Original article

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Altered Bladder and Bowel Function Following Cutaneous Electrical Field Stimulation in Children with Spina Bifida – Interim Results of a Randomized Double-Blind Placebo-Controlled Trial

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Summary

Bladder and bowel dysfunction in spina bifida are the result of abnormal electrical input, secondary to the neurological lesion of the spinal cord. Experimental attempts to correct this deficit with invasive electrical stimulation have demonstrated promising effects, as has a recent preliminary study of transcutaneous electrostimulation in children with myelomeningocoele.

A randomized controlled trial of non-invasive electrical stimulation in children with neuropathic bladder and bowel has been established. Interim results of 50 patients are presented. Treatment was performed at home for one hour daily for a mean period of 45 days. The only statistically significant difference between the active and placebo-groups was a 32% relative decrease in night-time urinary incontinence, favoring the placebo group. However there were non-significant trends of preferential improvement in the active group for the relative increases in maximum and average bladder content and episodes of spontaneous normal defecation. It is anticipated that a continued increase in patient numbers will overcome the large placebo effect observed and yield more significant results.

Key words: Spina Bifida – Bladder dysfunction – Neuropathic bladder – Urinary incontinence – Urodynamics – Bowel dysfunction – Neuropathic bowel – Faecal incontinence – Electrical stimulation

Introduction

Dissociation of the bladder and hindgut in spina bifida from central nervous system control may produce physically and socially disabling incontinence and constipation. Many affected children suffer ongoing upper urinary tract deterioration requiring operative intervention. Therefore any conservative therapy which reduces the need for life-long medication, frequent prolonged hospitalisation or major surgery would be a significant advance.

Experimental attempts to restore the electrical *milieu* of the neuropathic bladder by electrical stimulation began in the 1950's. The technique has since been employed in human and animal bladder and bowel dysfunction of various aetiologies and may be of benefit (3–9, 12–15, 19–20). Electrodes are either inserted into the vesical or rectal lumina (7–9), implanted directly into the bladder or rectal muscle-walls (20), the pelvic floor (14) or around the spinal cord (3), sacral (4, 13) or pelvic (6) nerves. However, the mode of action of such therapy is poorly understood and the data are sometimes conflicting (16). This may be related to poorly controlled experimentation and a lack of quantification of results. That electrical stimulation has a physiological effect is suggested by an increase in the level of various bladder enzymes (12, 19). *Kaplan* et al have revived interest in the use of electrostimulation in children with spina bifida, publishing a series which revealed significant increases in bladder capacity with maintenance of low filling pressures (7).

Surprisingly the use of *non-invasive* skin electrodes has received little attention since a Japanese trial over twenty years ago (15). The technique is used in some adults with urinary and fecal incontinence, particularly on the basis of pelvic floor weakness. Recently, a preliminary study in children with spina bifida reported elimination of fecal incontinence in half of the six subjects after six months of sacral cutaneous electrostimulation (5). Therefore an objective assessment of neuropathic bladder and bowel function in children following non-invasive electrical stimulation has been established.

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Methods

The study group is selected from a pool of approximately two hundred males and females aged 4- to 18-years who regularly attend the multidisciplinary Spina Bifida clinic at the Royal Belfast Hospital for Sick Children. No volunteers are excluded, except those with demand-pacemakers (the only contra-indication). Informed written consent is obtained. Each patient's pre-entry treatment remains unaltered.

On entry to the study parents and/or patients complete a one-week diary detailing daily episodes of normal micturition and defaecation, incontinence, urine volumes, and faecal bulk and consistency.

The child undergoes baseline video-urodynamic studies on an UIS 6000 machine (Lectromed, Letchworth Garden City, England).

Electrical stimulation is performed at home for one hour daily for at least six weeks, using a "Duet Continence Stimulator" (Dynamic Medical Instruments Ltd., Wigan, England; conforming to British Standard 5724; battery-powered; 10 × 6 × 3 cm). Electric current is automatically delivered in an asymmetrical biphasic waveform at 10 hertz with a pulse-width of 200 microseconds (mimicking normal physiology) for 2 seconds on / 2 seconds off. Half the patients are randomly double-blindly allocated (by computer) to receive instead placebo "stimulation" by equipment that delivers no impulse but is otherwise identical. After application of electrode gel, one electrode (4 cm^2, silicone rubber) is placed on the pre-sacral skin over the S 2/3/4 nerve roots (which supply the pudendal and pelvic nerves to the bladder, rectum and their respective sphincters) and is secured with surgical adhesive tape. Rather than locate the second electrode (3 × 5 cm, self-adhesive) over the anal orifice, as per the Liverpool technique (5), we use the perineal skin, with the aim of producing a field-effect on the bladder as well as the anorectum.

The patient and parents are instructed to increase the current amplitude up to the maximum level, or until the patient is only just aware of an effect (e.g., tingling or buzzing sensation at the electrode sites or a distal muscle contraction). Once established, patients are able to work, rest or play without distraction during treatment. Compliance is encouraged by regular telephone contact with the families, and later confirmed by testing the remaining charge on all batteries used: even placebo-units drain batteries at a predictable rate.

Children are reviewed after at least six weeks and the treatment terminated. The patient completes another one-week diary. Repeat video-urodynamics are performed, by the same observer as pre-treatment to minimise variability.

For every patient the proportional change in each urodynamic and diary parameter is calculated, and these changes are assembled together into active- and placebo-groups (on an "intention to treat" basis). The mean change of each parameter for the active-treatment group is then compared with that for the placebo-group. The parametric end-points are analysed with the Independent-Samples t-test, and categorical end-points with the Mann-Whitney U-test, using a computerised statistical software package (SPSS for Windows©).

Results

Of 50 participants so far, 29 (58%) were male and 21 (42%) female. Age at entry to the trial ranged from 4.3–18.2 years (mean = 9.1, standard deviation = 3.4). Active electrostimulation was performed by 26 patients (52%), while 24 (48%) received placebo units. The duration of electrical stimulation ranged from 0–97 days (mean = 44.9, standard deviation = 18.9) and was normally distributed. Before- and after-treatment urodynamic data were available for 47 patients, and reliable comparative diary data for 35 cases.

There was no significant difference between the active- and placebo-groups for any confounding factors (e.g., age at entry, weight, severity of neuropathy, degree of educational delay, or duration of and compliance with electrical stimulation).

No significant difference was exhibited between the active- and placebo-groups in any urodynamic parameter, i.e., relative change in: compliance, pressure-specific bladder volumes at 10, 20, 30 and 40 cm H_2O respectively, maximal detrusor pressure (MDP), bladder volume at MDP, maximum bladder capacity, maximum bladder capacity as a percentage of predicted bladder capacity for age, voided volume, maximum voiding flow rate and maximal voiding detrusor pressure. However in one patient unilateral grade II vesico-ureteric reflux, seen during his baseline video-urodynamic study, was no longer apparent after active electrical stimulation.

Urinary diaries revealed a significant 32% difference in the relative decrease in episodes of night-time urinary incontinence, favouring the placebo group ($p < 0.02$). The mean relative change in both the maximum and average bladder content was 100% and 47% greater respectively in the actively-stimulated group compared to the placebo group, but this was not significant. There was no significant difference between the active and placebo groups for the relative change in the number of episodes per week of day-time or day-and-night urinary incontinence.

The mean relative change in episodes of spontaneous normal defaecation (i.e., deliberate unaided events on the toilet) was 49% greater in the active-group than in the placebo group, but this was not significant. There was no significant difference between the active and placebo groups in any other bowel-diary measures (i.e., relative change in the number of episodes per week of day-time, night-time or day-and-night fecal incontinence).

When the data for all patients, whether in the active or placebo group, were collected together, a non-significant trend of improvement between the before- and after-treatment values was observed (confirmed by the paired samples t-test) for most parameters.

Discussion

The only statistically significant difference was in the relative decrease in night-time urinary incontinence, favouring the placebo group. However there were encouraging trends of improvement in the active group compared to the placebo group observed for relative increase in maximum and average bladder content and episodes of spontaneous normal defaecation.

The lack of statistically significant results in this interim analysis is probably multifactorial. Such a project must involve a heterogeneous group of children with a wide range of ages, degrees of bladder and bowel dysfunction, pre-entry treatment schedules, motivation and parental support. Such variation may be responsible for the wide statistical confidence-intervals observed, necessitating a much larger collection of patients in each group: a numbers-calculation, based on the variability of responses seen in an initial pilot study of twenty patients, suggests a sample size of approximately 100 cases will be required to generate statistically significant data. The general improvement in both objective and subjective measures seen in the actively treated group for most parameters has been partially hidden by the improvement also seen in the placebo-group. This effect may reduce as the patient-numbers continue to increase, but it illustrates the importance of randomised controlled trials of any treatment applied to such a diverse group of patients. This is particularly relevant for subjects at an age where bladder and bowel control may improve spontaneously with time. Parents of children with a disability such as spina bifida are often highly motivated so that bladder or bowel function may temporarily appear to improve as a result of the strict daily schedule and the encouragement that participation in this project imposes.

The apparent discrepancy between the promising preliminary data presented by *Holmes* et al (5) and our results may in part be explained by some of the above factors. It may also be due to minor differences in technique (particularly the placement of the distal electrode) or our shorter treatment duration.

The authors' anecdotal impression is that, for most individuals, subjective bowel function improves more than that of the bladder. Both organs should be stimulated equally by such direct nerve-root stimulation. This suggests that the bowel may be more sensitive to the effects of electrostimulation than the bladder. Alternatively, because of the position of the distal electrode, the bowel may preferentially receive additional electrical input via field-stimulation, whereby signals pass directly through all the tissues that lie between the two electrodes (rather than merely along the nerve roots).

In-vitro studies have shown that the bladder and/or rectum in spina bifida and other neuropathic conditions are intrinsically different from those of normal cases morphometrically, microscopically, physiochemically, and electrically (2, 11, 18). It is postulated that the absence of the usual incoming basal "electrical nutrition" is detrimental to gross and cellular bladder and bowel structure. This may then render them unable to respond appropriately to the stimulus of filling. Conversely, some children with spina bifida also have an excess of inappropriate spontaneous reflex activity from the isolated distal spinal cord (1, 17), producing high-pressure uninhibited detrusor contractions. If the increase in bladder volume that these results suggest is confirmed, it is conceivable that either imitation of the absent inhibitory impulses or anodal blocking (10) of the deleterious impulses to the bladder may be responsible.

The expectation is that cutaneous electrostimulation will improve bladder and bowel dysfunction in *some* children with spina bifida. This may depend on the neuropathic severity / the anatomical level of the lesion, on the age of an individual patient, or on other factors. Sub-group analysis may later allow prediction-criteria for which children are most likely to benefit from this treatment, but patient numbers are currently insufficient for this.

These interim results encourage continuation of the trial. If final results are sufficiently promising there is scope for evaluating the same technique in adults with spina bifida, as well as both children and adults with cerebral palsy, spinal injury and other neuromuscular disorders. It is

suspected that some patients with enuresis, encopresis, and idiopathic or post-surgical constipation may actually be suffering the effects of an occult neuropathy, hence they too may benefit from such electrical therapy.

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Abstract

Segmental Vertebral Malformations with Rare Forms of Neural Tube Defects

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Patients with spondylocostal dysostosis, spondylothoracic dysostosis and *Jarcho-Levin* syndrome present with variable associations of dysmorphic facies, short neck, dwarfism and deformed trunk. We report on seven cases of spondylocostal dysostosis associated with rare forms of neural tube defects: three patients had segmental spinal dysgenesis, two siblings had caudal regression syndrome, one case had diastematomyelia and one had anterior meningocele. Only fourteen cases of segmental spinal dysgenesis have been previously reported, none with spondylocostal dysgenesis. Our observation of three cases with both unusual entities suggests that the association may occur more often than suspected and may be substantially underdiagnosed. Animal models for costo-vertebral anomalies and for some forms of spina bifida exist and specific mutations have been associated with each. It is possible that genetic studies in humans with these unusual anomalies of ribs and spine could lead to a more precise delineation of the complex clinical entities and explain the timing of the developmental defects.