Vpliv trajanja zdravljenja na učinkovitost maksimalne električne stimulacije pri otrocih z nenevrogenim čezmerno aktivnim sečnim mehurjem in s težavami pri mokrenju

Influence of the duration of treatment on the effectiveness of anal maximal electrical stimulation in children with non-neurogenic overactive bladder and micturition problems

Bojan Tršinar,[1] Primož Tršinar[2]

[1] *Klinični oddelek za urologijo, Kirurška klinika, UKC Ljubljana, Zaloška c. 7, 1525 Ljubljana*

[2] *Oddelek za urologijo, Splošna bolnišnica Novo mesto, Šmihelska 1, 8000 Novo mesto*

Korespondenca/ Correspondence:
prof. dr. Bojan Tršinar dr. med., Klinični oddelek za urologijo, Kirurška klinika, UKC Ljubljana, Zaloška c. 7, 1525 Ljubljana
Fax: +386 1 522 32 33
Tel.: +386 1 522 32 17
e-mail: Bojan.Trsinar@siol.com

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Izvleček

Izhodišča: V raziskavi smo primerjali učinkovitost enomesečne in dvomesečne analne maksimalne električne stimulacije (MES) pri otrocih z nenevrogenim čezmerno aktivnim sečnim mehurjem in s težavami pri mokrenju.

Metode: 90 deklic s cistometrično potrjeno idiopatsko hiperaktivnostjo detruzorja, z nočno enurezo in/ali dnevno urinsko inkontinenco smo vključili v prospektivno randomizirano raziskavo. Deklice smo zdravili z MES po 20 minut dnevno 1 mesec (45 deklic) ali 2 meseca (45 deklic). Število nočnih in dnevnih inkontinenčnih epizod smo beležili 1 mesec pred začetkom zdravljenja in 1 mesec po koncu zdravljenja. Cistometrijo smo napravili 1 teden pred začetkom električne stimulacije in 1 mesec po koncu. Pri statistični obdelavi podatkov smo uporabili Wilcoxonov parni test in Mann-Whitneyev test.

Rezultati: Po zaključku MES v statistično obdelavo nismo vključili podatkov 17 od 90 deklic. 30 deklic, ki smo jih stimulirali 1 mesec, je imelo po MES pomembno zmanjšano mediano število mesečnih nočnih inkontinenčnih epizod (9,5 oz. 4,5; $p < 0,05$). Pri 43 deklicah, ki smo jih stimulirali 2 meseca, je prišlo do pomembnega zmanjšanja medianega števila mesečnih nočnih inkontinenčnih epizod (14,5 oz. 7,5; $p < 0,001$) kot tudi do pomembnega zmanjšanja medianega števila mesečnih dnevnih inkontinenčnih epizod (5 oz. 0; $p < 0,01$). Vendar pa klinični rezultati MES med obema skupinama niso bili statistično pomembno različni. V skupini bolnic z enomesečno MES je prišlo po zdravljenju do pomembnega zmanjšanja števila nehotenih krčenj detruzorja (3 oz. 1; $p< 0,05$). V skupini z dvomesečno MES pa smo ugotovili statistično pomembne spremembe v zmanjšanju števila nehotenih krčenj detruzorja (2 oz. 0; $p< 0,01$) in tudi statistično pomembno povečanje maksimalne cistometrične zmogljivosti mehurja (250 ml oz. 280 ml; $p < 0,001$) in raztegljivosti mehurja (12,5 ml/cm oz. 20,5 ml/cm; $p < 0,001$). Vendar pa tudi spremembe cistometričnih parametrov med skupinama niso bile statistično značilne.

Zaključki: Dvomesečna MES je bila pri zdravljenju otrok z nenevrogenim čezmerno aktivnim sečnim mehurjem in s težavami pri mokrenju sicer tako klinično kot urodinamsko učinkovitejša od enomesečne MES, vendar pa razlika statistično ni bila značilna.

Abstract

Background: To compare the effectiveness of one-month and two-month courses of maximal electrical stimulation (MES) in treating children with non-neurogenic overactive bladder and micturition problems.

Methods: 90 girls with cystometrically confirmed idiopathic detrusor hyperactivity associated with nocturnal enuresis and/or daytime urinary incontinence were enrolled in a prospective, randomized study and underwent pelvic floor stimulation treatment 20 minutes a day for either one month (45 girls) or two months (45 girls). All nocturnal and diurnal incontinence episodes were recorded for one month before the start of treatment and one month after its completion. Cystometry was performed one week before the beginning of treatment and one month after its completion. The Wilcoxon matched-pair test and Mann-Whitney test were used for statistical evaluation.

Results: After treatment with MES, 17 out of 90 patients were not included in the processing of statistical data. Thirty girls treated for one month had a significant decrease in the median num-

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ber of monthly nocturnal incontinence episodes (from 9.5 to 4.5, $p < 0.05$); 43 girls treated for two months had a significant reduction in the median number of monthly nocturnal incontinence episodes (from 14.5 to 7.5, $p < 0.001$) as well as in the median number of monthly daytime incontinence episodes (from 5 to 0, $p < 0.01$). However, the changes in clinical parameters observed after treatment with MES did not differ significantly between the two groups. In the one-month group only the number of involuntary detrusor contractions changed significantly (from 3 to 1, $p < 0.05$). In the two-month group there was a significant change in the number of involuntary detrusor contractions (from 2 to 0, $p < 0.01$) as well as in the maximum cystometric capacity (from 250 to 280 ml, $p < 0.001$) and compliance (from 12.5 to 20.5 ml/cm, $p < 0.001$). Again, the changes in cystometric parameters did not differ significantly between the two groups.

Conclusions: The two-month MES used in treating children with non-neurogenic overactive bladder and micturition problems had somewhat better but statistically insignificant clinical and cystometric results compared to the one-month MES.

Introduction

Overactive bladder is found in 60 to 70 % of children with nocturnal enuresis and daytime incontinence.[1]

A variety of more or less effective modalities are available for the treatment of micturition problems in children with overactive bladder. These include lower urinary tract rehabilitation (urotherapy) and pharmacological therapy (antimuscarinics, botulinum toxin). Specific forms of urotherapy are biofeedback therapy, physiotherapy and neuromodulation.

One form of neuromodulation is maximal electrical stimulation (MES), which involves short-term stimulation of the pelvic floor. It employs non-implantable vaginal or anal electrodes for the stimulation of the afferent pudendal nerves. Through a pudendal-pelvic spinal reflex, acute inhibition of the involuntary detrusor contractions can be induced.[2,3,4]

MES has been available for treating children with micturition problems at our Department since 1984.[5] Optimal treatment parameters for MES in children have not been established. Previous studies differed with regard to the number of stimulation treatments per week, duration of each treatment session, and the overall duration of treatment. Moreover, different stimulus frequencies and current intensity ranges were used.[6,7] It has been speculated that the intensity of stimulation and the number of treatment sessions may be the main outcome-determining factors.

The aim of the present study was to compare the effects of one-month and two-month courses of MES on micturition problems and cystometric parameters in children with nocturnal enuresis and/or daytime incontinence associated with overactive bladder. Our hypothesis was that two-month MES should be clinically and urodynamically more effective than one-month MES.

Materials and methods

The study population comprised 90 girls aged 5 to 17 years, mean age 9.7 years, with cystometrically confirmed detrusor hyperactivity and micturition problems. Thirty-nine girls had nocturnal enuresis, 14 daytime incontinence, and 37 had both nocturnal enuresis and daytime incontinence. Either unilateral (14 cases) or bilateral (4 cases) vesicoureteral reflux (VUR) was present in 18 patients: 7 VUR grade 1, 11 VUR grade 2, and 4 VUR grade 4. Patients with acute urinary tract infection (UTI) or a history of recurrent UTI were not enrolled in the study. Other exclusion criteria were neurogenic bladder, infravesical obstruction and organic bladder disease (including fibrosis and calculi), established by ultrasound, micturition cystography and cystoscopy.

All 90 girls had been treated with a bladder training regimen (instructions on voiding, treatment of underlying constipation) but with no improvement. All girls with nocturnal enuretic episodes (76) had received desmopressin for at least six months with no positive effect. Only 45 girls had received anticholinergic therapy for at least 3 months with transitory or no effect. Anticholinergic

Table 1: Pre-treatment clinical and urodynamic parameters between the two groups of patients treated with MES for one or two months.

Urodynamic variables	One month of treatment mean (range)	Two months of treatment mean (range)	P value
Number of patients	45	45	
Age (years)	9.6 (5–16)	9.4 (6–17)	N.S.
Nocturnal incontinence episodes per month	+9.5 (2–28)	14.5 (3–27)	N.S.
Daytime incontinence episodes per month	3 (1–30)	5 (2–28)	N.S.
First desire to void (ml)	100 (30–250)	100 (50–250)	N.S.
Maximum cystometric capacity (ml)	220 (110–355)	250 (100–420)	N.S.
Compliance (ml/cm)	9 (2–20)	12.5 (2–100)	N.S.
Number of involuntary detrusor contractions	3 (1–10)	2 (1–21)	N.S.

N.S. = non significant

therapy was discontinued at least one month before the start of stimulation treatment.

Informed consent for the study was obtained from the parents of each child. The patients were randomized into two groups to receive the MES treatment for one (45 patients) or two months (45 patients).

The primary endpoint of the study was to asses the clinical and urodynamic efficacy of anal MES in children with micturition problems and non-neurogenic overactive bladder. The second endpoint of the study was to asses the safety and tolerability of anal MES in children.

Stimulation device and therapeutic method used:

The treatment was initiated at our urodynamic unit by urotherapy-trained nurses, who taught the children and their parents how to administer the stimulation. A battery-powered stimulator connected by a cable to anal bipolar plug electrodes was used (Figure 1). The stimulator generated monophasic square current pulses with a duration of 1 ms and a frequency of 20 Hz. Each treatment session lasted 20 minutes. At the beginning of each session, stimulation intensity was gradually increased up to the level of tolerable discomfort. After 20 minutes of stimulation, the stimulator switched off automatically. MES was applied daily for one (45 patients) or two months (45 patients).

Evaluation

The patients were evaluated by micturition charts and water cystometry. The micturition chart was maintained by the patient for one month before the initiation of MES and for one month after its completion. All episodes of nocturnal and diurnal incontinence were recorded. Water cystometry was performed one week before the start of treatment and one month after its completion. With the patient lying supine, a 12F Foley catheter was introduced, and 0.9 % saline solution at body temperature was instilled into the bladder at a rate of 50 ml/min. Cough was provoked at each 100 ml increment of fluid. Intravesical pressure was measured by a 5F Portex catheter with the strain gauge transducer placed at the level of the symphysis. Intraabdominal pressure was recorded rectally. Detrusor pressure was derived by subtracting intraabdominal pressure from intravesical pressure.

The patients and their parents were asked to report any side effects of the stimulation treatment (abdominal or anal pain, increased defecation frequency). Patients who

Table 2: Urodynamic findings before and after one month of treatment with anal MES in 30 girls with nocturnal enuresis and/or daytime incontinence associated with detrusor instability.

Urodynamic variables	Before MES mean (range)	After MES mean (range)	P value
First desire to void (ml)	100 (30–250)	110 (60–180)	N.S.
Maximum cystometric capacity (ml)	220 (110–355)	265 (172–410)	N.S.
Compliance (ml/cm)	9 (2–20)	14 (2–33)	N.S.
Number of involuntary detrusor contractions	3 (1–10)	1 (1–7)	< 0.05

experienced side effects interrupted the treatment for at least a week.

The methods, definitions and units used in the study conformed with the ICS standards.[8] The Wilcoxon matched-pair test and Mann-Whitney test were used for statistical evaluation.

Results

After the end of treatment with MES, 17 out of 90 patients were not included in the processing of statistical data. Ten patients did not attend follow up for unknown reason, 4 girls failed to fill in the micturition chart, and 3 patients did not undergo cystometry.

There were no differences in pre-treatment clinical and urodynamic parameters between the two groups treated with MES for one and two months (Table 1).

After one month of treatment (30 girls), the median number of monthly nocturnal incontinence episodes fell from 9.5 (2–28) to 4.5 (0–27) ($p < 0.05$), and the median number of daytime incontinence episodes fell from 3 (1–30) to zero (0–30) (N.S.). After two months of stimulation (43 girls), the median number of monthly nocturnal incontinence episodes decreased from 14.5 (3–27) to 7.5 (2–28) ($p < 0.001$), and the median number of daytime incontinence episodes decreased from 5 (1–28) to zero (0–26) ($p < 0.01$).

The changes in clinical parameters observed after the treatment did not differ significantly between the two groups with one or two months of MES (p = N.S.).

One month after the termination of treatment, all patients had altered cystometric parameters as compared to the pre-treatment values. In the one-month group only the number of involuntary detrusor contractions changed significantly (from 3 to 1, $p < 0.05$) (Table 2). In the two-month group there was a significant change in the number of involuntary detrusor contractions (from 2 to 0, $p < 0.01$) as well as in the maximum cystometric capacity (from 250 to 280 ml, $p < 0.001$) and compliance (from 12.5 to 20.5 ml/cm, $p < 0.001$) (Table 3). However, the changes in these parameters did not differ significantly either between the two groups.

Twelve patients (5 in one-month group and 7 in two-month group) developed severe anal pain or diarrhoea during the treatment. None of the patients terminated the treatment prematurely because of side effects or technical problems.

Discussion

Very little data on the effectiveness and safety of anal MES in children with overactive bladder and on different clinical problems can be found in the literature. We have published some results of MES in children with overactive bladder and micturition problems, urinary tract infection, and vesicoureteral reflux (VUR).[5,9,10] In a placebo-controlled prospective randomised study, we found that anal MES was clinically and urodynamically effective in children with overactive bladder and micturition difficulties.[6] However, the optimal duration of stimulation and intervals between individual treatment sessions for this population has not been established.

Anogenital MES is a common method of treating stress or urge incontinence in adults, and different protocols have been reported

Table 3: Urodynamic findings before and after two months of treatment with anal MES in 43 girls with nocturnal enuresis and/or daytime incontinence and detrusor instability.

Urodynamic variables	Before MES mean (range)	After MES mean (range)	P value
First desire to void (ml)	100 (50–250)	120 (60–220)	N.S.
Maximum cystometric capacity (ml)	250 (100–420)	280 (120–450)	< 0.001
Compliance (ml/cm)	12.5 (2–100)	20.5 (2–220)	< 0.001
Number of involuntary detrusor contractions	2 (1–21)	0 (1–13)	< 0.01

in the literature. Godec et al. recommended no more than four to five perineal MES treatments, lasting 15 to 20 minutes each and given every two to three days.[11] Plevnik et al. found that in some patients with micturition disorders, the most noticeable improvement occurred after the first few treatment sessions; nevertheless, these authors felt that the stimulation should be continued for a month because its favourable results would then persist even a year after the end of treatment.[12] Nakamura et al., treating 21 patients with urge incontinence, used one to five MES sessions lasting 20 to 30 minutes each, distributed over a period of one month.[13] Esa et al. treated micturition problems in 48 patients with 20 MES sessions lasting 30 minutes each, administered at intervals of three to seven days.[14] Primus and Kramer recommended at least 10 treatment sessions for adult incontinent patients.[15] Siegel et al. found no significant difference in the treatment outcome when MES was administered daily or every second day.[16] Fehrling et al. published the results of 10 applications of MES, using the highest tolerable amplitude, in 60 adult patients with an overactive bladder.[17]

As for the relationship between the effects of anal MES and the duration of treatment in children, we can rely merely on our experience. In a previous study, we treated 53 mixed enuretics with five to 10 MES sessions administered at intervals of one week.[5] The clinical results were similar to those obtained in a subsequent study, in which children received 20-minute daily treatments over a period of one or two months.[6]

In our present study, we compared the clinical effects of one- and two-month courses of MES in 73 girls with micturition disorders. The group treated for two months had somewhat better results (statistically significant improvement in nocturnal and diurnal incontinence) than the group treated for only one month (significant improvement in nocturnal incontinence only). However, the difference in clinical outcome between the two groups was not statistically significant.

Gladh et al. published the clinical results of anogenital electrical stimulation in 48 children aged five to 14 years with overactive bladder and urge incontinence.[7] The treatment was limited to two or three sessions per week to avoid psychological stress. It was continued until the effects were optimal. All children started the treatment at the clinic, where the median number of sessions was nine (4–20). Thirty-one children continued with the stimulation at home for another 25 (5–96) sessions.

Both groups of children in our present study had improved urodynamic parameters after treatment with MES. The group treated for two months had somewhat better cystometric results after the treatment than the group treated for only a month, but the difference in urodynamic improvement between the two groups was not statistically significant.

In our previous study, a significant improvement in first desire to void and maximum bladder capacity occurred after six MES sessions in all enuretic subjects, and their detrusor hyperactivity was reduced by more than 50 per cent. In two enuretic patients, a significant increase in maximum capacity was attained with a single MES treatment.[18]

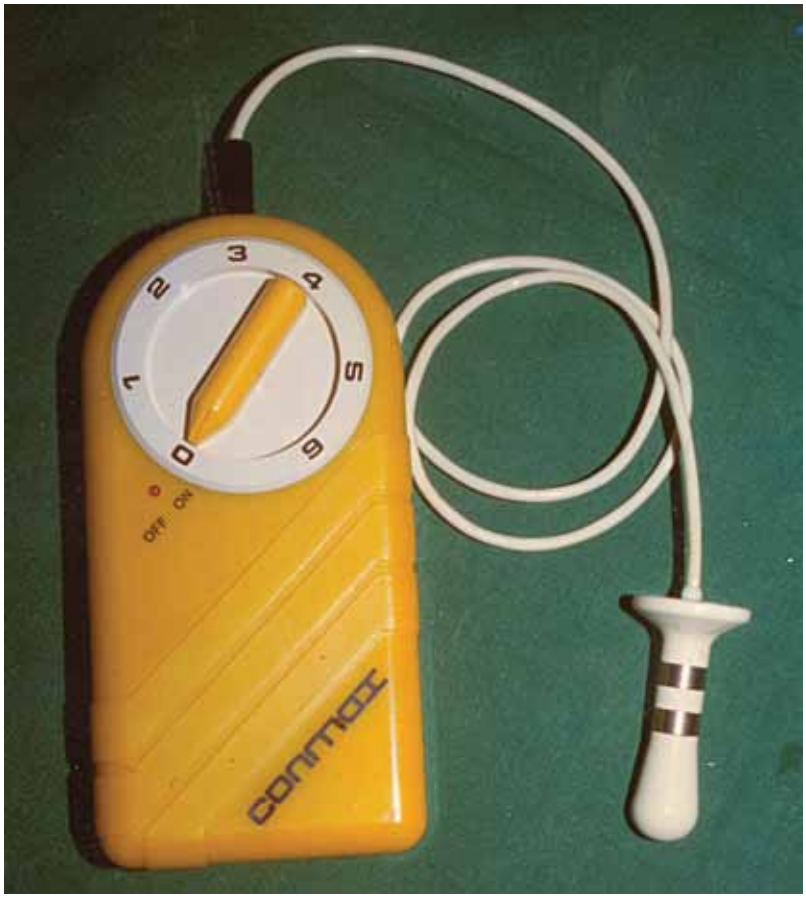

Figure 1: Electrical stimulator with anal plug.

Similar results of short-term MES were recorded by other authors treating adult patients with unstable bladder and urge incontinence. Ohlsson et al. achieved a statistically significant increase in maximum cystometric capacity (≥ 50 ml) in 4 of 21 patients with urge incontinence, and suppression of involuntary detrusor contractions in 2 of 6 patients with detrusor instability after only four MES treatments administered over a period of one week.[19] Janež noted intensified first desire to void and increased maximum cystometric capacity after 5 to 10 MES treatments; four of the five female patients with urge incontinence showed reduction in detrusor contractility.[20]

In our present study of MES in children with overactive bladder and micturition problems, the urodynamic findings in patients treated for two months were not statistically significantly better than those obtained in patients treated for only one month. These results may suggest that the clinical and urodynamic outcome in these patients also depends on some disturbances of neurologic control of the lower urinary tract rather than on the duration of stimulation. The efficacy of treatment with MES could be explained by well-known »peripheral« effects of electrical stimulation, i.e. hypertrophy of the closing mechanism of the urethra and changes of the bladder, as well as by less clear »central« effects, which seem to be able to replace the lost physiological neural control of micturition.[21,22] These »central« effects of stimulation include control of the threshold for micturition, adaptation of detrusor contractility and/or closing mechanism of the urethra, as well as restoration of the lost coordination of micturition.[23] Anyway, we have to admit that up to now we still have not found a proper mechanism for explaining long-term efficacy of MES. In some patients, just a few MES sessions are sufficient for lasting bladder inhibition. Bearing this in mind, we can often spare the treated child many unpleasant effects of MES and, at the same time, reduce the costs of therapy. If no improvement occurs after three to four months of MES, further stimulation is not recommended.[7]

It must be emphasized that the children in our study underwent MES only after failing to respond to other forms of treatment. All children had been treated with a bladder–training regimen, and nocturnal enuretics had received desmopressin. Only a small number of our patients had been treated with anticholinergics because many parents would not consent to medical therapy for their child's micturition problem.

Most children tolerated MES well with no major side effects. Only 12 children reported some anal pain or increased defecation frequency on treatment days. No one had to terminate the procedure prematurely. There were no significant differences in the number or severity of side effects between the groups stimulated for one and two months.

The children in our study were followed for only one month after the last MES session. Consequently, our results are limited to the short-term clinical and urodynamic outcomes of MES in our patients. No objective data on possible subsequent relapse of their micturition problems are available. Another

major weakness of our study is the relatively small number of patients.

Conclusions

MES appears to be an effective method for treating micturition problems in children with overactive bladder. In our study patients treated for two months with anal MES had somewhat better clinical and cystometric results compared to the group treated with MES for only one month but the difference between these two groups was not statistically significant.

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