.

To evaluate the symptoms, a structured questionnaire was used to acquire data on the presence of urgency, urge incontinency, UTI, frequency (more than 7 voids/day), nocturia, holding maneuvers, enuresis and constipation. UTI was defined as the presence of acute urinary symptoms and a positive urine culture. The Rome III criteria for children of 4-18 years of age were used to diagnose constipation, which was defined as the finding of positive answers to two or more of the six items, with the symptoms having been present for more than two months [4].

The same physiotherapist administered parasacral TENS in all cases. All the children were treated with 20 sessions of parasacral TENS applied for 20 minutes, three times weekly on alternating days. The frequency used was 10Hz, with a pulse width of 700 μs and intensity that varied as a function of the patient's sensitivity threshold. Two self-adhesive electrodes measuring 5x5 cm were placed between S2 and S4. The electric current generator was the Dualpex 961 (Quark, Piracicaba, Brazil).

No instructions were given to the participants with respect to diet, laxatives or pharmaceutical treatment for constipation throughout the study period. None of the patients used anticholinergics. Urotherapy was prescribed: the children were advised not to drink irritating fluids (caffeine, citric fruit juice, sodas) and they were instructed to urinate regularly and not to postpone urinating when they felt the need. The patients were reevaluated immediately following treatment.

All the parents/guardians signed an informed consent form. The study was approved by the internal review board of the Bahiana School of Medicine under protocol number CAAE 51086715.4.0000.5544.

For the data analysis, the patients were separated into two groups: (1) those with constipation and (2) those without this complaint. Means and standard deviations were used in the descriptive

analysis, while the chi-square test and odds ratios were used for the categorical data. McNemar's test was used to compare the variables before and after TENS treatment. The analysis was conducted using the Statistical Package for the Social Sciences (SPSS), version 14.0 for Windows.

Results

Fifty-one children were included in the study, 25 of whom were constipated prior to treatment. The mean age of the constipated children was 7.72 ± 2.9 (SD) years compared to 6.73 ± 2.44 years for the group of non-constipated children (p = 0.19). There was a predominance of girls in both groups and no statistically significant difference between the groups: 15 girls (60%) versus 17 girls (65.4%), respectively (p = 0.69).

Table 1 lists the LUTS recorded for these patients prior to TENS treatment. There was no statistically significant difference in urinary symptoms between the constipated and non-constipated children.

Table 1: Comparison of urinary symptoms in groups of constipated and non-constipated children

Variable	Constipated n=25	Non-Constipated n=26	p-value	OR
Urge incontinence	23 (92%)	20 (76%)	0.13	3.45 (0.62-19)
Frequency	15 (60%)	16 (61.5%)	0.91	0.93 (0.3-2.8)
Enuresis	16 (64%)	16 (61.5%)	0.85	1.1 (0.35-3.46)
Holding maneuvers	19 (76%)	23 (88.5%)	0.24	0.41 (0.09-1.87)
Urinary tract infection	17 (68%)	15 (57.7%)	0.44	1.55 (0.49-4.89)
Nocturia	11 (44%)	9 (37.5%)	0.64	1.31 (0.41-4.1)

Table 2 shows the urinary symptoms after TENS treatment. There was an improvement in urgency, urge incontinency and in holding maneuvers in both the constipated and non-constipated children; however, there was no significant improvement in enuresis. Complete resolution of the symptoms of OAB was registered in 25 children (49%). A further 13 participants (25%) reported an improvement of 90% in the symptoms of OAB, while 3 (6%) reported an improvement of 80%, 4 (8%) an improvement of 70%, 2 (4%) an improvement of 60% and 4 (8%) reported an improvement of less than 50%. Constipation was resolved in 15 cases (60%). As shown in Tables 3 and 4, the resolution of OAB was not associated with the resolution of constipation and vice-versa.

Discussion

According to the present results, TENS proved effective for the treatment of OAB and constipation. This positive effect on the symptoms of OAB was not associated with either the presence or absence of constipation prior to treatment. Furthermore, parasacral TENS resolved OAB irrespective of its positive effect on constipation. Likewise, the improvement in constipation was unrelated to any improvement in OAB.

Table 2: Comparison of urinary symptoms in the groups of constipated and non-constipated children prior to and following treatment

Variable	Constipated n=25			Non-constipated n=26		
	Before treatment	After treatment	p-value	Before treatment	After treatment	p-value
Urgency	25	6		26	11	
Urge incontinence	23	6	0.000	20	10	0.002
Enuresis	16	9	0.07	16	13	0.62
Holding maneuvers	18	8	0.002	23	7	0.000

Table 3: Resolution of overactive bladder alone by TENS in groups of constipated and non-constipated children

	Constipated n=25	Non-Constipated n=26	p-value
Complete resolution of overactive bladder	12 (48%)	13 (50%)	0.88
Incomplete resolution of overactive bladder	13 (52%)	13 (50%)	

TENS: transcutaneous electrical nerve stimulation

Table 4: Comparison of the resolution of constipation following treatment with TENS and resolution of overactive bladder alone

	Resolution of constipation n=15	Non-resolution of constipation n=10	p-value
Complete resolution of overactive bladder	8 (53.3%)	4 (40%)	0.51
Incomplete resolution of overactive bladder	7 (46.7%)	6 (60%)	

TENS: transcutaneous electrical nerve stimulation

Various studies have shown the positive effects of TENS on symptoms of OAB [13]. On the other hand, the routine use of anticholinergic drugs involves side effects that include constipation [14]. TENS was shown to improve constipation in two randomized studies. One double-blind, controlled study evaluated the acute effects of TENS on rectal motility in 20 children with OAB. After application of parasacral TENS from morning till evening and follow-up with urodynamics and manometry, an acute increase was found in bowel contractions [15]. In another study, the participants received twelve 20-minute sessions of transcutaneous electrical stimulation with interferential current. The transit time prior to and following electrical stimulation was evaluated and a significant increase was found in colonic transit time compared to a control group [9].

A previous study conducted by our group showed that children complaining of urinary symptoms of OAB alone are three-fold more likely to present with constipation compared to children without any urinary complaints (54.9% versus 29.7%; $p<0.005$; OR = 2.87; 95%CI: 1.3 – 6.0) [6]. Another study showed an interrelation between these two systems. Following urodynamic evaluation of constipated and non-constipated children with dysfunction of the lower urinary tract, the authors concluded that acute rectal distention affects bladder function in children with dysfunction of the lower urinary tract irrespective of whether or not chronic constipation is present [3].

One advantage of TENS over antimuscarinics for the treatment of OAB in children is that neuromodulation may improve not only the LUTS but also the constipation that is often present in these cases. In a recent study, a significant improvement in the symptoms of urge incontinence, holding maneuvers, enuresis and constipation (in 86% of cases), as well as a low rate of UTI was found following parasacral TENS [10]. It was also shown in a randomized clinical trial that oxybutynin and parasacral TENS were equally effective in improving LUTS; however, TENS had the advantage of exerting a positive effect on constipation [11].

Some studies have shown that improving constipation may improve LUTS [2,16] however, the results of the present study do not corroborate those findings, at least insofar as the patients with OAB alone who were submitted to TENS are concerned. A study evaluated the frequency of urinary incontinence and UTI in chronically constipated children, assessing the symptoms again following treatment of the constipation. The results were favorable for daily urinary incontinence in 89% of patients, for enuresis in 63% and for UTI in all patients. Nevertheless, unlike the present study, those authors failed to include a control group and this represents a limitation of that study [16]. Another prospective, controlled study used ultrasonography to evaluate urinary tract alterations in 29 constipated children and 451 children with no history of constipation. Post-void residual urine and kidney dilatation were more common in the constipated children; however, these symptoms improved following treatment with a laxative [2]. Nevertheless, the authors considered only a defecation frequency of less than three times a week as a diagnosis of constipation, possibly excluding more severe cases that would have been detected by using the Rome criteria. The sample may, therefore, differ from that of the present study.

Since patients with bladder and bowel dysfunction are normally treated for both conditions using cognitive-behavioral measures, it is difficult to associate the effect of, for example, laxatives as an independent predictor of the resolution of bladder dysfunction. Although this study failed to confirm that the successful treatment of OAB depends on an improvement in constipation, it does not

mean that fecal retention does not have to be managed. This is an extremely uncomfortable symptom that has to be treated. Furthermore, there is evidence that distention of the rectal ampulla hampers bladder function [3] and this may not be reflected in a recurrence of the symptoms. In addition, constipation is associated with greater post-void residual urine volume and urinary tract infection [1].

These findings showed that TENS acts both on the lower urinary tract and on bowel motility; however, in an independent manner. The mechanism of action of neuromodulation remains to be clarified. Nevertheless, the importance of the supraspinal effect of neuromodulation on the sacral region is becoming ever clearer [17-19], and neuroplasticity may justify its long-term effect on the lower urinary tract. This effect begins by stimulating the sensory fibers but not the motor fibers. That action increases the perception of bladder and rectal fullness [20]. The cingulate gyrus, the sensorimotor cortex and the mesencephalon act in this progressive sensation of fullness, which in turn modulates the efferent nerve impulses and micturition and defecation reflexes [21].

In a study conducted in Australia, evidence was found of an increase in colonic motility with the use of TENS [9]. As stimulation of the sympathetic nervous system reduces colon transit, it is improbable that direct stimulation of this system would be the principal mechanism of action in neuromodulation.

The limitations of the present study include the number of patients, which, although compatible with other samples in different studies, may have been too small to show any statistically significant differences. Constipation and urinary symptoms were evaluated using questionnaires, hence are subjective. Nevertheless, urinary symptoms are by nature inherently subjective and there is no other way of evaluating them. The Rome III criteria for constipation in children have been the most commonly used tool in the various studies conducted in this field. Some may argue that the improvement in LUTS and constipation could be due exclusively to the use of standard urotherapy or to a placebo effect. Although the possibility of this effect being present cannot be discarded, randomized studies have shown that TENS is more effective than sham therapy in resolving OAB and constipation in children [7,15].

Conclusion

Parasacral TENS improves OAB and constipation. The presence of constipation prior to treatment was not associated with a poorer prognosis insofar as the resolution of the symptoms of OAB was concerned. Likewise, there was no association between the resolution of constipation with parasacral TENS and the resolution of OAB.

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ANEXO G - Comprovante de aceite do artigo "Parasacral transcutaneous electrical stimulation for overactive bladder in children. The number of sessions required"

De: "Annette Fowler" <jpurol@elsevier.com>
Enviada: 2016/03/21 07:18:08
Para: ubarroso@uol.com.br
Assunto: Manuscript JPUROL-D-15-00394R1

Journal title: Journal of Pediatric Urology
Corresponding author: Prof. Ubirajara Barroso
Article title: Parasacral transcutaneous electrical stimulation for overactive bladder in children: An assessment per session.
Manuscript number: JPUROL-D-15-00394R1

Dear Prof. Barroso,

I am pleased to tell you that your work has provisionally been accepted for publication. It has been sent to the copy editor for some final amendments and we will notify you when the copy editing has been completed and your manuscript has been sent to the publisher.

Thank you for submitting your work to this journal.

With kind regards,

Annette Fowler
Editorial Office
Journal of Pediatric Urology

ANEXO H - Artigo "Parasacral transcutaneous electrical stimulation for overactive bladder in children. The number of sessions required"

Parasacral transcutaneous electrical stimulation for overactive bladder in children. The number of sessions required.

Maria Luiza Veiga, Ana Paula Queiroz, Maria Clara Carvalho, Ana Aparecida Nascimento Martineli Braga, Ariane Sampaio Sousa, Ubirajara Barroso Jr.

Center of Micturition Disturbance in Children (CEDIMI), Bahiana School of Medicine and Federal University of Bahia

Abstract

Objective- To evaluate the rate of complete response of overactive bladder (OAB) symptoms for each session of transcutaneous electrical stimulation (TENS), in a protocol of 20 sessions therapy.
Material and Methods- This is a prospective study of the improvement of LUTS after parasacral TENS in children with isolated OAB. Included in this study were children over the age of four with urgency, sinusoidal or tower-shaped uroflowmetry patterns and no significant post-void residual.
Results- 69 children with a mean age of 8.44 (±3.05) years were analyzed. Complete resolution of symptoms was found in some patients starting after the 3rd session. In the 10th and 20th (last) sessions, 12 (17.4%) and 38 (55.1%) patients reported a complete resolution of symptoms. At the end of treatment, all patients showed at least some improvement. Children who showed an improvement level greater than 50% in the 5th treatment session were 4.18 (p=0.007) times more likely to have success in the last treatment session.
Conclusion- Patient can experience complete symptom resolution as quickly as following the third session of TENS. The complete response rate progressively increases with the number of sessions, slowly until the 12th session and more rapidly after that. These results demonstrate that a minimum of 20 sessions are required to ensure a good outcome after parasacral TENS, and likely even more would be necessary in many cases. When symptom improvement of at least 50% is reported in the 5th session, there is a higher chance that the patient will have full resolution of symptoms at the end of treatment.

Key words: urinary bladder, overactive, transcutaneous electrical nerve stimulation, incontinence, children

Abbreviations and Acronyms
OAB = overactive bladder
TENS = transcutaneous electrical nerve stimulation
LUTS = lower urinary tract symptoms
VAS = visual analogic scale
SPSS = Statistical Package for the Social Sciences

Introduction:

Overactive bladder (OAB) is characterized by the presence of urgency, with or without urge incontinence, generally with frequency and nocturia, in the absence of a neurological or anatomical disease [1]. OAB is related to lower urinary tract infections, constipation, urinary incontinence and vesicoureteral reflux, and has psychological repercussions on children [2-4].

Electrical stimulation has emerged as an effective therapeutic option for treatment of these cases. In 2001, Hoebeke et al. and Bower et al. first described the results of the use of transcutaneous electrical nerve stimulation (TENS) in the treatment of lower urinary tract symptoms (LUTS) [5,6]. Although they reported success with this technique, the treatment was performed through daily sessions over the course of months.

In a study done in 2006, our group showed that electrical stimulation treatment done on an outpatient basis - 20 sessions, 3 times per week - provides a complete resolution of symptoms of OAB in 62% of patients [7]. In another long-term study with the same method, we showed that patients with urgency or urinary incontinence prior to the treatment (84% and 74%, respectively) remained asymptomatic for a minimum of 2 years after the parasacral TENS treatment [8].

Two randomized studies have shown parasacral TENS to be more effective than placebo treatment [9,10]. However, there is still no real standardization of electrical stimulation parameters. The studies show variation can be found in frequency, pulse width, application time and number of sessions [11,12].

Most studies report the success rate during the final session, with a few reporting in follow-up treatments over a longer term period [5-9]. The number and duration of sessions utilized in the different studies varies between 1 and 6 months, from daily to 3 times per week [12], which shows that there is empiricism in the choice of ideal treatment time. Parents often ask how long the treatment will last and when to expect a partial or complete resolution of symptoms. However, to our knowledge, no study has yet evaluated the result of neuromodulation on a session by session basis.

In our implementation of TENS, we use a total of 20 sessions as a standard, but are not sure if this number is ideal. The aim of this study is to evaluate the rate of complete response of overactive blader (OAB) symptoms for each session of transcutaneous electrical stimulation (TENS), in a protocol of 20 sessions therapy.

Materials and Methods:

This is a prospective study of the improvement of LUTS in children with isolated OAB. Included in this study were children over the age of four who complained of urinary urgency, with or without daytime incontinence, as perceived by their parents, bell or tower-shaped uroflowmetry patterns and post-void residual < 10% of expected capacity for their age (capacity in ML = (1 + age) x 30 or greater than 20 mL) [1] and/or less than 20 ml. No patient was treated with anticholinergic.

All children had the symptoms evaluated by one pediatric urologist. It was excluded children with lower urinary tract symptoms (LUTS) secondary to urinary tract abnormalities such as posterior urethral valves, ureterocele or ectopic ureter; children with neurological disorders; children who could not regularly attend the treatment and children whose guardians did not agree to sign the free and informed consent form.

The treatment consisted of the symmetric application of electric currents through surface electrodes in the parasacral region (between S2 and S4) and electrical stimulation was produced by an electrical stimulus generator: model Dualpex Uro 961 (Manufacturer Quark, Piracicaba, Brazil). The electrodes, are coated in rubber, self-adhering, and measure five by five centimeters. A symmetrical biphasic current was used with a frequency of 10 Hz, pulse width of 700 μs and the intensity was increased to the level just below the motor threshold, as tolerated, 3 times a week for a total of 20 sessions, each 20 minutes in length.

All patients were instructed to follow a very specific regimen which included the following: urinate every 3 hours; avoid ingesting coffee, tea, soda, chocolate and citrus fruits during treatment, urinate before going to sleep, intake a greater volume of fluids during the day, do not hold urine when experiencing urgency. If constipation occurs, the children were instructed to eat foods rich in fiber and were sent to a specialist. An illustrative booklet adapted for children was created with the above guidelines. Standard urotherapy was reinforced during each session.

To evaluate the success of the treatment the following criteria were used: 1) at the end of each session, parents/guardians were asked if they felt that the child was cured, if there had been slight or great improvement, or if the clinical picture remained unchanged; 2) the development of symptoms was observed right before each session using a visual analogue scale (VAS) in which 0 means the absence of improvement and 10 represents maximum improvement of symptoms; the value was multiplied by 10 to translate the data into a percentage. The symptoms were considered resolved if the parents reported that the child was asymptomatic and marked 10 on the VAS. The parents and children should consider the score 10 when all daytime symptoms were resolved.

For the descriptive analysis, mean and standard deviation were used. To compare complete resolution of symptoms with the number of sessions, we used the chi-square and the odds ratio tests. To analyze the data we used the program Statistical Package for the Social Sciences (SPSS) for Windows, version 21.0. All the parents and guardians signed the informed consent form. The project was approved by the Ethics Committee in Research, under protocol 06/2013 CAAE**:** 12141113.0.0000.5544, according to resolution 466/12.

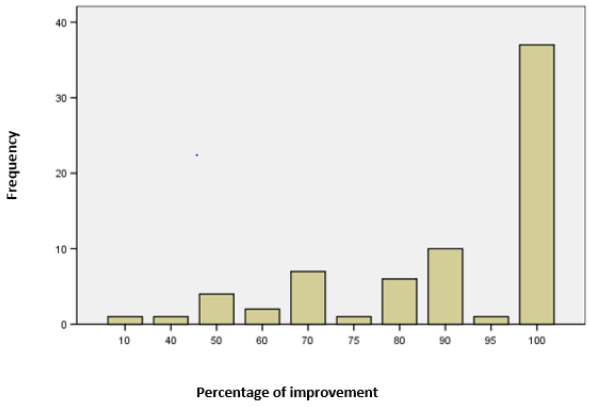
Results:

69 children with a mean age of 8.44 (±3.05) years were analyzed: 42 (60.9%) of them were girls. Of the patients evaluated, 29 (43.9%) of 66 patients with data available had daytime urinary incontinence, 42 (66,7%) of 63 experienced enuresis and 18 (50%) of 36 had constipation as evaluated by the Rome III criteria. 38 (55%) had a history of UTI, 54 (78%) had urgeincontinence, 45(65%) frequency and 46(66%) holding maneuvers.

The symptoms's complete resolution rate of each session is shown in Figure 1. We noted a complete resolution of symptoms (urgency, urgeincontinence, frequency, and holding maneuvers) in some patients starting after the 3rd session. In the 10th and 20th (last) sessions, 12 (17.4%) and 38 (55.1%) patients reported a complete resolution of symptoms. After complete resolution, 12(17.4%) reported that their symptoms worsened to a minimum level of 40% improvement, but this was temporary and all returned to 100% improvement. At the end of treatment, all patients showed at least some improvement (Figure 2). Children who showed an improvement level greater than 50% in the 5th treatment session were 4.18 (p=0.007) times more likely to have success in the last treatment session. There was no statistical significant difference between the success rate of the parasacral TENS in boys and in girls (43,2% X 56,8%, p= 0,33).

Figure 1. Correlation of Improvement percentage of symptoms and parasacral TENS session number

Figure 2. Global percentage of improvement after parasacral TENS



Discussion:

To the best of our knowledge, this study is the first to assess the outcome of neuromodulation on a session by session basis. We have shown a complete resolution of symptoms after as few as three sessions. The results tended to improve with time; 16% of patients saw a full resolution of symptoms after half the sessions and 55.1% had a full resolution at the end of all sessions. We observed a greater increase in the improvement curve after the 13th session. Since the curve continues to climb until the end, we suspect that we would continue to see an increase in the number of patients improving after the 20th session. Therefore, our current approach is to perform more sessions on patients that are showing improvement.

Children with OAB symptoms have frequently been treated by antimuscarinics, such as oxybutynine. On the other hand, a meta-analysis of several drugs [13] already demonstrated muscarinic receptor antagonists increase the likelihood of developing constipation. They also have other side effects due to the way that they react with the parasympathetic autonomic system. Thus, despite the rapid response to medication, parasacral TENS has emerged as a good therapeutic alternative due to issues such as adherence to treatment, length of use and adverse side effects. In a randomized clinical trial we recently compared oxybutynin and TENS and found that they are associated with similar rates of improvement in LUTS, but TENS is best to resolve constipation [14]. Although parasacral TENS is gaining increased acceptance around the world, the optimal duration of treatment is not yet known nor is it known how soon a patient can expect symptom improvement. Parents commonly ask about the duration of treatment and the response has always been empirical.

In this study, TENS had no effect in the first two sessions, showing that the results of this technique are evolutionary, and that there does not appear to be a significant acute effect on symptoms of OAB. This result tended to increase progressively with the number of sessions.

We found that at least 50% of the response by the 5th session predicts the final result. This may suggest that additional resources should be sought out to find the best response prior to the end of treatment for those patients who show less than 50% improvement during that period. The complete resolution of the symptoms progressively increased after the 13a session, doubling the rate of success from 15a to 20a session (26.1% - 55.1%). This may suggest a cumulative effect of the neuromodulation and/or the time of that neurons take for neuroplasticity. A study showed that children who underwent parassacral TENS for OAB maintained the long term response in a long term (90% in more than 2 years) [8]. There is now a good evidence that there is a supraspinal effect of sacral neuromodulation and an increase of perception of the bladder filling [15]. Centers in the cerebral cortex and midbrain are involved in the micturition control and they respond with blood flow and cell signal modification to the neuromodulation are involved [16-20].

This study has limitations. Although the number of patients studied is larger than that of other series, it is still not large to analyze all predictors of success. The evaluation of symptom relief is subjective and may be subject to bias. Therefore we may not exclude the

possible presence of the placebo effect. Additionally, all patients underwent standard urotherapy, which also has a positive effect on improving symptoms. In this study only 36 children had the constipation diagnosed by Rome 3 criteria.

Conclusion:

We found that a patient can experience complete symptom resolution as quickly as following the third session of TENS. The complete response rate progressively increases with the number of sessions, slowly until the 12th session and more rapidly after that. These results demonstrate that a minimum of 20 sessions are required to ensure a good outcome after parasacral TENS, and likely even more would be necessary in many cases. Some patients may have experienced a slight worsening of symptoms during treatment, but tended to improve over time. When symptom improvement of at least 50% is reported in the 5th session, there is a higher chance that the patient will have full resolution of symptoms at the end of treatment.

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ANEXO I – Carta aceite do artigo "Enuresis and overactive bladder in children: what is the relationship between these two conditions? The association between enuresis and overactive bladder in children".

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06-Jan-2016

Dear Dr. Sousa:

Your manuscript entitled "Enuresis and overactive bladder in children: what is the relationship between these two conditions?" has been successfully submitted online and is presently being given full consideration for publication in the International Braz J Urol.

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Sincerely,
International Braz J Urol Editorial Office

ANEXO J - Artigo "Enuresis and overactive bladder in children: what is the relationship between these two conditions? The association between enuresis and overactive bladder in children" aceito no *International Braz J Urol*.

Enuresis and overactive bladder in children: what is the relationship between these two conditions?

The association between enuresis and overactive bladder in children

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Keywords: enuresis; non-monosymptomatic enuresis; overactive bladder; child, incontinence

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Abstract

Objective: To evaluate clinical aspects associated with the presence of nocturnal enuresis (NE) in children with a diagnosis of overactive bladder (OAB).
Material and Methods: A database of 200 children who were evaluated by a structured questionnaire was analysed retrospectively. OAB was defined as the presence of urinary urgency (n=183 cases) and/or daytime urinary incontinence associated with holding maneuvers (n=168 cases). The inclusion criteria were a confirmed diagnosis of OAB, age 5-16 years, and no anatomical or neurological alterations of the urinary tract. The patients were divided into enuretics and non-enuretics. The two groups were compared with respect to sex, age, skin color, presence urinary infection, urgency, urge incontinence, non-urge incontinence, pollakiuria, urinary dysfunction, nocturia, holding maneuvers, number of episodes of enuresis and bowel alterations. In a univariate analysis, the chi-square test was used to compare proportions, with

p-values <0.05 being considered significant. A multivariate analysis was conducted to identify independent predictive factors.

Results: Enuresis was diagnosed in 141/200 children. The two groups were similar with respect to sex, age and skin color. No difference was found in relation to urinary infection, non-urge incontinence, urinary dysfunction, nocturia, encopresis or constipation. The two groups were significantly different with regard to some symptoms related to OAB such as urgency (p=0.001), urge incontinency (p=0.001) and holding maneuvers (p=0.033). Following multivariate analysis, only holding maneuvers (p=0.022) remained as an independent predictive factor.

Conclusion: The only independent predictive factor for resolution of enuresis in children with OAB, as detected in the multivariate analysis, was holding maneuvers.

Abbreviations:

LUTS: lower urinary tract symptoms

Non-MSE: non-monosymptomatic enuresis

OAB: overactive bladder

NE: nocturnal enuresis

LUTD: lower urinary tract dysfunction.

Introduction

The International Children's Continence Society classifies enuresis as monosymptomatic (MSE) when bedwetting is the only symptom and non-monosymptomatic (non-MSE) when lower urinary tract symptoms (LUTS) are present (1). Enuresis is a common condition in children, affecting around 15-20% of 5-year olds, 5-10% of 7-year olds, 5% of 10-year olds and 1-3% of children of 15 years of age (2-4). Older studies have reported daytime LUTS in around 15-40% of cases of enuresis (5,6). However, more recent data suggest that LUTS such as daytime incontinence, urgency, frequency and voiding postponement are present in 50-80% of cases (3,7). Daytime incontinence has been found more often in girls than in boys, whereas enuresis is more common in boys (8). In many cases, LUTS go unrecognized in patients with enuresis because doctors fail to ask about them or because parents are far more concerned about bedwetting (9,10). Because enuresis tends to have a greater effect on family dynamics than LUTS, it may be more perceptible to parents.

Differentiating between the types of enuresis (MSE and non-MSE) is relevant because the physiopathology and management may not be the same for the two conditions. Non-MSE is more commonly associated with urinary tract infections (UTI), vesicoureteral reflux, constipation and behavioral problems (11,12). Parents often believe that their child's treatment has failed entirely when enuresis persists even though complete resolution of LUTS was achieved. Since recognizing each condition individually is important, patients with enuresis should be investigated for LUTS and patients with LUTS should be asked about the presence of enuresis. Although OAB is commonly associated with enuresis, the clinical relationship between these two conditions remains to be clarified. In fact, identifying the characteristics of these patients is a crucial step towards gaining a better picture of the clinical scenario, prognosis and management of both conditions. Therefore, the objective of the present study was to evaluate the clinical aspects associated with enuresis in children and adolescents with OAB.

Material and Methods

A database of 200 children who were evaluated by a structured questionnaire was analysed retrospectively. OAB was defined as the presence of urgency (n=183 cases) and/or daytime incontinence (n=168 cases). The inclusion criteria were a confirmed diagnosis of OAB, age between 5 and 16 years and the absence of any anatomical alterations or neurogenic disorders of the lower urinary tract. Patients for whom the database information was incomplete, and those who had recorded fewer than 4 voids per day in the bladder diary were excluded from the study. The internal review board of the Escola Bahiana de Medicina e Saúde Pública approved the study protocol under reference number 12141113.0.0000.5544.

A structured questionnaire was administered to all the patients to obtain the following information: demographic data (age, sex and skin color), number of voids, the presence of nocturnal enuresis (and its intensity), daytime incontinence (and its intensity), nocturia, urgency, straining, holding maneuvers, constipation (in accordance with the Rome III criteria), and a history of UTI confirmed by culture. Daytime incontinence was classified as urge or non-urge incontinence. Daytime incontinence and enuresis were classified according to intensity as daily, three times a week or more, less than three times a week or occasional.

Holding maneuvers were considered present when the child's parents reported

typical body posturing such as squeezing the genitals, crossing the legs, going on tiptoe or squatting on the heel (Vincent's curtsy). All patients underwent uroflowmetry plus electromyography. Dysfunctional voiding was defined as an abnormal voiding pattern in the uroflow curve and activity on electromyography (flat curve plus activity on electromyography, staccato and interrupted voiding). Only 85 patients completed a 3-day bladder diary. The association between enuresis and the number of voids, the presence of daytime incontinence, and constipation was evaluated. Patients with and without enuresis were compared with respect to the presence of all the aforementioned clinical variables.

The SPSS software program, version 20.0 was used throughout analysis. In a univariate analysis, the chi-square test was used to compare proportions, with p-values <0.05 being considered statistically significant. Multivariate analysis was conducted for identifying the independent predictor variables. The variables that were significant in the univariate analysis were consecutively added to a multivariate hierarchical model, which started with a simple predictor.

Results

Of the 200 children with a diagnosis of OAB, 84 were boys (42%) and 116 girls (58%). Age ranged from 5 to 16 years, with a mean of 8.6 ± 2.9 years. NE was diagnosed in 141 children (70.5%). Of these children, 83 (58.9%) were female. The mean age of the children with enuresis was 8.6 ± 2.7 years, while the mean age of those without enuresis was 8.6 ± 3.2 years (p=0.831). In 112 patients (80.6%), NE occurred at least three times a week. NE rate of 68% (n = 87) in children ≤ 9 years and 75% (n = 54) in those 10 years of age or older.

Table 1: Demographic characteristics of the enuretic and non-enuretic children

Variable	Non-Enuretics (n)	Enuretics (n)	P-value
Male	26	58	
Female	33	83	p=0.702
Age ≤ 9 years	41	87	
Age ≥ 10 years	18	54	p=0.295
Skin color not black	14	29	
Skin color black	27	80	p=0.363
Total	**59**	**141**	

Table 2: Urinary symptoms in enuretic and non-enuretic children

Variable	Non-Enuretics (n/%)	Enuretics (n/%)	P-value
UTI without fever	24 (42.9)	45 (36.9)	p=0.448
UTI with fever	24 (44.4)	50 (40.7)	p=0.637
Urgency	**48 (81.4)**	**135 (95.7)**	**p=0.001**
Urge incontinence	**37 (63.8)**	**120 (85.7)**	**P=0.001**
Pollakiuria	**27 (46.6)**	**83 (60.6)**	**p=0.071**
Dysfunctional urination	23 (39.0)	44 (31.2)	p=0.288
Nocturia	19 (33.3)	35 (24.8)	p=0.223
Holding maneuvers	**34 (59.6)**	**102 (75.0)**	**p=0.033**
Non-urge incontinence	30 (51.7)	70 (50.4)	P=0.861

UTI: urinary tract infection

Regarding the demographic characteristics of the enuretic and non-enuretic patients with OAB. (table 1) No statistically significant difference was found between the two groups with respect to sex, age or skin color.

The clinical characteristics in both groups are showed in table 2. The symptoms associated with the presence of NE were urgency (p=0.001), urge incontinence (p=0.001) and holding maneuvers (p=0.033). There was no difference in relation to the presence of febrile or afebrile urinary infection, nocturia, constipation, straining or abnormal urine flow. In addition, there was no statistically significant difference between those

patients with severe enuresis (≥3 episodes/week) and the non-enuretic patients in relation to any of these factors. Following multivariate analysis, only one independent predictive factor was identified: the presence of holding maneuvers (p=0.022).

Discussion

Few studies have dealt with the subject of non-monosymptomatic NE. Since the principal complaint of families generally concerns nocturnal enuresis, daytime complaints are often undervalued and forgotten, hampering the implementation of appropriate treatment. In some cases, parents may even be unaware of daytime symptoms, since the frantic rhythm of modern life tends to leave parents with less time to participate in the day-to-day routine of their child's life. Nocturnal enuresis causes problems with socialization, resulting in low self-esteem and stress both in the child and in the family. In addition, NE has been found to be associated with behavioral alterations such as attention-deficit/hyperactivity disorder (13).

In the present sample, enuresis was shown to be a common symptom in patients with OAB, occurring in 70.5% of cases. Despite the extent to which NE distresses parents, little attention has been paid to factors potentially associated with NE in patients with LUTS. A better understanding of this relationship may help identify possible factors associated with more severe conditions. Consequently, physicians will be able to act more effectively by implementing more individualized treatments. When performing the clinical assessment of NE, physicians have frequently neglected daytime symptoms. To the best of our knowledge, this study is innovative in that an inverse analysis was used, i.e. the presence of enuresis was investigated in patients with symptoms of OAB.

In this series of patients, both the daytime urinary symptoms and enuresis were more common in girls. This finding in children with overactive bladder differs from cases of monosymptomatic NE, which tend to be more common in boys. In a study conducted with a group of 51 patients, Naseri et al. confirmed an association between enuresis and daytime incontinence, and reported twice as many girls being affected as boys (14). In the present group of 141 children with enuresis associated with OAB, the proportion of girls to boys was 1.45 to 1.

The frequency of monosymptomatic enuresis tends to decrease progressively with age until reaching a rate of 0.5 to 1%

in adults. In cases of non-monosymptomatic enuresis, however, some studies have shown that this does not occur, with the frequency of enuresis tending to remain the same in older children, possibly as a consequence of the mechanisms involved in overactive bladder (11,12,15). Accordingly, the present study also failed to detect any reduction in enuresis with increasing age in non-monosymptomatic enuresis.

Children and adolescents with symptoms of overactive bladder should be investigated for nocturnal enuresis, principally in the presence of holding maneuvers. The present results suggest that one of the principal mechanisms involved in non-MSE is nocturnal overactive bladder, given that the abovementioned symptoms are characteristic of this condition. The hypothesis that these children may have more difficulty waking up than non-enuretic children has to be investigated, since the involvement of assorted physiopathological mechanisms cannot be discarded. Furthermore, the psychological impact of NE in children with OAB, and the influence of NE in rendering prognosis poorer in these patients are factors that remain to be evaluated. It is important to note that it has been found a higher rate of psychiatric disorders in children who postpone voidind with holding maneuvers.[11] Futher studies should be performed in order to evaluate if it is also true for patients with non-monosymptomatic enuresis.

Constipation and bowel problems are often associated with urinary tract abnormalities and 90 (46.4%) of the patients in this series had at least one complaint. Nevertheless, the groups of enuretic and non-enuretic patients were not significantly different with respect to these symptoms. None of the other clinical characteristics of the patients with lower urinary tract dysfunction were found to be associated with NE. Factors such as the presence of urinary tract infection, irrespective of the number of episodes, and nocturia were not found to be significantly associated with enuresis.

This study has some limitations. For example, the subjective nature of the symptoms may have led to interpretation errors. Moreover, the severity of enuresis was assessed based on the responses provided by parents and children rather than by analyzing the number of dry nights recorded on a chart. However, to the best of our knowledge, although the association of OAB in patients with NE has been studied extensively, the association of NE in patients with OAB has not. The results of the present study may shed more light on

the actual rate of enuresis in children with OAB and on the profile of patients who are more prone to enuresis, thus opening perspectives for new studies. The impact of enuresis on both the patients with OAB and their caregivers remains to be evaluated. Nevertheless, understanding this impact is relevant since more than half of the patients present with this symptom. Furthermore, those patients with OAB who would benefit from a simultaneous treatment for enuresis should be clearly identified.

Conclusion

NE and OAB are commonly associated, with NE being present in 70.5% of children with OAB. In this study on children with overactive bladder, daytime urinary symptoms and non-monosymptomatic enuresis were both more common in girls. No reduction in enuresis was found with increasing age. Therefore, as long as overactive bladder and, consequently, daytime symptoms remain untreated, there will be no improvement in nocturnal symptoms. Of the OAB symptoms, only holding maneuvers were found to be associated with enuresis as an independent predictive factor. This suggests that when these daytime symptoms are present, OAB and NE probably share the same genesis.

Financial disclosures: None.

Funding sources: None.

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ANEXO K - Artigo publicado durante o doutorado: Transcutaneous Electrical Nerve Stimulation in Children With Overactive Bladder: A Randomized Clinical Trial

Transcutaneous Electrical Nerve Stimulation in Children With Overactive Bladder: A Randomized Clinical Trial

Patrícia Lordêlo, Alcina Teles, Maria Luiza Veiga, Luis Cláudio Correia and Ubirajara Barroso, Jr.*

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Purpose: We evaluated the effectiveness of parasacral transcutaneous electrical nerve stimulation to treat overactive bladder in children. We designed a prospective randomized trial with sham control for this evaluation.

Materials and Methods: We prospectively randomized 25 girls and 12 boys with an average age of 7.5 years (range 4 to 12) into the test (active treatment) or sham (superficial scapular electrical stimulation) group. A total of 20 sessions, 20 minutes each (10 Hz) were performed 3 times weekly. The criteria used to evaluate the rate of success were 1) self-reported cure, or significant, mild or no improvement; 2) visual analogue scale (level of success 0 to 10); 3) percent improvement; 4) modified Toronto score; and 5) maximum voided volume, average voided volume and number of voids daily based on bladder diary entries. After completion of the 20 sessions controls who were not cured underwent active treatment.

Results: A total of 21 patients in the test group and 16 in the sham group underwent treatment. Among the active treatment group 61.9% of parents reported cure. In the sham group no parent reported cure ($p < 0.001$). Regarding visual analogue scale a score of 10 was indicated by 13 parents in the test group, while 1 parent in the sham group indicated a score of 9 ($p = 0.002$). Additionally 100% improvement was reported by 12 parents in the test group and no parent in the sham group. Toronto score improved significantly in the test group ($p < 0.001$) and sham group ($p = 0.008$). However, the score was reduced more significantly in the test group compared to the sham group ($p = 0.011$). In the test group average and maximum voided volumes showed a statistically significant increase and the number of voids daily decreased. After superficial scapular electrical stimulation 13 of the 16 patients who underwent parasacral transcutaneous electrical nerve stimulation were cured.

Conclusions: This is the first known randomized clinical trial to demonstrate that parasacral transcutaneous electrical nerve stimulation is effective in the treatment of children with overactive bladder.

Key Words: child, transcutaneous electric nerve stimulation, urinary bladder, urinary incontinence

Abbreviations and Acronyms

AVV = average voided volume
MVV = maximum voided volume
NV = number of voids daily
OAB = overactive bladder
PSTENS = parasacral transcutaneous electrical nerve stimulation
TENS = transcutaneous electrical nerve stimulation
UTI = urinary tract infection
VAS = visual analogue scale

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See Editorial on page 417.

Lower urinary tract dysfunction is a disturbance found in neurologically normal children, and can occur in the filling and emptying phases of the lower urinary tract.[1] Overactive bladder is clinically characterized by urgency, daytime urinary incontinence and, often, frequency. Daytime urinary incontinence at age 7 years reportedly occurs at a rate of 3.5% in boys and 6% in girls, with 20% of these children demonstrating urgen-

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cy.[2] Daytime incontinence is a source of psychological stress and social discomfort, which in turn lowers self-esteem.[2] Moreover, lower urinary tract dysfunction is associated with urinary tract infection and vesicoureteral reflux, and presents a risk of renal scarring in children.[3–6]

Antimuscarinics are frequently used to treat OAB in children. However, to our knowledge there exists no published randomized, controlled, clinical trial of oxybutynin (the most commonly used medication in this group).

Electrical stimulation was introduced as an alternative to treat OAB in children. Hoebeke[7] and Bower[8] et al first described the use of PSTENS in children with refractory OAB, and found good results with daily sessions during a period of 5 to 6 months.

We were the first to report a short-course of PSTENS in children.[9] Treatments were scheduled 3 times weekly for a maximum of 20 sessions. Short-term results indicated a complete response for 63% of the cases and significant improvement in symptoms for 32%. We evaluated our long-term results with this procedure.[10] With a mean follow-up of 28.3 months (range 6 to 80) continued success was seen in 78% of the children. Both studies were performed without a control group. We evaluate the efficacy of PSTENS in treating OAB in children in a randomized clinical setting.

MATERIALS AND METHODS

This study was a single-blind, prospective, sham controlled, randomized, clinical trial in which participants were children older than 4 years with OAB. OAB was defined as the presence of characteristic symptoms of urgency, with or without daytime incontinence, accompanied by holding maneuvers to postpone voiding. Further conditions were no post-void residual urine and bell-shaped curve on uroflowmetry. The study was blinded for patients and parents as well as the providers who evaluated the outcome. These providers were not the same ones who administered treatment. All parents signed an agreement to participate in the study. Parents were told that 1 group of patients would receive inactive treatment.

Site of stimulation (parasacral or scapular) was not disclosed. Randomization was facilitated by a sealed, opaque envelope. The study was single center with on-site allocation. The study was approved by our hospital ethical committee (register 12/06).

A voiding diary was kept for 3 days as an assessment tool for all patients. Post-void residual urine was evaluated by ultrasound and was considered abnormal if greater than 10% of expected bladder capacity in ml ([age + 2] × 30),[11] or greater than 20 ml. A total of 34 patients had a post-void residual of less than 5 ml and 3 had a reading of 5 to 20 ml. Exclusion criteria consisted of lower urinary symptoms secondary to anatomical anomaly such as posterior urethral valves, ureterocele or ectopic ureter, neurogenic bladder, nonresident status (children who lived outside the city where the trial took place), and inability to comply with treatment requirements.

We used 4 criteria to evaluate the outcome in intent to treat analysis. First, parents were asked if their child symptomatically improved significantly, mildly or not at all. Additionally a VAS from 0 to 10 was used by parents, in which 0 meant no improvement and 10 meant complete resolution of symptoms. Also, a nonvalidated adapted Toronto score was obtained before and after treatment.[10] The number of voids daily, AVV and MVV before and after treatment were evaluated in a voiding diary.

All children underwent urotherapy. The training was presented in an attractive booklet containing demonstrative illustrations that reinforced the necessity of 1) voiding before sleeping, 2) increasing volume of liquid ingested daily, 3) eating foods rich in fiber and 4) refraining from postponement of voiding when experiencing symptoms of urgency. Girls were asked to prioritize voiding comfort by postponement. The booklet suggests options of toilet seat adapters and foot supports to adjust for height issues. The booklet further recommends that at the moment of urination the child should lightly flex the spine and relax the abdominal musculature. The booklet cites that the stomach "should be sleeping" at the time of urination. No medication was given to patients before or during treatment.

TENS was administered in the office by 3 different professionals who were highly experienced in the field. Two superficial 3.5 cm electrodes were placed on each side of S3 and S2. Electrodes were also placed in the scapular area 3 cm above the inferior scapular edge (fig. 1). Electrical energy was produced by a generator (Dualpex 961 URO, Quark®). The procedure consisted of 20 sessions of TENS. Frequency used was 10 Hz with a generated pulse of 700 μs. Current intensity was increased to the maximum level tolerated by the child. TENS was performed 3 times weekly, with sessions of 20 minutes. In the test group only the sacral electrodes were activated, while in the sham group the stimulation was at the scapular electrodes.

Patients were reevaluated immediately after finishing treatment. Patients from the sham group who did not have complete remission of symptoms continued with 20 more sessions of PSTENS. However, for these sessions the stimulus was only applied in the lower sacral area and the sham group became part of the test group.

The difference in categorical variables was analyzed by chi-square test or Fisher's exact test. Paired analysis was performed using paired Student t test or Mann-Whitney test. Student t test or Mann-Whitney test was also used to compare independent variables. The level of statistical significance considered was less than 5%.

RESULTS

A total of 25 girls and 12 boys with symptoms of OAB were included in the study. Average ± SD patient age was 7.5 ± 2.8 years (median 7, range 5 to 10). Patients were randomly assigned to either the test group (21) or the sham group (16).

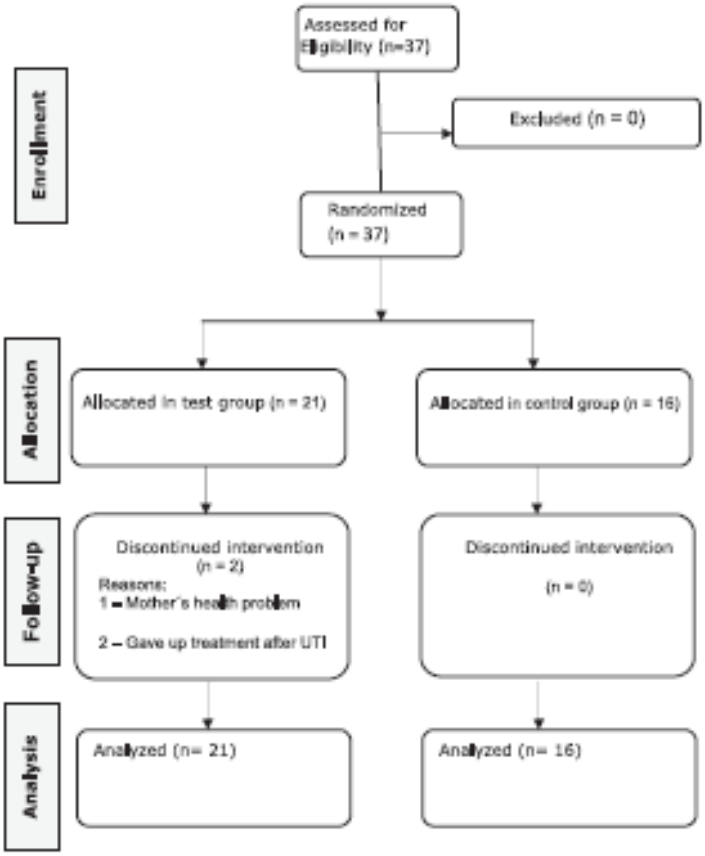

Figure 1. CONSORT fluxogram

Demographic and clinical characteristics of the patients are outlined in table 1. Female gender was predominant in both groups. The majority of the patients had daytime incontinence and enuresis, used holding maneuvers to prevent voiding and had a history of UTI.

Table 1. *Distribution of demographic and clinical data between groups*

Variable	Test group	Sham group	p Value
Mean ± SD yrs age	7.5 ± 3	7.4 ± 2.8	0.929
No. female (%)	18 (81.8)	12 (75)	0.691
No. daytime incontinence (%)	16 (76.2)	14 (87.5)	0.674
No. holding maneuvers (%)	15 (71.4)	12 (75)	1
No. nocturnal enuresis (%)	16 (76.2)	13 (81.3)	1
No. history UTI (%)	18 (81.8)	11 (68.8)	0.668
No. pyelonephritis (%)	8 (36.4)	7 (43.8)	0.729

Data regarding MVV, AVV and NV based on voiding diary, along with modified Toronto score before and after treatment, are presented in table 2. There was no statistical difference in values between the groups.

A total of 37 children underwent treatment (test 21, sham 16, fig. 2). In the test group 2 children did not finish treatment. One child left the group at

Table 2. *Data from voiding diary and modified Toronto score between groups*

Variable	Test group	Sham group	p Value
Median ml MVV (Q1–Q3)	150 (117–200)	140 (110–207.5)	0.928
Median ml AVV (Q1–Q3)	87.5 (63.2–107.6)	76.9 (69.7–88.3)	0.798
Median No. NV (Q1–Q3)	7 (5.5–9.5)	7.2 (6.2–8.9)	0.975
Mean ± SD Toronto score	9.6 ± 5.2	10.8 ± 5.6	0.523

Figure 2. Position of superficial electrodes in scapular and lower sacral regions during application of electrical stimulation.

session 8 because of a health problem in the mother. The other child presented with a UTI at session 15 and did not return to treatment.

Comparison of Results: Test vs Sham Group

Parents reported complete improvement of symptoms in 61.9% of the test group. By comparison, there was no case of complete resolution of symptoms in the sham group ($p < 0.001$). Significant improvement of symptoms was found in 38.1% of patients in the test group and 31.3% of those in the sham group.

VAS results are illustrated in figure 3. In the test group the lowest score was 5 and 13 parents indicated what was considered the highest therapeutic success (10). In the control group the highest score marked was 9 ($p = 0.002$).

Modified Toronto scores in the test and sham groups before and after treatment are presented in figures 4 and 5, respectively. There was a statistically significant difference in values of the scores before and after treatment in both groups, ($p < 0.001$ and $p = 0.008$, respectively). However, the score was reduced more significantly in the test group than in the sham group ($p = 0.011$).

Distribution of MVV and AVV is demonstrated in figures 6 and 7. There was a significant increase in MVV ($p = 0.001$) and AVV ($p = 0.002$) in the test group. However, the difference was not statistically significant in the sham group. NV before and after treatment is shown in figure 8. There was a significant decrease in NV in the test group compared to the sham group ($p = 0.013$). Figure 8 illustrates the Consolidated Standards of Reporting Trials (CONSORT) flowgram.

Results of Patients in Sham Group Who Underwent PSTENS

Of the 16 children in the sham group who underwent PSTENS 14 finished all 20 sessions. One child

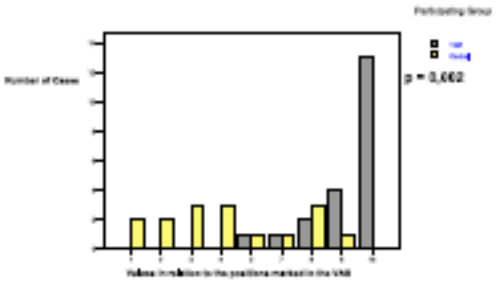

Figure 3. Distribution of values encountered in VAS for test and control groups.

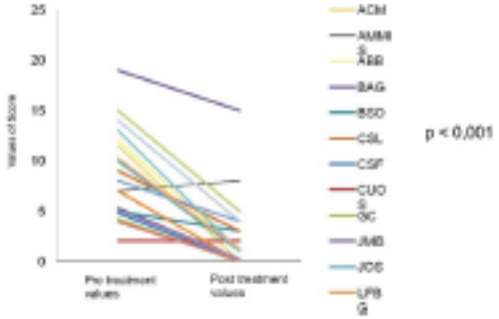

Figure 4. Modified Toronto score before and after treatment in test group. p value indicates difference in score before and after treatment.

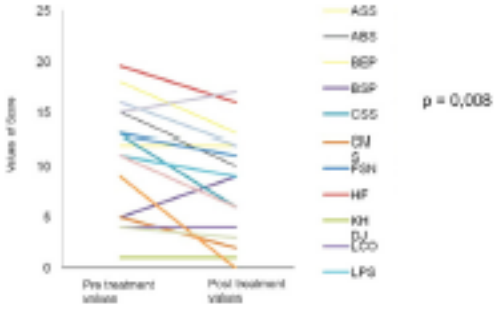

Figure 5. Modified Toronto score before and after treatment in sham group. p value indicates difference in score before and after treatment.

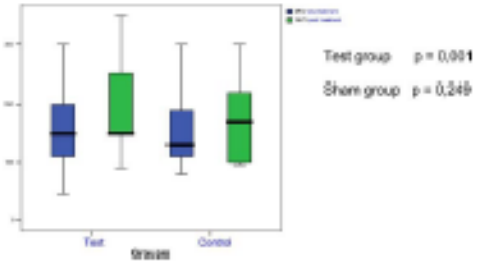

Figure 6. MVV before and after treatment between groups. p values represent intragroup differences through time.

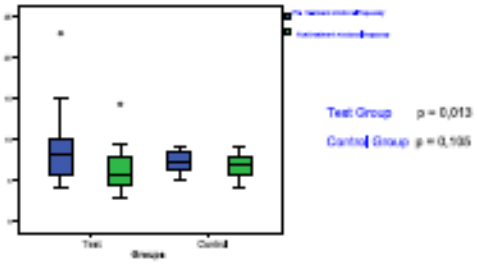

Figure 8. NV before and after treatment between groups. p values represent intragroup differences through time.

who stopped at session 18 had a reported 100% improvement. Another child who was not compliant since the beginning of the PSTENS abandoned treatment at session 14 with a reported 70% improvement in symptoms. Overall, 100% improvement was reported in 13 patients (81.25%), 90% in 1 (6.25%), 80% in 1 (6.25%) and 70% in 1 (6.25%).

Final Results in All PSTENS Treated Patients

Six children remained incontinent during the day after treatment. Two of these children are on anticholinergics. After a mean follow-up of 16.2 months (range 3 to 29) recurrence of symptoms was seen in 4 children (10.8%). Three of these patients are on anticholinergics. Four children presented with UTI, of whom 1 was operated on for grade IV vesicoureteral reflux, 1 had a 90% symptomatic improvement but eventually postponed voiding, 1 presented with recurrence of OAB and UTI after a period of complete improvement in symptoms, and 1

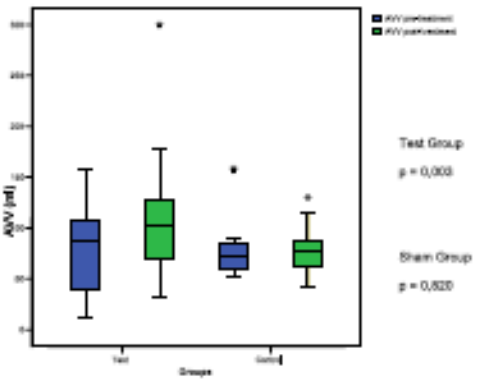

Figure 7. AVV before and after treatment between groups. p values represent intragroup differences through time.

presented with UTI at session 15 and was lost to follow-up.

DISCUSSION

For all criteria for success used in the study (improvement in symptoms, VAS, MVV, AVV, NV, Toronto score) the test group compared favorably with the sham group. These positive results reaffirm our recently published short-term and long-term PSTENS data, in which symptoms improved completely in 63% and 78% of patients, respectively.[9,10] Rate of recurrence after initial complete remission of symptoms was 10%.

To our knowledge this is the first study to show in a randomized clinical setting that electrical stimulation is effective in children with OAB. It is interesting that oxybutynin has been used for many years without the support of randomized studies. By comparison, in a randomized double-blind study there was no difference between tolterodine and placebo in children with OAB.[12] However, in 2 recent randomized clinical trials tolterodine and propiverine performed better than behavior modification plus placebo.[14,15] The use of anticholinergics has disadvantages, such as low compliance, prolonged use and side effects.[1,9]

Several authors have described PSTENS in children with good results, although invasive techniques of electrical stimulation preclude its widespread use in children.[17–19] Hoebeke[7] and Bower[8] et al reported the first 2 series of PSTENS over S3 for children with OAB. The treatment was performed at home under parental supervision. Treatment was daily for 1 to 2 hours during a period of 5 to 6 months. In the study by Hoebeke et al PSTENS was performed in 15 girls and 26 boys with OAB that was unresponsive to other kinds of treatment.[7] One year after treatment the rate of complete resolution of symptoms was 51.2%. Bower et al used PSTENS or TENS over the suprapubic area in 15 girls and 2

boys.[9] They used a frequency of 10 Hz, with PSTENS to the lower sacral area. Treatment was twice daily for 1 to 5 months. Each session lasted 1 hour. They reported complete resolution of symptoms in 7 of 15 children with daytime incontinence.

To our knowledge we reported the first ambulatory short-term study of PSTENS in children.[9] PSTENS was performed for 20 minutes 3 times weekly for a maximum of 20 sessions. Frequency used was 10 Hz. With a lower number of sessions the compliance with treatment may be higher. Moreover, when treatment is administered by a professional the current intensity can be increased until the sensitivity threshold is reached. This result is seldom possible when performed by the patient. We use the frequency of 10 Hz, which according to Lindstrom et al, causes better bladder inhibition in cats.[20] Also, this frequency has been widely successful in adults.[21]

The mechanics of electrical stimulation for OAB are far from being established. It is known that electrical stimulation acts directly not only on the muscle fibers, but also on the reflexes.[22] Activation of the inhibitory sympathetic neurons and inhibition of parasympathetic excitatory neurons that go to the bladder may have a role in the action mechanism of the electrical stimulation. These reflexogenic pathways have been described in intravaginal electrical stimulation in animals.[22] It has been also proposed that the pudendal nerve could be activated.[24] This mechanism consequently would relax the bladder and inhibit detrusor overactivity by external urethral sphincter contraction or by inhibition of interneurons.[25]

A supraspinal effect of electrical stimulation has also been reported. Lino et al investigated whether brain reorganization occurred along with clinical improvement after sacral root stimulation.[26] Six patients 33 to 68 years old with idiopathic OAB were included in the study. All patients demonstrated clinical improvement after sacral root stimulation. Transcranial magnetic stimulation results showed that sustained sacral root stimulation may reorganize the human brain and its ability to excite the motor cortex, in turn modulating lower urinary tract function.

Because all patients were treated with urotherapy, we did not know the results of PSTENS where this treatment had not taken place. Therefore, we recommend that urotherapy be performed concomitantly. Since no patient had complete resolution of symptoms in the sham group (low response rate associated with urotherapy only), at our department children with OAB are treated primarily with PSTENS in association with urotherapy.

Our study is limited by the unavoidable professional/patient interaction in the sham group. Also, the followup is short. However, our long-term study shows evidence that the positive outcome is sustained through time.[9] The negative influence of constipation on bladder function is well-known. Because electrical stimulation may improve constipation, it also may have indirectly improved lower urinary tract function in some of our patients. Future steps regarding PSTENS research include investigation of the effectiveness of a lower number of weekly sessions, alternative pulse width, alternative pulse frequency and addition of more sessions for patients who do not show complete improvement by session 20.

CONCLUSIONS

PSTENS was effective for treating OAB in children in a randomized clinical trial. There was greater improvement in symptoms, increased bladder capacity and reduction of number of voids in patients who underwent PSTENS compared to the sham group.

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EDITORIAL COMMENT

The authors are to be congratulated for this randomized, placebo controlled, clinical trial of transcutaneous neural stimulation in children with severe overactive bladder. Perhaps unsurprisingly both groups improved after the interventions, which were performed concurrent with behavioral therapy. However, the children who received active treatment were more likely to report a complete resolution of symptoms and a greater overall reduction in symptom scores than children who received the placebo treatment.

Neurologically normal patients with voiding dysfunction are, with rare exception, best treated with initial behavioral and/or medical therapy. For patients who cannot tolerate medications, or whose voiding dysfunction is severe and refractory to maximum medical therapy, a more invasive option such as PSTENS or sacral neuromodulation may be appropriate.[1–3] The authors have done an excellent job of demonstrating that in well selected patients treatment options such as this can be effective.

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ANEXO L – Artigo publicado durante o doutorado **“**The influence of positioning in urination: An electromyographic and uroflowmetric evaluation

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The influence of positioning in urination: An electromyographic and uroflowmetric evaluation

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KEYWORDS
Patient positioning;
Urination posture;
Uroflowmetry;
Electromyography;
Dysfunctional voiding;
Pelvic floor muscles

Abstract *Purpose:* We conducted a cross sectional study to evaluate whether the different positions during urination influence the electrical activity of the abdominal and perineal musculature, as well as the uroflowmetric parameters of children with lower urinary tract dysfunction (LUTD).

Materials and methods: Ninety four children between the ages of 3 and 14 years with symptoms of LUTD were evaluated. All underwent uroflowmetry and electromyography tests (abdominal and perineal) in two different positions: oriented position (trunk bent slightly forward and feet flat) and atypical position (standing on toes for boys and buttocks not in contact with the lavatory seat and legs flexed in girls). We excluded nine patients due to suspicions of outside interference or elements complicating the analysis of charts.

Results: Among patients evaluated 65 (64.7%) were girls and 30 (35.3%) were boys with an average age of 8.5 years. Children urinating in atypical position showed higher levels of perineal electrical activity than when they were in normal position ($p = 0.018$). However, there was no difference in the pattern of the curve if normal or abnormal when comparing the two groups ($p = 0.824$). When evaluated separately, the boys demonstrated no difference between positions, in relation to perineal electrical activity ($p = 0.412$) or abdominal electrical activity ($p = 0.202$).

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Conclusions: The electrical activity of the pelvic floor musculature is decreased in the oriented position when compared to atypical positions in female children. Our data suggest that special attention should be given to adopting an adequate posture during urination for girls with LUTD.

Introduction

Normal urination in children is characterized by a continuous curve that is smooth and bell shaped [1]. Furthermore, there is usually an electromyographic silence characterizing a relaxation of the pelvic floor muscles for urinary elimination to occur spontaneously [2]. According to the International Children's Continence Society (ICCS), normal urination should occur with complete absence of electrical activity in the pelvic floor muscles [1].

The position adopted during urination is one of the basic guidelines of behavior therapy in patients with lower urinary tract dysfunction [3]. The purpose of this position would be to assume a posture that allows a maximum relaxation of the pelvic floor. The girl should urinate with a suitably sized seat for children, with her legs slightly open, torso slightly leaning forward and feet flat on a stand if they do not reach the floor [4,5]. Boys should not assume a posture standing on the points of feet, when it is difficult to reach the toilet [4].

However, it is known that many children assume positions said to be inadequate at the moment of urination. It is common in our environment that girls are taught to urinate without making contact with the toilet via parental guidance when they are away from home, in order to avoid possible diseases. It is also very common that boys stand on their toes to urinate aiming to reach the toilet. To our knowledge, no studies exist that assess the impact of these atypical voiding positions.

This common manner in which children urinate may theoretically be associated with dysfunctional voiding as a result of activation of the guardian reflex at the moment of micturition. The guardian reflex is an excitatory reflex triggered by the sympathetic efferent pathways in response to the desire to urinate that contracts the urethral smooth muscle (internal urethral sphincter), preventing urination [6]. In these atypical positions, the abdominal musculature may contract, which in turn may activate contractions of the pelvic floor as a reflex.

The objective of the present study was to test the hypothesis that these atypical positions adopted by boys and girls are associated with greater activity of the perineal musculature and, as a result, with impaired urinary flow.

Materials and methods

We conducted a cross sectional analytical study, observing 94 children aged between 3 and 14 years with urinary complaints or symptoms of lower urinary tract dysfunction. Patients were not included in the study if they had neurological disorders or associated anatomical abnormalities of the urinary tract. Further, patients were excluded if they might interfere with the electromyography assessment chart.

We performed two uroflowmetry tests with each patient using the Urostym (Laborie, Canada) brand uroflowmeter. Two positions were evaluated: oriented position (trunk slightly bent forward and feet flat) and atypical position (standing on toes in boys and buttocks not in contact with the toilet seat and legs flexed in girls, Figs. 1 and 2). Two consecutive studies were conducted for each child by the same examiner, and the order of position (whether oriented or atypical) was chosen randomly. The flow was considered normal when the appearance was sinusoidal and abnormal when flat, staccato, or interrupted. We excluded samples when the final urine volume was less than 50 mL. The curves were analyzed in accordance with the International Children's Continence Society (ICCS) standardized terminology and criteria.

Electromyography was performed in conjunction with uroflowmetry in a private environment. Six disposable adhesive surface electrodes were placed on the subjects, two in the perianal region and four in the abdominal region. The parameters used to evaluate the results complied with the guidelines of ISEK (International Society of Electrophysiology and Kinesiology) [7].

The surface electrodes used were of the disk format, with a diameter of 1.5 cm and gel in its central portion. These electrodes were applied to the subjects after cleansing the skin with 70% alcohol; two of them were placed in the perianal region corresponding to three and nine o'clock in the circumference of an imaginary clock; two in the abdominal region along the internal oblique muscle, 5 cm apart from each other. Aside from these, two other electrodes were placed (one in each iliac crest) with the function of electrical conductor.

Figure 1 Atypical position in girls.

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Figure 2 Atypical position in boys.

Two physiotherapists experienced in the analysis of uroflowmetry and electromyography evaluated the results, remaining blind as to the position adopted by patients during the examination. The study evaluated the interobserver agreement (kappa index).

To build the database and analyze the results, the SPSS 17.0 program for Windows was used. We compared the values of abdominal and perineal electromyography, and the characteristics of the flow curves and other uroflowmetric parameters. We assessed the normalcy of the variables through the analysis of histograms and the Kolmogorov Smirnov test. For continuous variables, the normal data were analyzed using the Student t test; the values interpreted as abnormal were compared using the Wilcoxon test. Additionally, we used McNemar's test for analysis of information related to the type of position and presence or absence of electrical activity in muscles (abdominal and perineal). It was considered statistically significant when $p < 0.05$.

Results

Altogether 94 children were evaluated in the study. The mean age of patients was 8.5 years; 34 were boys (36.2%) and 60 were girls (63.8%). Nine patients were excluded due to suspicion of outside interference that could have affected the evaluation of the electromyography graph; 85 patients remained in the study (30 boys and 55 girls, Table 1). The symptoms of the patients included in the study were urinary urgency in 68 patients (80%), daytime incontinence in 48 patients (56.4%), and nocturnal enuresis in 40 patients (47%). Forty four patients (51.7%) had symptoms of urge incontinence, and 23 patients with nocturnal enuresis (27%) also had daytime urinary symptoms. Mean predicted bladder capacity for age in this whole group was 255 mL (age in years + 2 × 30) and the mean volume urinated by the patients was 162 mL. Only seven patients urinated less than 50% of estimated bladder capacity.

The mean maximum flow rate was 17 mL/s in boys and 22.8 mL/s in girls. There was no difference between the maximum flow of patients in the normal oriented position and patients in the atypical position (mean value of the maximum flow rate of 20.8 mL/s, $p = 0.507$), as well as in the volume urinated (mean volume urinated of 183.6 mL, $p = 0.969$), both in males ($p = 0.949$) and in females ($p = 0.955$). Although the meantime to maximum flow in the oriented position was between 14.8 s compared with 18.5 s in the atypical position, this difference was not statistically significant ($p = 0.129$).

Table 1 Distribution of the sample by sex and age.

	Age (yrs)										Total
	3	4	5	6	7	8	9	10	11	12	13	14	
Male			5		7		10		5		3		30
Female	8		9		8		16		12		2		55
Total	8		14		15		26		17		5		85

Regarding perineal electrical activity, the average values were 42.3 μV and 45.7 μV ($p = 0.018$, SD 26.8 μV) in normal and atypical positions, respectively, while the average values of abdominal electrical activity were 27.6 μV in the normal and 38.2 μV in the atypical position ($p = 0.01$, SD 25.6 μV). When analyzing the groups separately, we found that the boys did not differ between positions ($p = 0.412$ and $p = 0.202$ for perineal and abdominal activity, respectively) compared to females ($p = 0.034$ and $p =$, respectively, Fig. 3).

Using the Haycock formula for calculation of body surface area (0.024265 × weight (kg) 0.5378 × height (cm) 0.3964), we compared the values of abdominal and perineal electrical activity between the different groups according to the percentile. A statistically significant difference was observed among patients with weight above the 75th

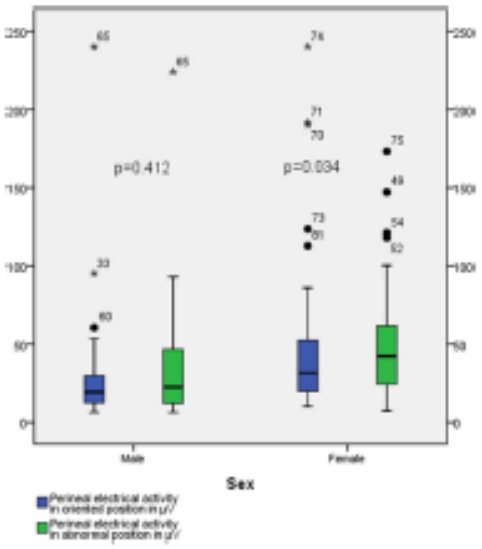

Figure 3 Perineal electrical activity (μV) according to sex.

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percentile between the values observed in the abdominal electrical activity (p = 0.021), but none of the groups (25th, 50th, and 75th percentiles) had abnormal perineal electrical activity (p = 0.508, p = 0.416, and p = 0.976, respectively). There were also no differences in electrical activity recorded in groups with lower abdominal weight (25th and 50th percentile, p = 0.050 and p = 0.057, respectively). In patients with a body surface area greater than 1.22 m^2 (in accordance with the Haycock formula), electrical activity in the abdominal muscles was found to be greater. When the overweight patients were excluded (p = 11), these results did not change.

The differences between the presence and absence of electrical activity in different positions were also analyzed. Among the 85 patients, 47 (55.2%) presented no electrical activity in either of the two positions, while 20 patients (23.5%) presented electrical activity in the atypical position, but not when they urinated in the normal position (p = 0.009). Analyzing the groups by sex, it was possible to observe that among boys there was no difference between the two positions (p = 0.219) while among the girls there was a difference in the electrical muscular activity when comparing the normal position with the atypical position (p = 0.031).

There was no important difference in the flow curve patterns in different positions (p = 0.824, Table 2). There were also no differences between the flow curve patterns when analyzing the groups of boys and girls separately (p = 1.00).

Forty seven patients (55.2%) that presented sinusoidal curves in one position maintained the same pattern when re evaluated in the second position. Interestingly, 11 children (12.9%) that presented sinusoidal curves in the atypical position began to exhibit abnormal curves when urinating in the oriented position. The reverse occurred with nine children (10.5%). Eighteen (21.1%) patients had abnormal curves in both positions. When the group of girls was analyzed, 34 of them were found to have symptoms compatible predominantly with an overactive bladder, whereas 21 had symptoms compatible with dysfunctional voiding. Of those with dysfunctional voiding, 16 maintained the same curve pattern irrespective of position, whereas in four cases the curve improved in the oriented position and in one case the curve worsened in this position. Of the girls with an overactive bladder, 27 maintained the same pattern in both positions, whereas in five cases the curve improved in the oriented position and in two patients the curve worsened in this position.

Table 2 Pattern of the curve of the flow in different positions.

		Atypical position		
		Sinusoidal curve	Abnormal curve	Total
Oriented position	Sinusoidal curve	47	9	56
	Abnormal curve	11	18	29
	Total	58	27	85 (p = 0.824)

We conducted the interobserver analysis in order to analyze the curve types that showed a kappa index of 0.80 for normal curves and 0.74 for abnormal curves. When we considered the sub classification of abnormal curves between flat, staccato, or interrupted we obtained a kappa index of 0.58. Further, in relation to the analysis of the presence or absence of electrical activity of the abdominal and perineal musculature by two different observers, we obtained higher kappa indices (0.83 and 0.82, respectively).

Discussion

Uroflowmetry is an important parameter in the study of urination and is an essential part of urodynamic studies [8]. Previous studies that evaluated flow rates in children without symptoms in the lower urinary tract found little variability between individuals as to the characteristics of urinary flow [9]. Further, it was also demonstrated that the majority of subjects studied had bell shaped flow curves [9]. In regards to the value of maximum flow in normal children, in a prospective study with 202 children, Farhane et al. [10] found that the flow increases with age and seems to be greater in females. In this latter group, the maximum flow was 15.8 mL/s between 5 and 6 years of age, and 26.2 mL/s between 13 and 15 years of age. In our sample, we found a maximum flow rate of 17 mL/s in boys and 22.8 mL/s in girls, confirming a value of higher maximum flow in females, suggesting no significant difference when compared to the maximum flow of children without symptoms of lower urinary tract.

Although data exist suggesting good acceptance of children when measured with needle electrodes, this procedure is more difficult to perform in children without neurological damage. In addition, there is the inconvenience of using needle electrodes in two consecutive tests on each individual, plus the different positions adopted during evaluation [11,12]. There are data that confirm a good correlation between the electrical activity of the muscles of the pelvic floor and the external urethral sphincter, except in cases of pelvic trauma or demyelinating disease [13]. However, attention must be given to possible interference in processing the data obtained by the software in the production of the graphs themselves, and we must seek to be strict with their inclusion in the results that are to be effectively analyzed.

Some studies have evaluated urodynamic changes and variations in accordance with changing posture, principally in adults. Al Hayek et al. [14] studied 16 articles which examined the influence of patient position during the urodynamic study in the detection of detrusor hyperactivity. It was possible to conclude that the cystometry performed in the supine position detected a significantly smaller number of patients with detrusor hyperactivity. However, to interpret the same results among pediatric patients would probably yield misleading comparisons.

As yet, there is no common protocol for non pharmacological treatment of children with voiding dysfunction that is advocated in different services. The

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term "urotherapy" has been used in conjunction with actions such as education of children and their families in relation to the functioning of bladder; fluid intake, and urination at scheduled times; directions in relation to bowel function; relaxation of pelvic floor muscles; biofeedback training and neuromodulation [15] One of the factors considered to be basic in urotherapy is the orientation relative to the position in which the child should urinate. There is a preoccupation in making sure that urination occurs in a situation where the abdominal muscles are not activated, which could stimulate the muscles of the pelvic floor and possibly the urethral sphincter [16]. Wennergren et al. [16] were the first authors to publish a study comparing the different positions of urination with the assistance of surface electromyography, although not related to the analysis of the flow curve in the group studied. Their results called attention to the importance of supporting the thighs on a surface to reduce the electrical activity of the pelvic floor muscles. In this work, which also used surface electromyography, 20 female children between 6 and 10 years of age were evaluated in three different positions. It was possible to observe that in positions with the thighs resting on a surface, relaxation of the pelvic floor muscles was observed in 94% of subjects; electromyography amplitude was significantly higher in atypical positions. Since this study, it has been suggested that children should always have both feet flat during urination, and, in the case of girls, the thighs should extend over the bowl to facilitate adequate relaxation of the pelvic floor muscles. In addition, the back should also be straight.

Hoebeke et al. [17] published important studies with respect to the role of pelvic floor training as part of the treatment of urinary dysfunction in children. Study guidelines included a diary of urination and of fluid intake, posture on the toilet, and biofeedback. In fact, our findings actually confirm the observation of a lower electrical activity in the pelvic floor during urination in girls in the oriented position. However, we could not perceive a difference between the two positions adopted in our study when separately analyzing only boys.

Body weight was also taken into account in the present study. Bai et al. [18] described the relationship between obesity and increased intra abdominal pressure in women with urinary incontinence.

Our study also highlighted the fact that there were no differences in time to maximum flow and in maximum urinary flow insofar as changes in posture were concerned, which leads us to believe that there may be some mechanism in the bladder that compensates for the increased perineal electrical activity in this second position.

Another interesting aspect of the study was the comparison between curve types and flow variations of the positions evaluated. The shape of the flow curve is considered the most important aspect in assessing uroflowmetry [19]. Contrary to our expectations, the results of our study were unable to demonstrate a significant improvement of the standard curve when the oriented position was adopted. Some patients even presented a worse curve in the oriented position. This may, however, be associated with the variability that is inherent to the procedure itself, especially in children. Vijverberg et al. [20] demonstrated such variability in a recent comparative analysis of uroflowmetric curves in pediatric patients. In this analysis of 480 uroflowmetry curves, Vijverberg et al. could understand the variation between different flows in intra observer assessment, suggesting that factors such as total volume urinated and maximum flow can influence the variation of the flow curve in pediatric patients. Although there was no improvement in the uroflowmetry curves in different positions, the design of our study does not allow us to assign the oriented position to a secondary role. The greater relaxation of the pelvic floor by itself suggests that there is some type of benefit to the oriented posture, which is certainly encouraging to us to continue undertaking this kind of practice.

No statistically significant differences were found in the present study with respect to the flow curve between the different positions that were adopted either in patients with dysfunctional voiding or in those with an overactive bladder.

The absence of a change in uroflowmetry leads us to two hypotheses. The first is that an atypical position for urinating would not yield any impact on bladder activity. In this case, the increased electrical activity of the pelvic floor would not have greater importance. The second hypothesis is that in order to overcome the greater resistance of the urethral sphincter muscles, the bladder would have to contract with more intensity, compensating for the maximum flow and not altering the curve. Therefore, the major limitation of this study is not performing urodynamic evaluation. However, urodynamic evaluation is generally not part of the routine investigation of children with LUTS. Furthermore, urination and the use of catheters are not physiological, and any change detected in one urodynamic study could not reflect the voiding reality of the child. Another limitation of the study is that only 30 male children were assessed. However, since the SWG variable measured is continuous, any more significant difference could be detected in the analysis [7]. We only evaluated children with LUTD. Because of this, our results should be analyzed with caution if applied to children without this dysfunction.

Finally, the interobserver analysis we performed coincided with other previously published data [9,20]. The kappa value between 0.4 and 0.6 demonstrated moderate agreement, between 0.61 and 0.80 substantial agreement, and greater than 0.8, almost perfect agreement. We realize that there is a correlation greater than 0.8 only when discriminating between normal and abnormal curves (kappa = 0.801), however to specify the exact type (whether flat, staccato or interrupted) between different types of abnormal curve may not be as reliable (kappa = 0.58). In relation to the assessment of the presence or absence of electrical muscular activity, it was possible to observe that the interpretation of this by different observers was reliable (kappa > 0.80).

There are some limitations associated with the study, including the small sample size, which hampered analysis of the sub groups, the fact that post void residual bladder volume was not obtained on the same day on which uroflowmetry was performed, and the lack of a control group.

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Conclusion

The electrical activity of the musculature of the pelvic floor is lower in the oriented position than the atypical positions of female children. The maximum flow and urine volume did not differ in the two positions. There was no difference between the types of flow curves when comparing the two positions. Our data suggest that special attention might be given to adopting adequate posture during urination for girls with LUTD.

Conflict of interest

None.

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None.

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ANEXO M – Artigo publicado durante o doutorado "Urodynamic outcome of parasacral transcutaneous electrical neural stimulation for overactive bladder in children

ORIGINAL ARTICLE

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Urodynamic outcome of parasacral transcutaneous electrical neural stimulation for overactive bladder in children

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ABSTRACT

Objective: To evaluate the urodynamic changes immediately after the first session (acute effect) and after the last session of parasacral TENS in children with idiopathic OAB.
Materials and methods: We performed urodynamic evaluation immediately before and after the first session of parasacral TENS and immediately after the last session (7 weeks later). Only children with idiopathic isolated OAB were included. Patients with dysfunctional voiding were not included.
Results: 18 children (4 boys and 14 girls, mean age of 8.7) were included in the first analysis (urodynamic study before and immediately after the first session) and 12 agreed to undergo the third urodynamic study. Urodynamic before and immediately after the first session: There was no change in the urodynamic parameters, namely low MCC, low bladder compliance, presence of IDC, the average number of IDC, or in the maximum detrusor pressure after the first exam. Urodynamic after the last session: The bladder capacity improved in most patients with low capacity (89% vs. 8%). Detrusor overactivity was observed in 11 (92%) before treatment and 9 (75%) after. There was not a significant reduction in the average number of inhibited contractions after TENS (p=0.560) or in the detrusor pressure during the inhibited contraction (p=0.205).
Conclusion: There was no change in the urodynamic parameters immediately after the first session of stimulation. After the last session, the only urodynamic finding that showed improvement was bladder capacity.

ARTICLE INFO

Key words:
Urodynamics; Transcutaneous Electric Nerve Stimulation; Child; Bladder

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INTRODUCTION

TENS has been used in the treatment of pediatric OAB bladder (1-3). Two randomized clinical trials have shown that parasacral TENS is an effective treatment of OAB in children (4, 5). Some authors have reported improvement in the urodynamic parameters during or after posterior tibial electrical neural stimulation (PTNS) in adults (4-6). However, despite that the effectiveness of TENS in children with idiopathic OAB has been demonstrated subjectively, to our knowledge, the urodynamic outcome after treatment has not been reported. The aim of this study is to evaluate the urodynamic changes immediately after the first session (acute effect) and after the last session of parasacral TENS in children with idiopathic OAB.

MATERIALS AND METHODS

We performed urodynamic evaluation immediately before and after the first session of parasacral TENS and immediately after the

last session (7 weeks later). The inclusion criteria was: 1 children with isolated OAB, defined as the presence of urgency, with or without daytime incontinence, associated with a bell shaped/tower uroflow curve and post void residual of less than 10% of the expected bladder capacity and less than 20 mL; and 2 patients without any neurological problem or any anatomical disease of the lower urinary tract. The exclusion criteria included the diagnosis of dysfunctional voiding or any anatomical or neurological problem of the lower urinary tract during the treatment, or the impossibility to perform the urodynamic study. This study was approved by our institutional Ethical Committee and all parents signed an informed consent. According to our IRB we were allowed to use urodynamic for any children with symptoms of OAB that underwent TENS.

Patients underwent 20 sessions of parasacral TENS with a duration of 20 minutes each. The frequency of current used was 10 HZ, the pulse width 700µ seconds and the current intensity was at the sensitivity threshold. Pads were placed on each side of *S3*. Three urodynamic studies (Dynamed®, São Paulo, Brazil) were performed: immediately before and after the first session and immediately after the last TENS session. For this procedure, two catheters 4 and 6 Fr were introduced in the bladder and one in the rectum to record the abdominal pressure. The rate of bladder feeling was 10% of the expected bladder capacity (30 x age+30) per minute (7). The same professional (MTC) performed all exams. The bladder and abdominal catheters were in place during the first parasacral TENS.

The endpoints used to evaluate the urodynamic effect of the parasacral TENS were: low MCC (less than 60% of the expected bladder capacity), compliance (less than 10), the presence of detrusor overactivity, the number of IDC, and the highest (maximum) pressure during IDC. For symptom evaluation we used visual analogic scale, where 0 was no improvement and 10 complete resolution of the symptoms.

We used *SPSS* 15.0 to perform the statistical analysis. Continuous variables were tested by the Wilcoxon test. A p value of less than 0.05 was considered significant.

RESULTS

Eighteen patients were included in the first analysis (urodynamic study before and immediately after the first session) and 12 agreed to undergo the third urodynamic study and could be included in the third analysis. Of these, all patients had urgency before treatment, 9 had daytime incontinence and 4 had frequency. Ten patients had a history of UTI before the beginning of the treatment.

Urodynamic before and immediately after the first session (Table-1): 18 children (4 boys and 14 girls, mean age of 8.7, ±2.9) were evaluated. The urodynamic findings of the two studies were as follows: No patient had a low bladder compliance before treatment. All patients with low MCC maintained this finding after TENS. Of 16 patients with detrusor overactivity, one presented a stable bladder after the session. There was no change in the average number of IDC (p=0.64), nor in the maximum detrusor pressure (p=0.2) during the inhibited contraction before and after TENS.

Urodynamic after the last session (Table-2)-Twelve patients underwent the third urodynamic study and participated on this analysis. The bladder capacity improved in 6 patients. Detrusor overactivity was demonstrated in 11 (92%) before treatment and in 8 (73%) after. There was no significant reduction neither in the average number of inhibited contractions after TENS (p=0.560) nor in the detrusor pressure during the involuntary bladder contraction (p=0.205). One patient who had a stable bladder before treatment maintained this state after the procedure. Among 10 patients who had information available about the symptoms, 9 had complete resolution of the LUTS. Seven patients who had the symptoms improved after TENS still had detrusor overactivity.

DISCUSSION

We demonstrated in this study of children with isolated OAB that, after the end of treatment, parasacral TENS improved the symptoms, but the only improved urodynamic finding was the MCC. Kabay et al. found improvement in the urodynamic findings after 12 weeks of PTNS in adults patients with neurogenic detrusor overactivity se-

Table 1 - Urodynamic outcome after the first parasacral TENS (N=18).

	Before	After
Low CMC	12	12
Low compliance	4	3
Presence of IDC	16	15
Number of IDC (SD)€	6.5 (6.4)	6.3 (5.7)*
Higher IDC (SD) £	49.6 (35.1)	42.9 (38.7) *

€ = Average; £ = Average of the highest pressure during IDC; * = p values were non-significant

Table 2 - Urodynamic outcome before the treatment after the last parasacral TENS (N=12).

	Before	After
Low CMC	7 (58%)	1 (8%)
Presence of IDC	11 (92%)	8 (73%)
Number of IDC (SD) €	6.0 (6.9)	5.33 (5.8) *
Higher IDC (SD) £	49.7 (35.1)	42.9 (38.7) *

€ = Average; £ = Average of the highest pressure during IDC; * = p values were non-significant

condary to multiple sclerosis (8). The average bladder volume during the first involuntary detrusor contraction on the first cystometry was 124.2 mL, while it was 217.5 mL after PTNS. MCC on standard cystometry was 199.7 mL, while it was 266.8 mL after stimulation. This last finding is in accordance with our results.

In our study, despite improving the symptoms, 73% of the patients still presented IDC and there was no change in the number of the IDC as well as in the pressure of the IDC before and after parasacral TENS. This confirms the findings of one previous study that demonstrated that the symptomatology can improve and the patients may persist with detrusor overactivity (9). We hypothesize that even after being treated, patients develop neuroplasticity but do not develop the capacity to inhibit the micturition reflex during the urodynamic study. However, this is not the case in the physiological bladder filling. Another interpretation is that the ENS modulates the symptom interpretation by the brain and, hence, there is no brain reaction to an IDC. Another hypothesis is that the urodynamic study is not reliable as a diagnosis method of OAB in children. The same explanations can be used to justify the absence of an acute urodynamic effect of TENS.

Amarenco et al. were the first to report data concerning acute stimulation and immediate cystometry modifications after PTNS (10). A total of 44 consecutive patients with urge incontinence, and frequency and urgency secondary to overactive bladder (37 with neurogenic and 7 with idiopathic OAB) were studied. Cystometry was done before PTNS and then it was repeated during the stimulation. PTNS was associated to significant improvement in IDC volume and to significant improvement in MCC. Kabay et al. evaluated the acute effects of PTNS on the urodynamic findings in adults with Parkinson disease and multiple sclerosis with neurogenic detrusor overactivity (8, 11). There was improvement in the average bladder capacity during the first involuntary contraction and in the MCC average before and during PTNS.

All three studies evaluated the urodynamic changes during the first session of ENS and differed from ours in that we evaluated it immediately after the first session. They found improvement

in the urodynamic parameters and we did not. This difference could relate to the different timing of the urodynamic study. The urodynamic effect could be present during the session due to a pudendal nerve or interneurons stimulation and be suppressed after the end of the session. Furthermore, the difference could also be the result of different types of stimulation and the differences in the samples studied. However, even though some effect on the bladder function may exist during stimulation, our study shows that this effect does not last after the first session.

Regarding the limitations of this study, we did not evaluate the lower urinary tract function during the stimulation. Therefore, we cannot know if there is an effect on the bladder filling phase when the patient is being neuro-stimulated. Also, the number of patients who underwent the third urodynamic is small. However, urodynamic is an uncomfortable method for toilet-trained children and it is not part of the mandatory work-up for children with OAB. Also, because of the retrospective nature of the symptoms evaluation, we did not have available the visual analogic scale evaluation of some patients. Another limitation is that we did not compare the averages of bladder capacity, compliance and pressure during bladder contraction. Instead, we used these data as categorical variables. Despite having low power for statistical evaluation, using urodynamic findings in categorical variables leads us to better clinical interpretation, since we know how many patients normalized their urodynamic parameters.

We reported the urodynamic outcome of patients with isolated OAB treated by a specific type of ENS. Therefore, these results may not be extrapolated to children with OAB associated with dysfunctional voiding or for those who underwent other kinds of ENS.

CONCLUSIONS

There is no change in the urodynamic parameters immediately after the first session of stimulation, demonstrating that there is no acute urodynamic effect of the parasacral TENS. Despite the symptoms of most patients have improved, after the last session, the only urodynamic finding that showed improvement was bladder capacity.

ABBREVIATIONS

OAB = Overactive bladder
ENS = Electric neural stimulation
IDC = Involuntary detrusor contraction
LUTS = Lower urinary tract symptoms
MCC = Maximum cystometric capacity
PTNS = Posterior tibial electrical neural stimulation
TENS = Transcutaneous electrical stimulation

CONFLICT OF INTEREST

None declared.

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ANEXO N – Artigo publicado durante o doutorado "A two-day bladder diary for children: Is it enough?

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A two-day bladder diary for children: Is it enough?

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Lower urinary tract dysfunction; Incontinence; Children; Lower urinary tract symptoms; Bladder diary

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Summary

Introduction
A bladder diary (BD) is a simple and non-invasive method of evaluating people with lower urinary tract symptoms (LUTS). Recently, the ICCS recommended a 48 h daytime frequency and volume chart (which does not need to be recorded on 2 consecutive days) to evaluate lower urinary tract (LUT) dysfunction. However, some studies on adults have demonstrated that a minimum of 3 days is required. It is believed that, to date, there are no studies in the literature that compare a 2 day BD with a 3 day BD. The advantages of a BD over a shorter period of time are the simplicity and possible better parent compliance.

Objective
The aim of this study was to evaluate if a 2 day BD is statistically and clinically comparable to a 3 day BD.

Study design
A voiding diary was filled in over a 3 day period for 92 children (ages ranged from to 3–16 years, mean 7.9 ± 3.07) attending the present institution. By using the voiding diary, the following parameters were calculated: urination frequency, maximum and average volumes of urine (MVV and AVV) and fluid intake. The diary considered the 2 days as the first and second days of the 3 day diary.

Results
Out of the 92 children, eight (8.7%) did not properly complete the diary. The sample predominantly comprised females (n = 55, 59.8%). No differences were seen between 2 day and 3 day bladder diaries regarding fluid intake, maximum and average voided volume. The sensitivity, specificity, positive and negative predictive values of the 2 day bladder diary for detecting frequency were 83.4%, 91.7%, 80% and 93.2%, and for low bladder capacity they were 97.2%, 90.9%, 99% and 83%, respectively (Table).

Discussion
In a 2006 document, the ICCS recommended that a bladder diary be kept for 3 days, but in new documentation (2014) there is a reference stating that 2 days are enough. Bladder capacity is an important parameter in evaluating LUTS. Using a 2 day BD, the data showed that only a small percentage of reduced bladder capacity diagnosis would be lost.

Conclusion
When using the 2 day diary, a 16% false negative rate for frequency should be expected. A 2 day bladder diary is sufficient to evaluate bladder capacity and fluid intake.

Table Comparison of 2 day and 3 day voiding diaries for the number of voids and low bladder capacity.

2 day voiding diary	3 day voiding diary					
	Higher number of voids (>8 voids/day)			Low bladder capacity (<65% of the expected bladder capacity)		
	Yes	No	Total	Yes	No	Total
Yes	20 (83.4%)	5 (8.3%)	25	70 (97.2%)	1 (9.1%)	71
No	4 (16.6%)	55 (91.7%)	59	2 (2.8%)	10 (90.9%)	12
Total	24	60	84	72	11	83

*Sample of 92 children. Missing value for number of voids, eight (8.7%), for bladder capacity, nine (9.7%).

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Introduction

A bladder diary (BD) is simple and non invasive method of evaluating people with lower urinary tract symptoms (LUTS). It logs the time and volume of fluid intake (in ml) and the time and volume of urine output (in ml) [1]. Bladder diaries have evolved over time and address many issues that are important for the clinical evaluation of people with LUTS. According to the International Continence Society standardization: micturition charts register only urination times during the day; frequency volume (FV) charts log the time and volume of each urination; and bladder diaries register the time and volume of fluid intake, the time and volume of each urination, the presence of incontinence, and the time of LUTS [2]. Although the clinical history is of great importance when evaluating and managing children with LUTS, questionnaires are very subjective and are associated with memory bias; therefore, the symptoms may be under or overestimated [3,4]. Furthermore, there is a weak correlation between the diary and questionnaire data, which means that the symptoms should not be relied on when evaluating children with LUTS [4–7].

Despite diaries being routinely recommended, it is surprising that there are few publications regarding this subject for adults and even fewer for children. Recently, the International Children's Continence Society recommended a 48 h daytime frequency and volume chart (which does not need to be recorded on 2 consecutive days) to evaluate lower urinary tract (LUT) dysfunction [8]. Studies on adults that have evaluated a BD period ranging from 1 to 14 days [3,6,9–11] have demonstrated that a minimum of 3 days is required [12–16]. It is believed that, to date, there are no studies in the literature that compare a 2 day BD with a 3 day BD. The advantages of a BD over a shorter period of time are the simplicity and possible better parent compliance. The aim of the present study was to evaluate if a 2 day BD is statistically and clinically comparable to a 3 day BD.

Material and methods

Over a 3 day period, a voiding diary was completed for 92 children attending the present institution for lower urinary tract symptoms (LUTS). The population comprised children who were referred to the incontinence clinic and presented with daytime urinary symptoms and no neurological or anatomical alterations of the lower urinary tract. Exclusion criteria were diary illegibility and non compliance over the 3 day period. The children's ages ranged from to 3–16 years (mean 7.9 ± 3.07). By using the voiding diary, the following parameters were calculated: urination frequency, maximum and average volumes of urine (MVV and AVV, respectively) and fluid intake (in ml).

The diary was completed over 3 consecutive days, usually at weekends because all the children were of school age. At the first visit, all of the parents/guardians were instructed on how to complete the diary. Records had to be kept over 24 h for 3 sequential days, noting times and volume of urine for all urinations, and recording fluid intake (time, amount and type of fluid consumed). The 2 day diary resulted from the first and second days of the 3 day diary. An increased urination frequency was considered to be an average of more than or equal to eight urinations. For the calculation of the expected bladder capacity (EBC) the formula Age + 1 x 30 was used. A reduced bladder capacity was regarded to be any value <65% of the expected bladder capacity (not considering the first morning urine) [3].

Statistical analyses

All the statistical analyses were performed using a commercially available statistics program (SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc.). Probability values of <0.05 were considered statistically significant, and presented as mean ± SD. To compare the averages between 2 day and 3 day BD the Wilcoxon test was used. Considering the 3 day diary as standard, the sensitivity, specificity, negative and positive predictive values of a 2 day diary were calculated for detecting low bladder capacity and increased voiding frequency.

Results

Out of 92 children, eight (8.7%) did not properly complete the diary. These children were excluded from the analysis, which compares the 2 day and 3 day BD. The sample predominantly comprised females (n = 55, 59.8%). As shown in Table 1, there were no differences between 2 day and 3 day BD regarding fluid intake, MVV and AVV. However, there were a higher average number of urinations per day in the 2 day diary when compared to the 3 day diary (Table 1).

The comparison of clinical parameters that are diagnosed by the diary, such as frequency and low bladder capacity, are demonstrated in Table 2. Regarding the number of urinations, the 2 day BD was unable to detect 16.6% of the frequency and 2.3% of the low bladder capacity; this gave a false positive diagnosis of 8.3% and 9.1%, respectively. The sensitivity, specificity, positive and negative predictive values of the 2 day BD for detecting frequency were 83.4%, 91.7%, 80% and 93.2%, and for low bladder capacity they were 97.2%, 90.9%, 95% and 88%, respectively.

Table 1 Comparison of data between 2 day and 3 day bladder diary.

	2 days	3 days	*P* value (first + second vs. 3 days)
	Mean ± SD	Mean ± SD	
Number of voids/day	7.06 ± 3.83	6.87 ± 3.85	0.007
AVV (in ml)[a]	103.7 ± 62.3	108.7 ± 67.3	0.999
MVV (in ml)[b]	192.7 ± 110.8	196.3 ± 100.7	0.305
Fluid intake (in ml)	1233.4 ± 911.7	1221.6 ± 900.2	0.234

[a] AVV = average voiding volume in ml.
[b] MVV = maximum voided volume in ml (or maximum bladder capacity).

Table 2 Rates of frequency and low bladder capacity in 2 day and 3 day bladder diaries.

	3 day diary [%]	2 day diary [%]
Higher number of voids (>8 voids/day)	24 (28.6%)	25 (29.7%)
Low bladder capacity (<65% of the expected bladder capacity)	72 (85.7%)	71 (84.6%)

Discussion

Objective measures of lower urinary tract symptoms have been a clinical challenge. Bladder diaries or FV charts are routinely used in practice for the primary evaluation of these patients. However, there are few studies on the use of a BD for children. The first result from the present study that is important was that parents/guardians of around 92% of the children were able to complete the BD appropriately. The vast majority of parents, if not all, were made up of low income families with low and medium levels of education. This goes against the myth that using a BD is difficult, even if used over 3 days.

Regarding the ideal minimal time for completing the bladder diary for adults: in 1998, Wyman et al. [3] compared 1 week and 2 week FV charts for a group of women suffering from incontinence. They concluded that the 1 week FV chart was sufficient to document urinary frequency and incontinence episodes and, since then, the 7 day FV has been used as the gold standard. Palmas Hansen and Klaskorv [12] demonstrated that a 3 day FV chart is valid and useful for investigating patients with voiding symptoms. For women aged 18–77 years with various lower urinary tract symptoms, Shick et al. [16] analyzed and compared 14 variables of the diary for various periods of FV charts (1–6 days) with the then gold standard of 7 days. They found that the 7 day diary was unnecessarily long and that the same valid information could be obtained with a 4 day diary. Tincello et al. [13] reported a completion rate of 90.7% compared to 50% with diaries of 3 and 7 days, respectively. Other authors have supported that the 3 day diary is reliable [14,17,18]. In a 2006 document, the ICCS recommended a 3 day BD, but in new documentation there is a reference that 2 days are enough; however, this statement does not appear to be based on any data in the literature.

Bladder capacity is an important parameter for evaluating the lower urinary tract. In both adult and pediatric populations, some studies have shown the importance of a urinary diary for evaluating bladder capacity along with other objective methods such as uroflowmetry and cystometry [19,20]. The bladder diary has advantages over other methods because it more reliably reflects the daily urine output. Kim et al. [21] used 48 h FV charts to assess bladder capacity in previously healthy Korean children and concluded that this instrument is of great importance when evaluating this variable, which is essential for evaluating children with urinary symptoms. The present data showed no statistically significant differences in the measured maximum voided volume between the 2 day and 3 day BD; however, by using a 2 day diary a small percentage of reduced bladder capacity diagnosis (2.3% false negative and 9.7% false positive) was lost. In another study, Ulucak et al. [20] evaluated 34 children (predominantly females) and the urinary diary showed no difference when compared to cystometry, for example, and was the least invasive method and had the advantage of been carried out under the most physiological conditions. Following this line, given the results of the present study, it is believed that the 2 day diary can be used in a reliable manner without any major losses to the evaluation and follow up of patients with lower urinary tract symptoms. The present data show that the 3 day diary compared to the 2 day diary regarding urinary frequency (the presence of increased frequency of urination) was in agreement for 80.4% of cases. However, the average number of urinations was greater than in the 2 day BD. Despite the statistical differences, the clinical significance of this finding was evaluated. For the diagnosis of frequency, there was a relatively high percentage of false negatives (16.6%) in the 2 day diary compared to the 3 day diary. Kwak et al. [22] evaluated children with nocturnal enuresis (mono and not monosymptomatic) and compared the 3 day diary with a questionnaire on the assessment of the number of urinations per day. Although other variables were disparate, they noted no difference regarding the number of urinations. This shows that the medical history can help in this regard, as it may reduce the significance of the difference between the diaries that were found in the present study. However, it is believed that the number of urinations will not affect the choice of treatment for children with symptoms of an overactive bladder.

A limitation of the present study was that the same 3 day diary was used to assess whether the 2 day diary gave similar results. This certainly makes the findings of the two diaries similar. Another way to conduct such a study would be keeping two diaries: one 2 day and one 3 day at different times. However, there would be great difficulty in performing this study in children, as the analyzed parameters would vary according to the fluid intake, which tends to be higher at weekends. Furthermore, it could be difficult to get parental motivation to complete a second diary in a short time.

Conclusion

The 2 day diary allows comparison of the results over 3 days; however, a larger average number of urinations was found in the 2 day diary. When using the 2 day diary, a 16% rate of false negative for frequency should be expected. A 2 day bladder diary is sufficient to evaluate bladder capacity and fluid intake.

Conflict of interest statement

There is no disclosure.

Funding source

Nil.

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ANEXO O – Artigo publicado sobre o tema "Constipation in children with isolated overactive bladders

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ELSEVIER

Journal of Pediatric urology

Constipation in children with isolated overactive bladders

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KEYWORDS
Prevalence;
Constipation;
Child;
Isolated overactive bladder

Abstract *Objective:* To evaluate the prevalence of constipation in children with isolated overactive bladder (IOAB) and no micturition complaints.
Materials and methods: A questionnaire was used to evaluate constipation in 51 children with IOAB, as well as in a control group of 74 children between the ages of 4 and 14 years. The Rome III criteria for children were used to assess constipation. IOAB was defined as the presence of symptoms such as urgency with or without daytime incontinence or frequency, a bell shaped uroflow, and no post residual urine.
Results: Mean patient ages were 7.94 (±2.8) and 8.28 (±3.4) years in the OAB and control group, respectively (p = 0.54). Twenty eight (54.9%) of the OAB group were girls, and 34 (45.9%) were girls in the control group (p = 0.32). More of the children with IOAB had constipation than those without urinary symptoms (54.9% vs. 29.7%, p = 0.005; or 2.87, 95% CI: 1.3–6.0). The results were statistically significant regarding the following Rome III criteria: "history of stool retention", "presence of painful or hard bowel movements", "the presence of a large fecal mass in the rectum" and "large diameter stools which may obstruct the toilet". Within the group with OAB, constipation was more common among males (p = 0.05). There was no association between the type of OAB symptoms and constipation. The average dysfunctional voiding symptom score was 9.76 (±4.1). Eleven children (21.6%) presented alterations on ultrasound. Girls with OAB presented more frequently with UTI than boys (18 vs. 10, p = 0.13).
Conclusion: This was the first comparative study with respect to constipation in children with IOAB and without urinary symptoms. Children with IOAB have a greater risk of having constipation compared to those with no urinary symptoms.

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Introduction

Intestinal constipation is not considered a disorder as such, but a complex symptom which is the most common intestinal problem among children [1]. Initially, it is a matter of little concern for parents. This delay in treatment aggravates the symptoms and makes treatment difficult. Currently, constipation is considered a public health problem because of its impact on health networks, mainly because of its increased prevalence in the general population. Constipation accounts for 25% of visits to the pediatric gastroenterologist [2].

Constipation can be classified as organic when it arises from a known cause such as an anatomical, neurological, or metabolic abnormality. Functional constipation corresponds to 95% of infant constipation [3]. It is believed that this constipation occurs because of badly adapted behavior, as it can be improved through behavioral training.

Many children tend to develop functional constipation by inhibiting their desire and refusing to defecate. It can be a result of trauma or distress, a way to receive attention from parents or fight with siblings, or because of the memory or anticipation of pain while defecating, anxiety or fear of using the toilet, or a low intake of fiber and incoordination of the puborectalis muscle [1,3,4].

Constipation has been linked to dysfunctional voiding and subsequently termed dysfunctional elimination syndrome (DES), defining children who abnormally evacuate urine and feces [5]. Although the reason for this association lacks better clarification, it is reasonable that both disorders be treated together, under the penalty of the treatment not being successful. OAB is an abnormality commonly found in girls and boys. Children with OAB may experience more constipation because of a common neurophysiological immaturity in bladder and bowel function, by successive contractions of the pelvic floor muscles, or by the children's personal habits [6]. To our knowledge, no study has yet addressed the frequency of constipation in children with OAB without dysfunctional voiding (OAB). The objective of this study was to test the hypothesis that children with OAB have a higher rate of constipation than the general population.

Methodology

Patients with and without (control group) OAB, and between the age of 4 and 14 years, were interviewed. For the patient group, data were collected prior to treatment from the reference center for Children's Urinary Disorders, and for the control group data were collected in the waiting room of the general pediatric outpatient clinic.

Patients were defined as having OAB if there was urgency with or without daytime incontinence or frequency [7], uroflowmetry with a bell shaped curve, electromyography demonstrating perineal relaxation during urination, the presence of less than 10% post void residual urine of the capacity expected for age (using the formula (age + 2) × 30) and a negative urine culture [8]. Children with neurological or anatomical abnormalities were excluded. In the OAB group the presence of symptoms was investigated by the following questions:

1) When your child needs to urinate, does he/she have to rush to the bathroom in order to prevent wetting his/her clothing?
2) Does your child urinate on clothing (pants or shorts) during the day?
3) Does your child void at a higher than normal frequency?

The control group included children with no urinary complaints. They were questioned using the dysfunctional voiding symptom score (DVSS) [9,10] to exclude children with symptoms such as urinary urgency, incontinence and holding maneuvers. Only patients with zero points for these questions were included in the study. The DVSS questions related to constipation were not performed.

The Rome III [11] criteria for children were used to diagnose constipation; constipation was considered present when the child presented at least two of the six symptoms for longer than two months. The questions and the way in which they were presented to the child can be seen in Table 1.

The urinary symptoms evaluated in the patients with OAB were urge incontinence, frequency, enuresis, nocturia and holding maneuvers. History of urinary tract infection (UTI) was also noted.

The questionnaire was administered by two previously trained interviewers (one for each group).

The statistical analysis was done using mean and standard deviation, the t test for numeric variables, the chi squared test for categorical variables, and relative risk with 80% power and a significance level of 95%. The analysis of the data was done using SPSS version 14.0 for Windows.

This study was approved by the institution's ethics committee under protocol 107/2008. All legal guardians signed consent forms.

Results

The study included 51 children in the group with OAB and 74 children in the control group. The mean age was 7.94

Table 1 Rome III criteria for children and the adapted questions.

1. Two or fewer defecations in the toilet per week (the child poops two or fewer times per week)	Yes [ ] No [ ]
2. At least one episode of fecal incontinence per week (the child poops in his/her underwear at least once a week)	Yes [ ] No [ ]
1. History of retentive posturing or voluntary retention (the child holds his/her legs or squeezes his/her butt to avoid going to the bathroom to poop)	Yes [ ] No [ ]
2. History of painful or hard bowel movements (the child experiences pain or needs to use force to poop)	Yes [ ] No [ ]
3. Presence of a large fecal mass in the rectum (the child feels or complains that he/she feels stool stored in the butt)	Yes [ ] No [ ]
4. Large diameter stools which obstruct the toilet (the child's poop is large and clogs the toilet)	Yes [ ] No [ ]

(±2.3) and 8.23 (±3.4) years in the IOAB and control group, respectively (p — 0.54). There were more girls in group IOAB, but this difference was not statistically significant (28, 54.9% vs. 24, 45.9%; p — 0.22).

Children with IOAB had more constipation than those children with no urinary symptoms (54.9% vs. 29.7%, p — 0.005) when evaluated by Rome III with an odds ratio of 2.87 (CI 95%: 1.3 6.0).

Evaluating each item independently between the groups using the Rome III criteria (Table 2), statistical significance was found with regard to the following items: "history of stool retention", "history of painful or hard bowel movements", "presence of a large fecal mass in the rectum" and "history of large diameter stools which may obstruct the toilet".

In evaluating the group with IOAB, constipation was more common among males (p — 0.05), but there was no significance when compared with urinary symptoms such as urge incontinence, frequency, nocturia, holding maneuvers, nocturnal enuresis and history of UTI (Table 3). The average DVSS was 9.76 (±4.1), and 11 (21.6%) children presented alterations on ultrasound such as hydronephrosis and bladder wall thickness. Girls with OAB presented more frequently with UTI than boys (13 vs. 10, p — 0.13).

Table 3 Comparison of gender and urinary symptoms with constipation in the IOAB group constipation (n%).

Variable (n)	Constipation (n%)		
	Yes	No	p
Males (23)	16 (69.6)	7 (30.4)	0.05
Urge incontinence (41)	21 (51.2)	20 (48.8)	0.28
UTI (28)	13 (46.4)	15 (53.6)	0.18
Frequency (31)	16 (51.6)	15 (48.4)	0.55
Nocturia (15)	10 (66.7)	5 (33.3)	0.26
Holding maneuvers (39)	21 (53.8)	19 (46.2)	0.78
Enuresis (33)	19 (57.6)	14 (42.4)	0.60

Discussion

Despite the publication of various articles regarding constipation and lower urinary tract dysfunction (LUTD) [12 16], it is still unclear which type of LUTD is more associated with the retention of feces. It seems logical that children who do not have good coordination of their pelvic floor muscles during urination lack the same coordination for the evacuation of feces. However, OAB is a very common form of LUTD and frequently found in its isolated form with good perineal relaxation during urination.

Children with IOAB were found to have constipation up to three times more frequently than those without such symptoms. Koff et al. called to attention the association between constipation and dysfunctional voiding, which they termed dysfunctional elimination syndrome. It was found to be correlated with UTI and vesicoureteral persistence [5]. The present study demonstrates that not only children with dysfunctional voiding but also those with IOAB have a higher risk of presenting constipation. We think the term dysfunction elimination syndrome is inaccurate, because it does not cover the whole spectrum of the association between constipation and LUTD. Also, we do not know if those constipated children will have a worse outcome than those without it. Future studies should characterize the type of LUTD that each patient has and its association with constipation, instead of describing the patients as having dysfunctional elimination syndrome.

There are possible justifications for the association of constipation and OAB. Both bladder function and intestinal function are controlled by the supraspinal regions, such as the anterior cingulate gyrus, prefrontal cortex, and the insular region of the cerebral cortex [17 20]. Consequently, the dysfunction of both the bladder and intestines may be a result of the same pathophysiology, such as supraspinal neurophysiological immaturity [21]. However, no studies were found which used functional magnetic resonance imaging to assess regions of the brain in constipated patients. On the other hand, there are studies which evaluate the sensation of discomfort and pain using a rectal balloon in patients with irritable bowel syndrome. Through the use of functional magnetic resonance imaging, activation was shown in the anterior cingulate gyrus region [22 24]. The idea that OAB and constipation arise from one single pathophysiology is reinforced by the successful use of electrotherapy for the treatment of both constipation and OAB [20,24 26].

It is also possible that constipation causes OAB in some cases. Studies have shown that the filled rectum may worsen bladder function [17,27]. In a study in which a balloon was inflated in the rectum to simulate rectal fullness in two groups (children with LUTD associated with constipation and children with LUTD alone), Koff et al. showed that acute rectal distension affects bladder function in children with LUTD independent of the presence of chronic constipation through an excitatory response to rectal distention [27].

In contrast, OAB may also cause constipation. It is known that children with OAB contract the pelvic floor when they

Table 2 Distribution of Rome III criteria in each group.

Variable	IOAB n — 51 n (%)	Control n — 74 n (%)	p	OR (IC 95%)
<2 evacuations/week	13 (25.5)	16 (21.6)	0.61	1.24 (0.53 2.95)
>1 fecal incontinence/week	8 (15.7)	5 (6.8)	0.10	2.56 (0.78 8.35)
Stool retention	17 (33.3)	13 (17.6)	0.04	2.34 (1.01 5.40)
Pain or force	25 (49)	19 (25.7)	0.007	2.78 (1.30 5.93)
Fecal mass	19 (37.3)	11 (14.9)	0.004	3.40 (1.44 8.00)
Large stools	16 (31.4)	4 (5.4)	0.001	8.00 (2.48 25.74)

perform holding maneuvers to prevent urinary incontinence. The contraction of the anal sphincter muscles causes negative feedback, inhibiting rectal contraction and thus stimulating fecal retention [23]. The presence of this maneuver several times a day might cause constipation in many children. However, this theory is not supported by our findings in this study, because no association between holding maneuvers and constipation was found. Another factor which may be responsible for the association between OAB and constipation is a low fluid intake. Many children with OAB avoid drinking fluids during the day so as not to experience urinary incontinence, especially during school. This low fluid intake may cause fecal retention or worsen light constipation. It is probable that the association between OAB and constipation is multifactorial.

Recurrent UTI is normally cited as being associated with constipation, and its symptoms can be resolved with treatment for stool related complaints [21,22]. We expected children with constipation to have more UTI and less urinary tract symptoms such as daytime incontinence and frequency.

Surprisingly, it was shown that types of LUTS as well as nocturnal enuresis and the presence of UTI are not associated with the presence of constipation. It is possible that constipation has a greater influence on bladder dynamics in more serious cases with poor vesicoperineal coordination, low voiding frequency, and high post void residual.

In agreement with a large part of the literature [2,13,29,30], the majority of constipated children in this study were male, in the OAB group as well the control group. However, there is still no concrete explanation for the association between the masculine gender and constipation. May be, some genetic influence or some differences between gender behavior and diet could impact this dynamic. Since there was no correlation between constipation and the rate of UTI, and since girls have more frequent UTI than boys (trend to significance), despite being less constipated, we indeed think that constipation alone has no impact on UTI incidence in children with overactive bladder. However, in the general population things are different. Many authors have been reporting the association of constipation and UTI in children [23,31,34]. Also, the rate of UTI decreases after treatment for constipation [2]. We hypothesize that the association between constipation and UTI that we find in the literature in the general pediatric population is due to the fact that constipated patients also have LUTD. Therefore, the presence of LUTD and not the constipation itself would be the most important variable for UTI in this population.

Conclusion

The results demonstrate that, according to the Rome III criteria, children with IOAB have constipation more frequently than children without urinary symptoms. Constipation was more common among boys with IOAB. Constipation was not associated with any symptoms related to the lower urinary tract, nor to the presence of UTI in the group with IOAB.

Conflict of interest

None.

Funding

None.

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ANEXO P – Artigo publicado sobre o tema "Evaluation of constipation after parassacral transcutaneous electrical nerve stimulation in children with lower urinary tract dysfunction - A pilot study

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Evaluation of constipation after parasacral transcutaneous electrical nerve stimulation in children with lower urinary tract dysfunction – A pilot study

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KEYWORDS
Constipation;
Child;
Lower urinary tract dysfunction;
Transcutaneous electrical nerve stimulation

Abstract *Objective:* To evaluate the efficacy of parasacral transcutaneous electrical nerve stimulation (TENS) for the treatment of constipation in children with lower urinary tract dysfunction (LUTD).
Materials and methods: We treated 9 boys and 5 girls with a mean age of 8.07 ± 2.72 years. 10 (71.4%) had overactive bladder and 4 (28.6%) had voiding dysfunction. A total of 20 parasacral TENS sessions, 20 min each (10 Hz), were performed 3 times per week. The criteria used to assess constipation were the Rome III criteria for children, the Bristol Stool Chart, and a visual analog scale (pain from 0 to 10). The children were reassessed immediately after treatment. No specific treatment of constipation was performed.
Results: After treatment, 85.7% ($p < 0.001$) of the children's constipation symptoms had improved following the Rome III criteria. Parasacral TENS significantly impacted the following symptoms: "the presence of at least one episode of fecal incontinence per week", "history of stool retention", and "the presence of a large fecal mass in the rectum." There was no significant change in the Bristol Stool Chart evaluation ($p < 0.25$), but there was a significant improving trend in level of pain before and after treatment ($p < 0.063$). All urinary symptoms evaluated showed improvement after TENS treatment. There was a decrease in post void residual urine.
Conclusion: In this first study to evaluate the results of parasacral TENS on constipation in children with LUTD, satisfactory results were obtained for both complaints.

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Introduction

Constipation is the most common chronic defecation disorder in children and is frequently associated with fecal soiling [1]. It is responsible for 3–5% of visits to the pediatrician [2] and for 25% of consultations with a gastroenterologist [3,4].

In addition to related emotional consequences such as anxiety and withdrawal from social life (principally in school), constipation is related to other problems such as urinary tract infection (UTI), bladder abnormalities and lower urinary tract dysfunction (LUTD) [4].

LUTD is related to voiding abnormalities that can occur during the filling or emptying of the bladder in children without neurological or anatomical disorders. Many children have urgency as a result of overactive bladder (OAB) or combined with detrusor sphincter dyssynergia. Other symptoms include daytime incontinence, pollakiuria or infrequent urination, nocturnal enuresis, as well as a general association with maneuvers done to postpone voiding [5].

These types of dysfunction, and especially OAB, have been historically treated with anticholinergics. However, these drugs cause constipation as one of their major side effects. In contrast, parasacral transcutaneous electrical nerve stimulation effectively treats voiding dysfunction as well as constipation, due to the anatomo-physiological relationship between the two tracts.

The objective of this study was to evaluate, in the short term, the resolution of constipation in children with LUTD after parasacral TENS treatment, as well as to assess voiding responses to the treatment.

Materials and methods

Children over the age of 4 with LUTD and associated functional constipation were given parasacral TENS treatment and evaluated prospectively.

The following tests were used to evaluate LUTD: uroflowmetry combined with electromyography, and urinary tract ultrasonography with an evaluation of post-void residual volume. Post-voiding levels higher than 10% of bladder capacity for this age in ml ([age + 2] × 30) or greater than 20 ml were considered residual. LUTD was classified according to the guidelines of the International Children's Continence Society. Children with neurological problems or genetic syndromes as well those with anatomic alterations of the lower urinary tract were excluded from the study.

The Rome III criteria [6] (Table 1) for children were used to diagnose constipation; constipation was considered present when the child presented at least two of the six symptoms for longer than two months. The Bristol Stool Chart [7] (Fig. 1) was used to classify the stool shape into seven types (1 and 2 indicate constipation; 3–5 are "ideal" stools; 6 and 7 show paradoxical diarrhea). The visual analog scale evaluated pain during defecation on a scale from 0 to 10, divided into six groups with 0 indicating no pain and 10 maximum pain. These last two questionnaires were categorized into two groups, who had constipation (types 1, 2) and did not have constipation (type 3–7), and had pain between "0 and 5" and between "6 and 10".

A physical examination was performed and consisted of the following: abdominal palpation to test for the presence of hard stool; assessment of perineal contractions to evaluate coordination; neurological exam to assess perineal and lower limb sensitivity; anal and bulbocavernosus reflex tests in all children, and a cremasteric reflex test in boys; inspection and palpation of the lumbar spine to identify spina bifida occulta (tufts of hair, stains and lipomas may be present).

Electrical stimulation was applied by two experienced professionals in the field, and followed a protocol previously published by our department [8]. The treatment consisted of 20 sessions at a frequency of 10 Hz and a pulse width of 700 ms. The intensity of the current was increased to the maximum level tolerated by the child, but without reaching the motor point, using two self-adhesive 3.5 cm electrodes placed to the side of S2 and S4. The electrical stimulation was performed three times weekly, for sessions of 20 min each. The 961 Dualpex Uro, Quark was used.

No patients had been treated for constipation before this study. No patient had ever used anticholinergics before TENS. Uroflowmetry was performed in all patients. All children were instructed to follow urotherapy, guiding them not to ingest bladder irritants (caffeine, soft drinks, citrus fruits), to urinate every 4 h, and not to delay urination at times of emergency. The instructions have been described in detail [8]. We did not ask to increase fiber in the diet to avoid this bias to the study. No specific treatment was instituted for constipation. Patients were re-evaluated immediately after treatment.

All responsible parties signed an informed consent form. This study was approved by the institution's ethics committee under protocol 107/2008.

Mean and standard deviation measurements were used for statistical analysis, and McNemar's test was used for the analysis of paired categorical variables with a significance level of 5%. Data analysis was done using the SPSS program for Windows, version 14.0.

Results

The study included 9 girls and 5 boys with symptoms of LUTD. The mean age was 8.07 ± 2.72 years (median: 7,

Table 1 The Rome III criteria for pediatric functional constipation.

2 or more of the following features in a child with developmental age of at least 4 years and occurring at least once per week for at least 2 months before diagnosis

- ≤ 2 bowel defecations in the toilet per week
- At least 1 episode of fecal incontinence per week
- History of retentive posturing or excessive volitional stool retention
- History of painful or hard bowel movements
- Presence of a large fecal mass in the rectum
- Presence of large-diameter stools that may obstruct the toilet

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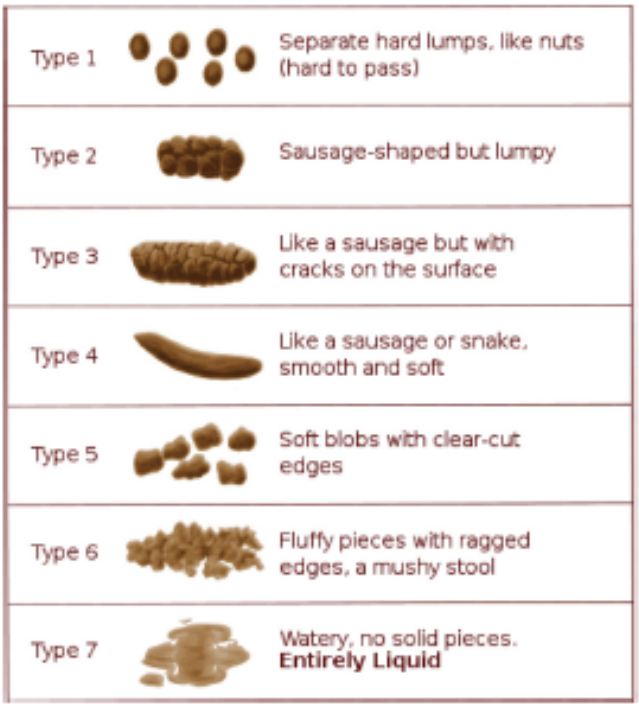

Figure 1 Bristol stool chart, with Spanish translation.

range: 5–11). Regarding the diagnosis of LUTD, 10 (71.4%) had OAB and 4 (28.6%) had voiding dysfunction.

After treatment, 85.7% ($p < 0.001$) of the children's constipation symptoms had improved following the Rome III criteria. Evaluating each item independently using the Rome III criteria (Table 2), parasacral TENS effectively treated the following: "the presence of at least one episode of fecal incontinence per week", "history of stool retention", and "the presence of a large fecal mass in the rectum." The improvement was found to be statistically significant.

Regarding evaluations based on the other criteria, there was no significant change based on the Bristol Stool Chart, but there was a significant improving trend in the level of pain experienced before and after treatment (Table 3).

With relation to urinary symptoms, children had fewer episodes of enuresis, UTI, holding maneuvers and urge incontinence. All these results were found to be statistically significant, as can be seen in Table 4. Four children with voiding dysfunction had elevated post void residual urine with respect to their age (mean 60 mL) which became negligible after treatment. Regarding the uroflowmetry findings, before treatment 10 children had a bell shape and one had a staccato curve. This curve became normal (bell shaped) after treatment.

Discussion

This is the first study to evaluate the result of transcutaneous electrical nerve stimulation on constipation in children with LUTD, but others have already evaluated the efficacy of TENS on children with constipation and no urinary symptoms [9–11].

Table 2 Distribution of Rome III criteria before and after treatment.

Variable	Before treatment n (%)	After treatment n (%)	p
<2 defecations/week	2 (14.3%)	2 (14.3%)	1
>1 fecal incontinence/week	7 (50%)	1 (7.1%)	0.031*
Stool retention	6 (42.9%)	0 (0%)	0.001*
Pain or force	9 (64.3%)	5 (37.5%)	0.21
Fecal mass	11 (78.6%)	1 (7.1%)	0.002*
Large stools	7 (50%)	3 (21.4%)	0.21

* Statistical significance.

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Table 3 Comparison before and after treatment using the Bristol stool chart and visual analog scale.

Variable	Before TENS n (%)	After TENS n (%)	p
Bristol stool chart			
Constipation	4 (28.6%)	1 (7.1%)	0.25
Normal	10 (71.4%)	13 (92.9%)	
Visual analog scale			
0–5	6 (42.9%)	11 (78.6%)	0.063
6–10	8 (57.1%)	3 (21.4%)	

LUTD has been linked with neurophysiological immaturity of the central nervous system. As constipation is closely linked with LUTD due to the anatomical and nervous relationship between the urinary and gastrointestinal tracts, it is not surprising that LUTD is associated with the retention of feces, which has been called dysfunctional elimination syndrome [12]. A child with urgency tends to try to inhibit urination through maneuvers such as crossing their legs, squatting, or compressing the glans to counter the desire to void. Such maneuvers inevitably lead to the postponement of defecation as well [13]. On the other hand, retained stool in the rectum creates an increase in bladder pressure, leading to urgency. Constipation increases the potential for urinary incontinence, uncoordinated voiding, post void residual urine and recurrent urinary tract infection [3]. In this study, almost all of the evaluated items showed improvement after the use of parasacral TENS and uro therapy, which emphasizes the close relationship between these two systems.

For decades, anticholinergics were used as primary therapy for patients with LUTD, especially OAB. However, constipation is one of the undesirable effects of this medication, and a contributing or aggravating factor to this dysfunction in the children with LUTD who are under treatment. This is because the parasympathetic system is responsible for the disposal of feces and urine.

We have obtained significant results regarding parasacral TENS on the treatment of diurnal and nocturnal incontinence [3,14–16]. In one study we show that 20 treatment sessions, 3 times weekly, prompted a 63% resolution of the symptoms and 32% significant improvement in children between the ages of 4 and 14. Out of these patients, 78% had continued success after two years of follow up. We performed a randomized clinical trial involving children with OAB that demonstrated that parasacral TENS is more effective than a placebo, even though both of the patient groups were instructed to follow urotherapy. In the current study, all urinary symptoms showed statistically significant improvement using the same protocol.

Table 4 Comparison of urinary symptoms before and after treatment.

Variable	Before treatment n (%)	After treatment n (%)	p
Enuresis	13 (92.9%)	5 (38.5%)	0.001
UTI	10 (71.4%)[a]	0 (0%)	0.001
Holding maneuvers	13 (92.9%)	4 (28.6%)	0.001
Urge incontinence	13 (92.9%)	2 (15.4%)	0.001

[a] 4 out of the 10 had episodes of febrile UTI.

TENS has been shown to effectively treat children with functional constipation as well. In a randomized and controlled clinical trial [11] with constipated children, TENS and interferential current were used for 1 h daily for at least two months at a frequency of 4 kHz. There was a significant increase in stool frequency per week ($p = 0.008$). Another randomized clinical trial [10] demonstrated that the use of interferential current on children for 12 sessions of 20 min each over the course of 4 weeks significantly improved constipation when compared to the use of a placebo.

The current study differs from others by evaluating children with LUTD. The results show a significant improvement in constipation, demonstrated through the evaluation of constipation based on the Rome III criteria overall, and three of the items evaluated independently. Additionally, all urinary symptoms showed improvement, making TENS a good treatment option for constipated children with urinary symptoms, despite the need for additional treatment such as diet modification or the use of medication such as laxatives. There was no nutritional or behavioral advice given regarding constipation during this treatment.

In 1988, a committee of experts gathered to standardize the knowledge and classification of functional disorders of the digestive tract, and create what are known as the Rome Criteria. In 1999, a reviewed version of this consensus called the Rome II Criteria was published, and the Rome III Criteria was published in 2006 [17]. The Bristol Stool Chart is a simple evaluation tool to measure the shape and consistency of human feces due to intestinal transit time. This scale was validated in healthy subjects and in patients with gastrointestinal disorders, and its efficacy has been demonstrated for research purposes and clinical analysis [18,19]. Currently, the Rome III criteria [6] and the Bristol Stool Chart [7] are recommended for the diagnosis of functional constipation and recognized for clinical and research application. Both of these diagnostic tools are low cost and easily applicable. There was no statistical significance found in this study with relation to the Bristol Stool Chart before and after treatment, probably due to the small number of patients. Before the treatment, 28% of patients were constipated and only 8% were constipated after treatment.

A limitation of this study was the small number of participants with LUTD and constipation. Also, the follow up time was short. Long term studies need to be performed in order to establish whether this modality of treatment for constipation lasts. Additionally, all children were treated in combination with urotherapy, which might have acted as a therapeutic agent and influenced the results.

Conflict of interest

The authors of this study declare no conflict of interest or funding.

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ANEXO Q – Artigo publicado sobre o tema "Transcutaneous Parasacral Electrical Stimulation vs Oxybutyn for the Treatment of Overactive Bladder in Children: A Randomized Clinical Trial

+ MODEL ARTICLE IN PRESS

Transcutaneous Parasacral Electrical Stimulation vs Oxybutynin for the Treatment of Overactive Bladder in Children: A Randomized Clinical Trial

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Purpose: We determined the effectiveness of 2 methods to treat overactive bladder in children using intragroup and intergroup comparisons in a randomized clinical trial.

Materials and Methods: Nine boys and 19 girls with a mean ± SD age of 6.4 ± 2.18 years were randomly divided into group 1—parasacral transcutaneous electrical stimulation with placebo drug and group 2—oxybutynin with sham scapular electrical therapy. Success was assessed by 1) the rate of complete symptom resolution, 2) a visual analog scale of 0 to 10, 3) the dysfunctional voiding score system, 4) voiding diary records, 5) Rome III criteria and 6) side effect frequency in each group.

Results: A total of 13 and 15 patients were randomized to groups 1 and 2, respectively. Symptoms completely resolved in 6 patients in group 1 (46%) and 3 in group 2 (20%) (p 0.204). A statistically significant improvement was found in the 2 groups in the dysfunctional voiding score system and voiding diary records. However, no statistically significant difference was found between the groups in the visual analog scale score, voiding frequency, and maximum and mean voided volume (p 0.295, 0.098, 0.538 and 0.650, respectively). Constipation improved in 100% of group 1 patients but in only 55% in group 2 (p 0.031 vs 0.073). Group 1 showed no side effects while dry mouth, hyperthermia and hyperemia developed in 58%, 25% and 50% of group 2 patients (p 0.002, 0.096 and 0.005, respectively). Treatment was discontinued by 13.3% of patients in group 2.

Conclusions: Parasacral transcutaneous electrical stimulation was as effective as oxybutynin to treat overactive bladder in children. However, transcutaneous parasacral electrical stimulation was more effective against constipation and showed no detectable side effects. Oxybutynin was more effective for decreasing voiding frequency.

Key Words: urinary bladder, overactive; transcutaneous electric nerve stimulation; oxybutynin; constipation; adverse effects

Abbreviations and Acronyms

DVSS — dysfunctional voiding score system
OAB — overactive bladder
PTENS — parasacral transcutaneous electrical stimulation
UTI — urinary tract infection
VAS — visual analog scale
VF — voiding frequency
VUR — vesicoureteral reflux
VV — voided volume

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OVERACTIVE bladder in children is defined as voiding urgency usually associated with daytime urinary incontinence, frequency and constipation, in addition to nocturnal enuresis or nocturia in some cases.[1]

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It is present in approximately 6% of girls and 3.8% of boys at age 7 years.[2] It is also associated with emotional and behavior changes such as low self-esteem, social isolation, shyness, aggression, transgression and attention deficit hyperactivity disorder.[3,4] OAB is a major cause of UTI in children older than 4 years and a risk factor for VUR.[5,6] The risk of renal scarring increases substantially in children with UTIs and VUR.[7] Therefore, OAB must be diagnosed and properly treated.

Behavioral therapy can improve OAB symptoms but frequently other therapy is required. Anti muscarinics, especially oxybutynin, were claimed to improve approximately 60% of cases,[8,9] although the rate of complete resolution of symptoms has been lower than 30%.[10,11] Side effects such as dry mouth, constipation, hyperemia and hyperthermia develop in about 50% of patients and 10% need to interrupt treatment.[12]

Based on previous studies of home electrical stimulation[13] we began performing outpatient treatment with 20 sessions of PTENS at 10 Hz for 20 minutes each 3 times per week. This treatment achieved complete resolution of symptoms or significant improvement in 94% of cases[14] and long term (at least 2 years) symptom resolution in 73%.[15] In a randomized clinical trial PTENS was more effective than sham treatment.[16]

Although there are studies of oxybutynin and PTENS to treat OAB in children, to our knowledge no group has compared the 2 methods. In a randomized clinical trial we compared the efficacy of oxybutynin and PTENS in children with OAB. Because oxybutynin has been used for decades and it is a well established treatment for OAB in children, we hypothesized that PTENS would not be inferior to this medication.

MATERIAL AND METHODS

The current prospective, randomized, blinded clinical trial was approved by the institutional review board. We selected children for study inclusion at ages between 4 and 17 years who had urgency, a bell-shaped uroflowmetry curve, post-void residual urine volume less than 10% of bladder capacity expected for age or greater than 20 ml, DVSS greater than normal (6 in boys and 9 in girls), voiding urgency at least 3 times per week and no previous treatment. Patients with signs of neurological disease or urinary tract anatomical problems were excluded from study or excluded if diagnosed after allocation. All parents or legal guardians of participants agreed to treatment and provided free, informed consent.

After the sessions patients were instructed to return for medical appointments at the scheduled time, or as soon as UTI symptoms or changes in the urinary pattern were present.

Each child completed a questionnaire on urinary and intestinal history. Constipation was assessed using Rome III criteria, on which at least 2 positive answers of the 6 questions were considered sufficient for diagnosis. A DVSS score questionnaire validated in Portuguese was applied to the child to assess voiding dysfunction.[17] Physical examination consisted of neurological examination to rule out changes related to dermatome innervations from S2 to S4. If any change was detected, the child was referred to a pediatric neurosurgeon.

We instructed patients to complete a voiding diary for 3 consecutive days, mainly to record VF, and mean and maximum VV. Urinalysis, urine culture, urinary tract ultrasound, post-void residual urine volume measurement, uroflowmetry and voiding cystourethrogram were done in patients with a history of febrile UTI in infancy. When VUR was diagnosed, patients underwent renal scintigraphy with dimercaptosuccinic acid to identify possible renal scarring.

All children received voiding and intestinal instructions, representing standard urotherapy. Instructions included scheduled voiding every 3 hours or not allowing 4 hours to pass without voiding, avoiding the ingestion of coffee, tea, soda, chocolate and citrus fruits during treatment, urinating before bedtime, ingesting a greater amount of liquid during the day, not retaining urine when there was urinary urgency, eating high fiber foods, using the toilet seat reducer when necessary and using a footrest when the toilet was high and the feet of the child could not reach the ground.

We selected 22 patients by randomization using a website (http://randomized.com/). Group 1 included 13 patients who underwent PTENS 3 times per week and received placebo daily. Group 2 included 15 patients treated with oxybutynin daily and with scapular electrical stimulation (sham treatment) 3 times per week. Patients and parents were blinded to treatment type.

The colors and flavors of oxybutynin and placebo were identical. All patients received the same dose of 0.3 mg/kg per day twice daily for the duration of the electrical stimulation sessions.

The electrical stimulation technique consisted of the application of electrical current produced by a Dualpex Uro 961 generator (Quark®) using surface electrodes for a total of 20 sessions of 20 minutes each 3 times per week on alternate days. We used a symmetrical biphasic square current pulse with a frequency of 10 Hz, pulse width 700 milliseconds and intensity increased up to the level of below the motor threshold (fig. 1). Two surface electrodes were placed symmetrically on the parasacral region and 2 were placed symmetrically on 1 scapula. Stimulation was done using the parasacral and scapular electrodes in groups 1 and 2, respectively.

Posttreatment evaluation was performed 3 months after the beginning of treatment using a questionnaire administered by a professional blinded to patient group. We made intragroup and intergroup comparisons using a VAS to evaluate symptoms, the DVSS, comparative evaluation of voiding diaries, Rome III criteria to assess whether constipation improved and the frequency of side effects in the 2 groups.

If necessary, an active search was performed by telephone to discover why patients discontinued treatment and did not return and why those who completed treatment did not return for consultation. Any study

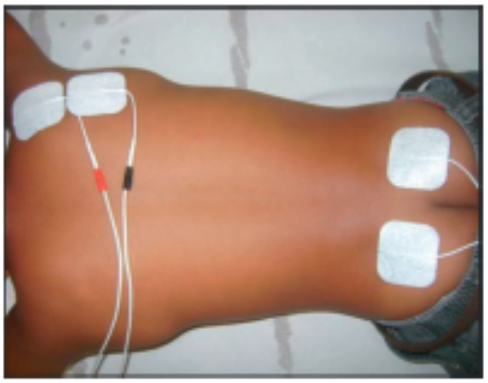

Figure 1. Patient using surface electrodes on scapula and parasacral area.

withdrawal was considered failure as an intent to treat analysis. Treatment success was considered to be achieved when there was complete resolution of symptoms.

For descriptive and analytical analysis we used SPSS(r), version 17.0 for Windows(r). We calculated statistical inferences for categorical variables using the Fisher exact and McNemar tests. For continuous variables the Wilcoxon and Mann-Whitney tests were used to compare dependent and independent means, respectively. The tests were nonparametric with $p < 0.05$ considered statistically significant.

RESULTS

Table 1 lists patient clinical and demographic characteristics. We evaluated 28 patients, including 13 in group 1 and 15 in group 2. Two children withdrew from treatment. Their guardians informed us by telephone that the condition of the children had worsened with fever and body redness presenting after therapy started. Three group 1 and 2 group 2 patients crossed over after treatment.

Table 1. Pretreatment clinical and demographic characteristics in 28 patients

	PTENS	Oxybutynin	p Value (Fisher test)
No. pts (%)	13 (46)	15 (54)	
No. female (%)	9 (69)	10 (67)	1.000
No. race (%)			
White	9 (69)	12 (80)	0.670
Nonwhite	4 (31)	3 (20)	
No. UTI (%)			
Nonfebrile	3 (37)	4 (50)	0.664
Febrile	4 (50)	8 (73)	0.377
Mean ± SD age (yrs)	6.3 ± 2.4	6.5 ± 2.0	0.555
Mean ± SD wt (kg)	26.2 ± 11.9	23.40 ± 12.8	0.717
No. urge incontinence (%)	11 (85)	14 (93)	0.583
No. frequency (%)	9 (69)	10 (67)	1.000
No. nocturia (%)	3 (23)	2 (13)	0.639
No. enuresis (%)	9 (69)	10 (67)	1.000
No. constipation (%)	6 (46)	10 (67)	0.445

VAS and DVSS

Six group 1 patients (46%) showed complete symptom resolution, as did 3 (20%) in group 2 ($p = 0.204$, fig. 2). Mean DVSS significantly improved after treatment in groups 1 and 2 (table 2). However, no difference was seen between the treatments.

Voiding Diary Data

All voiding diary parameters improved after treatment except the number of voids per day. This was significantly decreased only in group 2, although there was a significant trend in group 1 (table 2). There were fewer than 4 voids per day in 4 group 2 patients (41%) but in no group 1 patient. No difference was found between the groups (table 3).

Constipation Assessment

Constipation was noted in 15 patients (53%) before treatment. After treatment constipation improved in all 6 patients in group 1. In group 2 only 5 of 9 patients with constipation were improved after treatment.

Side Effects

No group 1 patient presented with side effects. However, in group 2 dry mouth, hyperthermia and hyperemia developed in 59%, 25% and 50% of patients, respectively.

DISCUSSION

Regarding symptom resolution the results were similar in the 2 groups. However, although there was no statistical significance, the rate of complete symptom resolution was about twofold in favor of PTENS (46% vs 20%). The absence of statistical significance was possibly due to our small sample size, resulting in a type II error. The reported rate of complete symptom resolution using oxybutynin is less than 30%.[8,10] In the PTENS group we found complete resolution in only 46% of patients, a slightly lower rate than in previous studies.[14,16]

Each method effectively decreased DVSS. Our results represent short term followup. PTENS was previously associated with a lasting result with complete resolution of symptoms in 73% of cases.[15] However, to our knowledge there is no long term study in the literature with oxybutynin. Studies of the results of using oxybutynin after months of interruption must be performed to assess the rate of recurrent symptoms.

Only group 2 attained a decreased number of voids per day. However, the reduction reached values

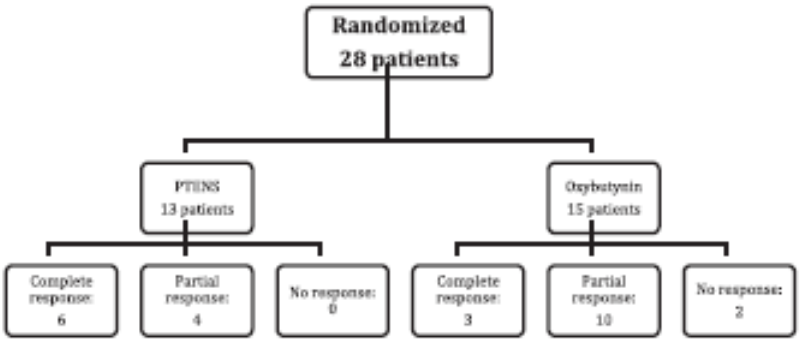

Figure 2. Distribution and results after randomization

that were considered abnormal (3 or fewer voids per day) in 5 patients (41%) on the medication. This difference may have been due to the different mechanisms of action of oxybutynin and PTENS. Due to the action of the *M2* and *M3* muscarinic receptor subtypes oxybutynin stimulates the bladder wall, decreases afferent impulse intensity, and the frequency and intensity of involuntary contractions, increases functional bladder capacity and reduces urinary frequency.[18,19] On the other hand, PTENS acts on neural pathways that modulate afferent efferent stimuli in the spinal and supraspinal areas. It affects reflexes more and detrusor relaxation less.[20] Further studies should be done to determine whether children with prominent urinary frequency could benefit more from medication than from neuromodulation.

Treating constipation is crucial when dealing with OAB in children. According to studies in animals and humans stool retained in the rectum is related to worsening bladder function.[21] A critique of oxybutynin treatment is the negative action that the drug causes on intestinal motility due to its nonselective antimuscarinic action, which favors constipation.[22] In the current study 57% of patients were constipated according to Rome III criteria. As expected we found that PTENS significantly improved constipation while oxybutynin did not.

Sympathetic stimulation and parasympathetic inhibition may be responsible for the acceleration of intestinal transit. Two randomized clinical trials demonstrated that electrical stimulation accelerated intestinal motility more than sham treatment.[23,24] Since all patients in our study received instructions (high fiber and fluid intake) on how to improve constipation, the instructions could possibly have influenced the improvement in some children, including those who received oxybutynin, in whom a poorer result was expected. It is also possible that the improvement in urinary symptoms in some patients was related to the treatment for constipation and not exactly to the therapeutic effect on the lower urinary tract.

PTENS was not associated with detectable side effects. In contrast, more than half of the patients on oxybutynin presented with side effects and 2 (13%) discontinued treatment, in agreement with other series.[8,12]

This study has some limitations. The number of patients was small and perhaps some differences between groups were not detected due to low power. However, because our hypothesis was that PTENS

Table 2 PTENS and oxybutynin groups before and after treatment

	Mean ± SD Pretreatment	Mean ± SD Posttreatment	p Value (Wilcoxon test)
PTENS.			
DVSS	11 ± 2.2	3.5 ± 2.7	0.000
VF (No./day)	7.5 ± 2.8	6.5 ± 2.2	0.101
Max VV (ml)	176.5 ± 78.3	256.5 ± 117.9	0.000
Mean VV (ml)	113.4 ± 60.2	159.7 ± 62.4	0.000
Oxybutynin.			
DVSS	12.2 ± 2.9	3.6 ± 1.8	0.000
VF (No./day)	8.5 ± 3.5	5.4 ± 2.1	0.002
Max VV (ml)	166.3 ± 84.9	238.1 ± 68.5	0.006
Mean VV (ml)	90.2 ± 35.0	152.1 ± 49.8	0.001

Table 3 Comparison of PTENS and oxybutynin groups

	Mean ± SD Overall	Mean ± SD PTENS	Mean ± SD Oxybutynin	p Value (Mann Whitney test)
DVSS	8.16 ± 3.68	7.46 ± 3.36	8.92 ± 3.88	0.295
VF (No./day)	1.96 ± 2.70	1.00 ± 2.00	3.00 ± 3.05	0.068
Max VV (ml)	70.20 ± 54.90	80.00 ± 53.77	59.58 ± 56.43	0.528
Mean VV (ml)	48.48 ± 30.93	46.31 ± 29.28	52.92 ± 33.57	0.650

would be noninferior to oxybutynin, fewer patients could be enrolled. If the hypothesis had been to prove the superiority of one method over the other, a higher number of patients would have been needed. Another limitation was the possibility of parents and patients not being blinded. Despite this possibility we noted no comments from patients regarding the group in which they were placed. It is possible that side effects and sensation in the sacral area may have made patients aware that they were in the oxybutynin or PTENS group. Outcome assessment was blinded, which decreased the assessment bias. Future studies should include more patients to evaluate the long-term efficacy, cost effectiveness, compliance, and acceptance of parents and patients for the 2 treatments.

CONCLUSIONS

PTENS and oxybutynin were similarly efficacious for treating OAB in children. Oxybutynin was more effective in decreasing voiding frequency and PTENS was more effective in improving constipation. Detectable side effects developed only in children who received oxybutynin. Each method was well accepted by families.

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