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Transabdominal electrical stimulation increases colonic propagating pressure waves in paediatric slow transit constipation☆,☆☆,★

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Abstract

Background and aims: In slow-transit constipation (STC) pancolonic manometry shows significantly reduced antegrade propagating sequences (PS) and no response to physiological stimuli. This study aimed to determine whether transcutaneous electrical stimulation using interferential current (IFC) applied to the abdomen increased colonic PS in STC children.

Methods: Eight children (8–18 years) with confirmed STC had 24-h colonic manometry using a water-perfused, 8-channel catheter with 7.5 cm sidehole distance introduced via appendix stomas. They then received 12 sessions (20 min/3× per week) of IFC stimulation (2 paraspinal and 2 abdominal electrodes), applied at a comfortable intensity (<40 mA, carrier frequency 4 kHz, varying beat frequency 80–150 Hz). Colonic manometry was repeated 2 (n=6) and 7 (n=2) months after IFC.

Results: IFC significantly increased frequency of total PS/24 h (mean±SEM, pre 78±34 vs post 210±62, p=0.008, n=7), antegrade PS/24 h (43±16 vs 112±20, p=0.01) and high amplitude PS (HAPS/24 h, 5±2:10±3, p=0.04), with amplitude, velocity, or propagating distance unchanged. There was increased activity on waking and 4/8 ceased using antegrade continence enemas.

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Conclusions and inferences: Transcutaneous IFC increased colonic PS frequency in STC children with effects lasting 2–7 months. IFC may provide a treatment for children with treatment-resistant STC.

Many children with chronic constipation respond to medical therapy and behavioural modification programmes, but 1/3 remain constipated into adulthood [1]. Constipation may be caused by slow colon transit (slow-transit constipation, STC), diagnosed via radio-nuclear or sitz (plastic) marker colon transit studies [2-4]. In STC, soiling and fecal impaction have significant social and emotional consequences for the child and family, resulting in a low quality of life (QOL) [5].

Children with STC can be managed by antegrade continence enemas (ACE) [6], and we have previously reported the analysis of colonic motor activity performed by inserting the manometry catheter via the appendix stoma [7,8]. Significant abnormalities in colonic motor function were identified, including reduced frequency of antegrade propagating sequences (PS) and lack of response to meals and waking.

Transcutaneous electrical stimulation using interferential current (IFC) has been used for pain management [9] and urinary incontinence, with diarrhoea reported as a side effect [10,11]. IFC increased defecation frequency in children with chronic constipation [12] and reduced colonic transit times in STC [13,14]. Symptom improvement lasted 3–6 months in 1/3 and more than 2 years in 1/3 of patients [15,16]. The aim of this study was to determine the effects of IFC upon colonic PSs. Specifically, we hypothesised that IFC increases the frequency of PS in children with STC.

1. Methods

Children (n=62) with STC were recruited during a larger randomised control trial (Ethics: HEC 23040C) [13,14]. Thirteen of these children had appendix stomas, and 8/13 volunteered for colonic manometry forming the cohort of this study.

All 8 children had >2 years chronic constipation that had not responded to medical therapies (diet, laxatives, behaviour modification). STC was diagnosed by radionuclear transit studies (defined by retention of radioisotope in the ascending/transverse colon) performed within the previous year [17]. Patients had existing appendix stomas placed more than 6 months before the study. All had long-standing constipation (6–19 years of symptoms). Half had symptoms since birth. Most had soiling but only 2 had daily soiling. For management, they performed antegrade continence enemas to wash out their colons every second day and recorded 3–4 defecations/week.

1.1. IFC Stimulation

Briefly, physiotherapists were provided with IFC machines (Vectorsurge 5 VS470, Metron Medical, Carrum Downs, Victoria, Australia) that delivered two channels of alternating current. One at a fixed frequency (4 kHz), whilst the other varied from 4080 to 4150 Hz, producing a varying beat frequency of 80 to 150 Hz. The current (<40 mA) was applied via 4 self-adhesive conducting electrodes (40 mm×40 mm, Verity Medical Ltd, Hampshire, England),with 2 paraspinal (T9-L2), and the paired electrodes positioned diagonally opposite on the anterior abdominal wall below the costal margin [12]. Current was applied just at the sensory level and sub-motor intensity so children felt no more than low sensory stimulation and no skeletal muscle contractions occurred. IFC stimulation was given for 20 min, ×3/week for 4 weeks.

1.2. 24-h colonic manometry

Eight children had 24-h colonic manometry immediately before electrical stimulation and 2 months (n=6, 5 male, 9–19 years) or 7 months (n=2, 1 male, 16–18 years) after completing stimulation. Patients ceased washouts 5 days before and during the manometry. Manometry was performed as previously described [7]. Briefly, an 8-channel multi-lumen catheter with 7.5 cm sidehole spacing, was inserted via the appendix stoma and advanced anally with bisacodyl infusion (2.5 ml of 0.5 mg/ml solution). The catheter position was established by fluoroscopy. Water was perfused at 0.25 ml/min. Polygram software (Medtronic Australasia, Gladesville, NSW, Australia) was used for recording, commencing 24 h after bisacodyl [7], with children remaining in bed for 24 h. They drank water and ate a meal of 17% protein, 34% carbohydrate and 48% fat, with 1255 kJ for breakfast, 4184 kJ for lunch and 4184 kJ for dinner. They completed an event diary recording eating, postural changes, sleep/waking, urine and defecation, abdominal sensation and flatus. After 24 h, 20 min of electrical stimulation was applied.

Colonic motility studies were examined and analysed visually, as previously described [7] to identify antegrade PS, retrograde PS and high amplitude PS, the latter defined as >116 mmHg in 3 adjacent channels (shown as ‘extent’ in Table 1). Frequency, amplitude and velocity of PS and distance travelled were compared before and after stimulation for each patient (paired t-test). Linked PSs were identified. Sequential PSs were defined as being ‘regionally-linked’ if they started at different side-holes, were in the same direction and had overlapping side-hole

Table 1 Frequency, extent and velocity of propagating sequences.

A. APS		Frequency/wk			Extent (side-holes)		Velocity (cm/s)	
Pt #		Pre	Post	% change	Pre	Post	Pre	Post
1	2 mth	26	93	358	4	3	0.83	2.15
2	2 mth	1	128	12800	8	3	4.77	2.01
3	2 mth	31	57	184	3	3	1.7	1.18
4	2 mth	61	155	254	3	3	1.66	1.41
5	2 mth	128	140	109	3	3	2.35	1.67
6	7 mth	11	35	318	5	3	0.7	1.1
7	7 mth	40	175	438	4	4	2.5	1.1
	mean	43	112	2066	4.3	3.1	2.07	1.52
	SD	42	52	4735	1.8	0.4	1.37	0.44

B. HAPS		Frequency/wk			Extent (side-holes)		Velocity (cm/s)	
Pt #		Pre	Post	% change	Pre	Post	Pre	Post
1	2 mth	13	18	138	4	3	0.96	1.05
2	2 mth	3	14	467	5	7	0	2.68
3	2 mth	10	16	160	7	4	0.6	0.89
4	2 mth	2	8	400	6	8	1.17	1.27
5	2 mth	0	0	0	0	0	0	0
6	7 mth	6	3	50	5	3	0.8	0.4
7	7 mth	0	11	1100	0	5	0	1.1
	mean	5	10	331	3.9	4.3	0.50	1.06
	SD	5	7	381	2.8	2.7	0.50	0.84

C. RPS		Frequency/wk			Extent (side-holes)		Velocity (cm/s)	
Pt #		Pre	Post	% change	Pre	Post	Pre	Post
1	2 mth	0	20	2000	3	6	0	2.81
2	2 mth	4	37	925	3	3	2.08	1.31
3	2 mth	7	14	200	3	3	2.4	1.66
4	2 mth	53	78	147	3	3	1.98	1.53
5	2 mth	134	384	287	3	3	1.57	1.97
6	7 mth	6	19	317	3	4	1.5	1
7	7 mth	41	124	302	5	4	2.1	2.2
	mean	35	97	597	3.3	3.7	1.66	1.78
	SD	48	133	671	0.8	1.1	0.80	0.60

D. Frequency of total colonic propagating sequences					E. APS:RPS ratio		
Pt #		Total Pre	Total Post	% change	Pre	Post	Change
1	2 mth	26	113	435	26	4.65	0.2
2	2 mth	5	165	3300	0.25	3.46	13.8
3	2 mth	38	71	187	4.43	4.07	0.9
4	2 mth	114	233	204	1.15	1.99	1.7
5	2 mth	262	524	200	0.96	0.36	0.4
6	7 mth	23	57	248	1.83	1.84	1.0
7	7 mth	81	310	383	0.98	1.41	1.4
	mean	78	210	708	5	3	3
	stdev	89	165	1147	9	2	5

activity [18]. If 3 or more regionally-linked PSs occurred sequentially, this was defined as a 'colonic complex'. Waking and postprandial responses were analysed using area-under-the-curve analysis.

1.3. Statistics

Samples were tested for normality and then compared pre and post TES using students t-test. $P<0.05$ was considered statistically significant. For one patient, recording stopped during the 2nd session and this patient was not included in analysis.

2. Results

Children had colonic manometry before and 2 months (n=6) or 7 months (n=2) after 1 month of IFC stimulation. Data from one time period (9 am to 5 pm) from one child 2 months after stimulation were lost, and this child is not included in the analysis of PS.

Following stimulation 5 patients had an increase in antegrade, high amplitude and retrograde PS, with the antegrade:retrograde PS ratio becoming greater than 1.0 (1.4 to 4.6, Table 1). One patient (#5) had no change in antegrade or high amplitude PS, a doubling in retrograde PS and reduction in antegrade:retrograde PS ratio. Another patient (#6) had a three-fold increase in antegrade and retrograde PS but a reduction (halving) in high amplitude PS. Results were similar for patients at 2 or 7 months post-stimulation. Table 1 shows the change in frequency of PS in 7 children, 2 months after stimulation (n=5) and 7 months after stimulation (n=2). In the combined group (n=7), there was a significant increase in frequency of antegrade, high amplitude and total PS, with a non-significant increase in frequency of retrograde PS (Fig. 1). Increases were into the normal range [7].

If data for two months after stimulation were assessed separately, there was still a significant increase in the frequency of total PS (/24 h mean±SEM, pre 89±47: post 221±80, p=0.03, n=5), antegrade PS (/24 h, 49±22:115±18, p=0.03) and high amplitude PS (/24 h, 5±3:11±3, p=0.06), compared with activity before stimulation (paired t-test). There was a non-significant increase in retrograde PS (/24 h, 40±25 pre, 107±70, p=0.22). There was no apparent change in velocity or propagating distance.

The most common site of initiation of propagation of antegrade PS was the cecum, both before and after stimulation. For retrograde PS, the most common site of initiation moved from the splenic flexure before stimulation, to the rectosigmoid after stimulation. Pre-treatment 4/5 patients had antegrade and 2/5 had retrograde colonic complexes, whilst post-treatment all 5 had antegrade and 3/5 had retrograde colonic complexes. There was no change in percent of antegrade linked-sequences (pre-treatment 65%±8%, mean±SEM, post-treatment 56%±4.5%), but unexpectedly, there was a significant decrease in retrograde linked-sequences (61%±4.5%, 33%±9.8%, p=0.04 t-test).

Data on responses to meal and waking were available for 4/6 patients given the second manometry 2 months after IFC and 2/2 patients 7 months after IFC. None of these 6 patients had an increase in high amplitude PS activity on waking before stimulation. Two months post-stimulation, there was an increase in the number of subjects showing a waking response (0/4 and 0/2 pre, 3/4 and 1/2 post). At 2 months post-stimulation, there was also a small increase in patients with an increase in high amplitude PS after a meal (3 meals, 4 subjects, 3/12 pre, 6/12 post). There was an increase in total motility index but no greater response after a meal in the 2 patients at 7 months post-treatment.

All patients were using ACE to washout the colon every 2–3 days for management. There was no difference in the number of defecations/week in the pre-treatment (mean±SEM, 3.6±0.6), treatment (3.1±0.4), 1st month post treatment (4.6±0.5) or 2nd month post treatment (3.3±0.4). However, 2/6 patients were able to defecate without the use of antegrade enemas 2 months after stimulation as were the 2 patients with 7 month follow up. Continuing to defecate without needing washouts suggests their constipation symptoms were gone.

3. Discussion

In a long-term follow-up of patients in an RCT of IFC to treat paediatric STC, 1/3 of patients had no improvement, 1/3 of the patients had improvement that lasted more than 2 years and 1/3 had improvement lasting 3–6 months [15]. In this study we examined a subset of these patients and demon-

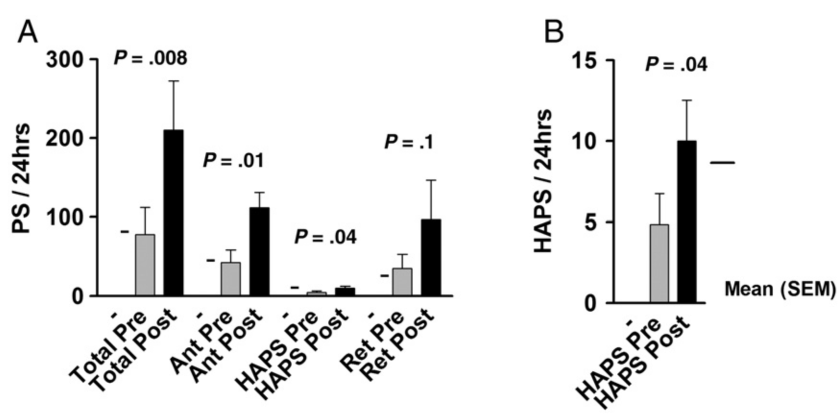

Fig. 1 Frequency of propagating sequences (PS). (A) Total, antegrade (Ant), high amplitude (HAPS) and retrograde (Ret) PS. Mean (SEM) values of all 7 patients. (B) HAPS values of all 7 patients.

strated that transcutaneous electrical stimulation using IFC increased frequency of colonic PS in 5/7 STC children.. There was also a 3-fold increase in high amplitude PS frequency. Four of 8 patients stopped using ACE, as soiling stopped. The increased activity persisted for 7 months in the 2 patients who were followed for the longer period.

Colonic PS and high amplitude PS are temporally associated with both defecation and luminal transit [19] in healthy controls. More frequent high amplitude PS after morning waking or a high calorie meal can also be used as a measure of a "normal' colonic response to physiological stimuli [7]. Adults and children with STC have an absent or diminished response to such stimuli [7,8]. An absent colonic response has been reported by some to be an indicator of an intrinsic neuropathy/mesenchymopathy [20]. Therefore as the majority of our patients demonstrated an increased frequency of PS and high amplitude PS after treatment with IFC, these data are likely to be of clinical significance.

The mechanism of action of IFC remains unclear. With the electrode positions used, the current could affect local sensory and motor nerves in the skin, spinal nerves (sensory and motor, T9 to L2), sympathetic (thoraco-lumbar) and parasympathetic nerves, enteric nerves, pacemaker cells (interstitial cells of Cajal) or smooth muscle cells in the intestinal wall. The stimulation was just at the sensory threshold and did not produce striated muscle contraction or pain, so was not stimulating A-δ or C (nociceptor/pain) fibres. The effects took months to develop and lasted for months, suggesting it was changing nerve circuits or overall neuronal health, rather than causing direct contraction of muscle.

We have previously reported on the use of IFC to treat chronic constipation [12] and STC in children [13,14,21]. Other groups have demonstrated that IFC increased gastrointestinal motility producing diarrhoea [10,11], improved gastric emptying [22], improved functional dyspepsia symptoms [23] and increased rate of swallowing [24]. Dinning et al. performed 24-h colonic manometry in 8 adults with STC during direct stimulation of sacral nerve S3 and showed there was increased pancolonic PS [25].

The electrical parameters used in this study were those previously used for bladder stimulation. Stimulation was performed by physiotherapists with patients visiting clinics 3 times a week. Following 1 month of IFC, symptoms improved over the following 2 months after stimulation, with more improvement at 7 months (both patients had stopped using their appendix stomas and doing washouts, and were defecating regularly with no impaction). We have previously reported the long-term follow-up of the randomised control trial and crossover treatment [26] and this showed that symptom improvement lasted 3–6 months or more than 2 years and that 2 months' stimulation produced greater improvement than 1 month. Following the release of battery-operated machines, daily stimulation at home was tested and this produced increased defecation [13], suggesting a dose response. Further studies on larger numbers of patients with daily stimulation for more than 2 months support that symptoms continue to improve with more stimulation [16]. Patients are accustomed to using laxatives or ACE, and graded removal of these treatments may need to be planned and measured as specific outcomes.

Unfortunately the numbers studied are small, as each study requires the family and child to spend 3 days in the hospital and few are able to do this twice. Because of the difficulties of doing this assessment, we did not attempt an RCT. We cannot discount that these changes in bowel activity could occur as a placebo or due to time. As we think it would be very difficult to perform an RCT, large animal studies may be necessary to perform an RCT.

Children with STC have reduced antegrade PS. Transcutaneous IFC 3-times a week for 1 month increased the frequency of colonic PS 3–5 fold in most of the children and increased colonic motor activity on waking and after meals. The effects persisted 2–7 months after stimulation. Further studies on larger numbers of patients are warranted to determine if IFC can provide a treatment for children with treatment-resistant STC.

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