Original Research Paper

The effect of abdominal functional electrical stimulation on bowel function in multiple sclerosis: a cohort study

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Abstract

Background: Chronic constipation is prevalent in people with multiple sclerosis, with current treatments usually only partially effective.

Objectives: This study aims to evaluate the efficacy of abdominal functional electrical stimulation to reduce whole gut and colonic transit times and improve bowel and bladder-related quality of life.

Methods: A total of 23 people with multiple sclerosis who fulfilled the Rome III criteria for functional constipation applied abdominal functional electrical stimulation for 1 hour per day, 5 days per week, for 6 weeks. Whole gut and colonic transit times and bowel and bladder-related quality of life were measured before and after the intervention period.

Results: Whole gut (mean 81.3 (standard deviation 28.7) hours pre vs. 96.1 (standard deviation 53.6) hours post-intervention, $P = 0.160$) and colonic transit time (65.1 (31.4) vs. 74.8 (51.1) hours, $P = 0.304$) were unchanged following 6 weeks of abdominal functional electrical stimulation. There was a significant improvement in bowel (mean 1.78 (SD: 0.64) pre vs. 1.28 (SD: 0.54) post, $P = 0.001$) and bladder (50.6 (26.49) vs. 64.5 (21.92), $p = 0.007$) related quality of life after the intervention period.

Conclusion: While abdominal functional electrical stimulation did not reduce whole gut and colonic transit times for people with multiple sclerosis, a significant improvement in bowel and bladder-related quality of life was reported.

Keywords: Multiple sclerosis, bowel, bladder, constipation, electrical stimulation, abdominal functional electrical stimulation

Introduction

Bowel problems including chronic constipation are estimated to affect more than half of people with multiple sclerosis (MS).[1] A primary reason for this is that MS can cause autonomic dysregulation, which can result in decreased gastrointestinal motility and colonic motor activity,[2,3] while other gastrointestinal tract abnormalities have also been reported to cause constipation for people with MS.[2,4,5] In addition, MS-related problems such as muscle weakness, fatigue, or cognitive impairment may lead to ignoring or suppressing the urge to defecate, thereby leading to constipation.[6] Pharmacological agents (such as anticholinergics and antispasmodics) frequently used in the treatment of MS symptoms can also result in constipation.[7]

Chronic constipation can cause abdominal bloating, pain and discomfort, resulting in substantial physical discomfort and psychosocial distress to the individual.[2,8] Consequently, individuals may also experience constipation-related complications including haemorrhoids, anal fissures, faecal impaction or rectal prolapse.[1] Despite the high burden of

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morbidity, there is currently a lack of well-established, effective therapies for the management of bowel dysfunction in MS.[2] At present, this chronic constipation is typically managed with a range of manual and pharmacological methods, but these interventions remain only partially effective, with little evidence to support their efficacy.[9]

In humans, defecation is initiated by straining, which involves the contraction of the abdominal muscles.[10] However, muscle weakness is a common clinical feature of MS, with weakness of the abdominal wall musculature reported in the MS population.[11,12] Transcutaneous electrical stimulation of the abdominal muscles, termed abdominal functional electrical stimulation (FES), has shown promise in the treatment of chronic constipation in people with central neurological disorders such as spinal cord injury and MS.[13–17] However, larger studies are needed to confirm the accuracy and validity of these findings. The aim of this study was to investigate the effect of abdominal FES on whole gut transit time (WGTT), colonic transit time (CTT) and quality of life in people with MS.

Methods

This was a prospective cohort study. Ethics approval was granted by the University of New South Wales human research ethics committee (HC180005) and the procedures conformed to the Declaration of Helsinki (2013). All participants provided written informed consent and the study was prospectively registered on the Australia New Zealand Clinical Trials Registry (ACTRN12618000464268).

Participants

Participants were recruited from the urology clinic at the Studdy MS Centre, Lidcombe, Sydney with the following inclusion criteria: 18 years of age or older, clinical diagnosis of MS, fulfilment of Rome III criteria[18] for functional constipation with ongoing constipation for more than 3 months, and able to eat and drink normally. The following exclusion criteria were applied: current urinary tract infection, pregnancy, history of irritable bowel syndrome, organic bowel obstruction or other gastrointestinal disorders including diverticulitis, ulcerative colitis or Crohn's disease, contraindications to FES (e.g. pacemakers), no response to abdominal FES (e.g. lower motor neuron impairment), unable to provide informed consent.

Participants' diet, medications and other treatments were not changed by the study team. Participants

were asked to document any changes in the use of bowel management strategies throughout the study.

Sample size calculation

A pilot study involving four participants with MS reported that abdominal FES improved WGTT with an effect size of 1.42.[13] The small sample size is likely to have resulted in an overestimation of effect size.[19] As such, 24 participants were required to detect an effect size of 0.71 (Wilcoxon signed rank, $\alpha = 0.05$, power 0.9).

Intervention

Abdominal FES was applied bilaterally via surface electrodes (5 cm × 10 cm; Axelgaard, USA) placed over the posterolateral abdominal wall for 1 hour per day, 5 days per week, for 6 weeks.[20] Participants were at liberty to apply stimulation at any time of day, with the time of application varying between participants. Stimulation current (20–70 mA) was adjusted to achieve a strong visible muscle contraction at a level that could be tolerated by the participant (frequency 40 Hz, pulse width 300 μs). Participants were visited at home on day 1 of the intervention, and the equipment demonstrated to them. Subsequently, abdominal FES was applied by the participants or their carers at home, with compliance monitored via a training diary. Weekly compliance rates (%) to the intervention were calculated by dividing the number of completed abdominal FES training sessions per week by 5.

Outcome measures

The primary outcome measures of whole gut and colonic transit times were measured twice, once directly before and once directly after the 6-week intervention period, using the SmartPill motility system (Medtronic, Minneapolis, USA).[21] The smart pill records pressure, temperature and pH as it passes through the gastrointestinal tract and transmits the information to a data receiver worn around the body of the participant for offline analysis.

The secondary outcome of quality of life was assessed using the patient assessment of constipation – quality of life (PAC-QOL) and incontinence – quality of life (I-QOL) questionnaires. The PAC-QOL is a 28-item questionnaire that makes use of a five-point Likert scale to assess the impact of constipation-related symptoms on quality of life, with no specific time frame specified.[22] Similarly, the I-QOL consists of 22 items and is used primarily to evaluate the impact of urinary incontinence on quality of life previously.[23] Both questionnaires

were administered before and after the 6-week intervention period.

Analysis

Whole gut and colonic transit times were computed electronically using the SmartPill MotiliGI software (MotiliGI version 3.0.20; Medtronic, Minneapolis, USA). Capsule ingestion was identified as the point at which pill temperature began to increase to body temperature. Gastric emptying was identified as the start of the first sustained increase in pH greater than 3.0. The ileo-caecal junction was identified as the point where following a gradual, consistent rise in pH there was a drop in the value of pH greater than 1.0 points. Body exit was identified by a sharp drop in temperature that coincided with a bowel movement and an abrupt loss of pressure signals.

All response scales for the PAC-QOL questionnaire for bowel constipation were re-coded to a score of 0 to 4 to ensure uniformity and consistency of scores across the various subscales. The response scale for items 25–28 (satisfaction subscale) was reversed so that lower scores represented higher levels of satisfaction and quality of life.[22] Scores for each item were then totalled for each participant and divided by the total number of items to compute the mean PAC-QOL score for constipation. A one-point decrease in total PAC-QOL scores has been shown to be clinically significant.[24] In the context of our study where mean PAC-QOL scores were calculated, a decrease in mean PAC-QOL scores by 0.0357 points would indicate clinical significance. Participants' I-QOL scores for urinary incontinence were computed by adding up individual scores of each item, subtracting the lowest possible total score, and then dividing them by the raw score range. Total scores were then multiplied by 100 to range from 0 (minimum quality of life) to 100 (maximum quality of life). A change of 2.5 in the I-QOL has been shown to be clinically significant.[25]

Statistics

All data passed the Shapiro–Wilks test for normality, thus paired t-tests were used to test for any difference between baseline and post-intervention WGTT and CTT, I-QOL and mean PAC-QOL scores. The missing measurements of gut transit times in seven participants (as marked by a '–' in the Results section) were mostly attributed to either low capsule voltages when the transition to the ileocaecal junction was uncertain, or technical faults in the data receivers, when exit time could be ascertained by visual inspection of the pill as it exited the body.

A Friedman test was used to test for any significant difference in compliance rates between each week of the intervention period. Relationships between anthropometric data (specifically, age, height, weight, body mass index and the Expanded Disability Status Scale (EDSS)) and baseline measures of constipation (CTT, WGTT and PAC-QOL), and also the relationships between the anthropometric data, baseline measures of constipation, and treatment compliance and change in gut transit times were calculated using Pearson's correlations or Spearman's rank correlations for non-parametric data. All results are reported as mean ($\pm$ standard deviation) unless otherwise stated and a P value less than 0.05 was considered statistically significant.

Results

A total of 23 participants were recruited for this study (Table 1), with recruitment stopped at this point based on a preliminary analysis of the data due to restrictions on time.

Out of the 23 participants, 19 (82.6%) successfully completed 6 weeks of abdominal FES.

Three participants dropped out due to health issues unrelated to the study. One participant withdrew due to an adverse event (reaction to the electrodes). The median weekly compliance among the 19 participants who completed the study was 100% (Figure 1). There was no significant difference ($P = 0.965$) in median weekly compliance rates across the 6-week intervention period for 18 participants who completed the intervention period. One participant who completed the intervention did not record their compliance.

Gut transit times

There was no significant change in whole gut ($P = 0.160$) and colonic transit times ($P = 0.304$) before and after 6 weeks of abdominal FES (Table 2).

Quality of life

There was a significant improvement in both constipation-related ($P = 0.001$) and urinary incontinence-related quality of life ($P = 0.007$) before and after 6 weeks of abdominal FES (Table 3).

Correlations

We found no significant relationships between anthropometric variables such as age, height, weight, body mass index or EDSS and the baseline assessments of the baseline level of constipation

Table 1. Demographics of study population (n = 23).

Age (years)	
Mean (SD) (range)	52.1 (11.4) (32–73)
Body mass index	
Mean (SD) (range)	28.2 (8.3) (20.1–56.5)
Gender	
Male	7 (30.4%)
Female	16 (69.6%)
Type of MS	
Relapse–remitting	13 (56.5%)
Secondary progressive	7 (30.4%)
Primary progressive	1 (4.4%)
Unknown	2 (8.7%)
No. of years since diagnosis	
Mean (SD) (range)	15.5 (9.0) (5–36)
Age of MS onset (years)	
Mean (SD) (range)	36.6 (11.9) (13–61)
EDSS scores	
Mean (SD) (range)	5.1 (1.7) (1.5–8)
0–4.5 (fully ambulatory)	11 (47.8%)
5–7.5 (ambulatory with aid)	10 (43.5%)
8–10 (non-ambulatory)	2 (8.7%)

EDSS: Expanded Disability Status Scale; SD: standard deviation; MS: multiple sclerosis.

(CTT, WGTT and mean PAC-QOL scores) (Table 4).

We also found no significant relationships between anthropometric data, baseline measures of constipation, or treatment compliance and the change in CTTs and WGTTs after 6 weeks of the intervention (Table 5).

Discussion

The aim of this study was to perform a practical investigation of the effect of abdominal FES on bowel and bladder function for people with MS. The application of abdominal FES for one hour per day, 5 days per week for 6 weeks did not result in a significant change in WGTTs or CTTs. However, participants reported improved bowel and bladder-related quality of life after the intervention period. As such, the effectiveness of abdominal FES to improve bowel function in MS is worthy of further exploration in a randomised controlled trial.

The finding that there was no change in WGTTs and CTTs is in contrast to a small study by Singleton et al.,[13] in which the application of 6 weeks of abdominal FES to four people with MS was reported as improving WGTTs and CTTs. Our data show wide variability in both intrasubject and intersubject gut transit times, with WGTTs ranging from 22.6 to 221.3 hours (normal range 10–73 hours for the healthy population).[18,26] It is highly likely that the
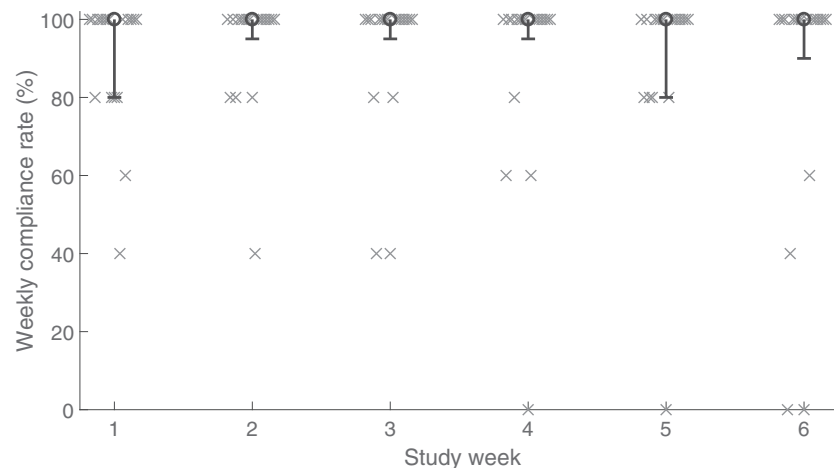

Figure 1. Compliance with the intervention of 18 participants who completed the intervention. Individual participants' compliance rates (grey cross) and overall median weekly compliance rates (black circle) to abdominal functional electrical stimulation (FES) during the 6-week intervention period are shown. Error bars represent the interquartile range. One participant who completed the intervention did not record their compliance.

Table 2. Participants' whole gut transit times and colonic transit times before (baseline) and after (post-FES) 6 weeks of abdominal FES.

Participant	Whole gut transit time (hours)				Colonic transit time (hours)			
	Baseline	Post-FES	Δ	P value	Baseline	Post-FES	Δ	P value
1	68.5	Withdrew			44.9	Withdrew		
2	97.8	159.8	+62.0		75.7	136.9	+61.3	
3	100.9	Withdrew			78.0	Withdrew		
4	102.9	71.3	−31.6		96.4	58.7	−37.7	
5	128.5	Withdrew			–	Withdrew		
6	71.0	128.5	+57.5		44.8	118.0	+73.2	
7	47.8	22.6	−25.3		26.6	14.7	−11.9	
8	81.8	113.6	+31.8		55.3	91.7	+36.4	
9	74.3	55.0	−19.3		63.1	–	–	
10	114.5	221.3	+106.7		100.2	208.4	+108.2	
11	82.3	44.8	−37.5		–	30.0	–	
12	43.2	79.3	+36.2	**0.160**	35.2	67.9	+32.7	**0.304**
13	136.0	39.8	−96.3		126.1	27.8	−98.3	
14	32.3	51.2	+18.9		13.6	27.8	+14.2	
15	64.7	74.3	+9.6		56.4	57.4	+1.0	
16	50.9	42.0	−8.9		–	26.0	–	
17	70.0	Withdrew			59.0	Withdrew		
18	114.8	98.7	−16.1		104.7	74.8	−29.9	
19	117.5	121.5	+4.0		96.5	–	–	
20	78.3	187.8	+109.4		–	–	–	
21	79.4	122.1	+42.7		72.7	101.2	+28.5	
22	42.0	67.2	+25.2		22.3	50.2	+27.9	
23	70.6	125.2	+54.6		–	106.1	–	
Mean (SD)	**81.3 (28.7)**	**96.1 (53.6)**	**+17.0 (50.7)**		**65.1 (31.4)**	**74.8 (51.1)**	**+15.8 (53.1)**	

FES: functional electrical stimulation; SD: standard deviation.
'–' represents data loss due to equipment failure.
Note: significance of boldface values is to-improve-presentation

recruited trial participants ($n = 23$), although having met the Rome III criteria for functional constipation, had varied underlying pathophysiological mechanisms that contributed to their symptoms of constipation.[2,27] The intrasubject variability is likely to be associated with intrinsic, physiological factors of the human gut, which has been documented in previous studies.[28] While unlikely to be due to a relatively short follow-up time, variability in both WGTTs and CTTs may also be attributed to lifestyle factors such as changes in fluid intake, diet, exercise and/or laxative use. While a diary to record medication use was provided to participants, compliance was so low that the data could not be analysed.

There were no significant relationship between participants' individual baseline characteristics (age, body habitus, level of disability) and constipation severity (assessed by gut transit times and quality of life). This

is not surprising, given the multifactorial aetiology of constipation in MS and the complex interplay between causative factors that contribute to the underlying pathophysiology of constipation in MS. Notably, we found a significant correlation between average weekly compliance rates and changes in CTTs ($P = 0.026$). Contradictory to our hypothesis, our results indicate that participants with lower compliance rates had a greater reduction in CTTs. This significant finding is more likely to be reflective of the wide intraparticipant variability in gut transit times (measured at different time periods), rather than any actual effect of compliance on gut transit time. In addition, these correlation analyses are exploratory at best, and it is important to take into account the potential for confounding in these analyses.

It is possible that abdominal FES may be an effective treatment modality for constipation in a

Table 3. Bowel and bladder-related quality of life before (baseline) and after (post-FES) 6 weeks of abdominal FES.

Participant	PAC-QOL bowel constipation				I-QOL urinary incontinence			
	Baseline	Post-FES	Δ	*P* value	Baseline	Post-FES	Δ	*P* value
1	1.71	Withdrew			26.14	Withdrew		
2	3.00	2.11	−0.89		10.23	37.50	+27.27	
3	1.43	Withdrew			48.86	Withdrew		
4	2.36	1.39	−0.97		51.14	54.55	+3.41	
5	1.00	Withdrew			12.50	Withdrew		
6	1.25	1.68	+0.43		52.27	47.73	−4.55	
7	1.50	1.21	−0.29		65.91	63.64	−2.27	
8	2.57	1.96	−0.61		22.73	30.68	+7.95	
9	2.50	0.86	−1.64		26.14	77.27	+51.14	
10	0.93	1.00	+0.07		75.00	78.41	+3.41	
11	1.29	0.43	−0.86		71.59	100.00	+28.41	
12	2.79	2.29	−0.50	**0.001**	22.73	26.14	+3.41	**0.007**
13	1.39	0.86	−0.54		56.82	80.68	+23.86	
14	1.86	1.82	−0.04		48.86	53.41	+4.55	
15	2.18	1.64	−0.54		18.18	43.18	+25.00	
16	1.82	0.86	−0.96		68.18	81.82	+13.64	
17	Withdrew				Withdrew			
18	0.50	1.11	+0.61		76.14	64.77	−11.36	
19	1.71	1.61	−0.11		100.00	100.00	+0.00	
20	1.79	1.18	−0.61		42.05	62.50	+20.45	
21	1.93	0.64	−1.29		73.86	79.55	+5.68	
22	2.36	0.46	−1.89		–	78.41	–	
23	1.32	1.18	−0.14		93.18	–	–	
Mean (SD)	**1.78 (0.64)**	**1.28 (0.54)**	**−0.57 (0.64)**		**50.60 (26.49)**	**64.46 (21.92)**	**+11.76 (15.65)**	

FES: functional electrical stimulation; SD: standard deviation; PAC-QOL: patient assessment of constipation – quality of life. I-QOL: incontinence quality of life.
'–' indicates participants who did not complete the questionnaire.
Note: significance of boldface values is to-improve-presentation.

particular subgroup of patients with certain demographic or clinical characteristics. As abdominal FES causes a contraction of the abdominal muscles, it may be more likely to have a positive effect in people with slow- transit constipation due to the association between electrical stimulation of the abdominal wall musculature and improved CTTs, which has previously been demonstrated in cats and in people with central neurological disorders such as spinal cord injury and MS.[13,17,29] Consequently, abdominal FES may be less likely to relieve constipation due to functional obstruction caused by pelvic floor dyssnergia. Given that there are many variations in the underlying pathophysiological mechanisms of chronic constipation in persons with MS,[30] it may be worthwhile evaluating other outcomes of bowel function in future studies, such as time to first stool, number of defecations per week, changes in anal and rectal pressures, or changes in abdominal muscle mass.[16,31]

Despite the intervention leading to no significant difference in WGTTs and CTTs, participants reported improved quality of life. Mean PAC-QOL scores in our study cohort decreased by an average of 0.57 points (clinically significant threshold of 0.0357 points), while I-QOL scores increased by 11.76 points (clinically significant threshold of 2.5 points) after the intervention. This indicates that gut transit times may not be the sole indicator of the severity of constipation in people with MS. Abdominal FES has been reported to have helped relieve the physical discomfort and symptoms associated with constipation, thereby improving quality of life and overall wellbeing in individuals with MS.[14]

Limitations
The limitations of this study include the lack of a placebo control group. The SmartPill wireless

Table 4. Correlation between study variables.

Variables		Baseline CTT ($n = 18$)	Baseline WGTT ($n = 23$)	△CTT ($n = 13$)	△WGTT ($n = 19$)	Mean baseline PAC-QOL ($n = 22$)
Age	Pearson's r	−0.360	−0.349	0.444	0.431	−0.225
	(95% CI)	(−0.673, 0.065)	(−0.639, −0.036)	(−0.069, 0.769)	(0.009, 0.728)	(−0.647, 0.237)
	P value	0.142	0.103	0.128	0.065	0.315
Height (m)	Pearson's r	0.004	−0.232	0.097	0.047	0.051
	(95% CI)	(−0.514, 0.552)	(−0.686, 0.313)	(−0.419, 0.439)	(−0.393, 0.387)	(−0.363, 0.498)
	P value	0.987	0.288	0.753	0.849	0.823
Weight (kg)	Spearman's ρ	0.065	0.285	0.403	−0.213	−0.099
	(95% CI)	(−0.442, 0.559)	(−0.155, 0.648)	(−0.060, 0.753)	(−0.587, 0.248)	(−0.476, 0.310)
	P value	0.797	0.188	0.172	0.382	0.662
Body mass index	Spearman's ρ	0.096	0.382	0.275	−0.249	−0.069
	(95% CI)	(−0.472, 0.601)	(0.006, 0.694)	(−0.376, 0.823)	(−0.660, 0.208)	(−0.561, 0.424)
	P value	0.705	0.072	0.364	0.304	0.761
EDSS	Pearson's r	0.171	0.257	0.227	0.355	−0.325
	(95% CI)	(−0.309, 0.742)	(−0.125, 0.652)	(−0.380, 0.652)	(−0.056, 0.634)	(−0.666, 0.106)
	P value	0.497	0.236	0.455	0.135	0.140

EDSS: Expanded Disability Status Scale; △: change; CTT: colon transit time; WGTT: whole gut transit time; PAC-QOL: patient assessment of constipation – quality of life; CI: confidence interval.

Table 5. Correlation between anthropometric data and baseline measurements with respective changes in gut transit times.

Variables		△CTT ($n = 13$)	△WGTT ($n = 19$)
Age	Pearson 's r (95% CI)	0.444 (−0.066, 0.787)	0.431 (−0.088, 0.758)
	P value	0.128	0.065
Height (m)	Pearson's r (95% CI)	0.097 (−0.548, 0.512)	0.047 (−0.406, 0.403)
	P value	0.753	0.849
Weight (kg)	Spearman's ρ (95% CI)	0.403 (−0.043, 0.721)	−0.213 (−0.583, 0.233)
	P value	0.172	0.382
Body mass index	Spearman's ρ (95% CI)	0.275 (−0.485, 0.793)	−0.249 (−0.650, 0.215)
	P value	0.364	0.304
EDSS	Pearson's r (95% CI)	0.227 (−0.526, 0.715)	0.355 (−0.047, 0.633)
	P value	0.455	0.135
Baseline CTT	Pearson's r (95% CI)	−0.342 (−0.847, 0.655)	−0.285 (−0.755, 0.434)
	P value	0.253	0.304
Baseline WGTT	Pearson's r (95% CI)	−0.268 (−0.808, 0.621)	−0.183 (−0.654, 0.514)
	P value	0.376	0.452
Average weekly compliance rates (%)	Spearman's ρ (95% CI)	0.612* (0.177, 0.852)	0.375 (−0.108, 0.723)
	P value	0.026	0.125

*Correlation is significant at the 0.05 level (2-tailed).
EDSS: Expanded Disability Status Scale; △: change; CTT: colonic transit time; WGTT: whole gut transit time; CI: confidence interval.

capsules cost A\$660 per unit, and the funding of 48 additional capsules for the recruitment of a placebo control group was not within the scope of this project. The study was also highly dependent on participant compliance. While all participants tolerated the abdominal FES well, compliance rates were generally only acceptable, and not all participants used it five times per week. Of note, nine

participants achieved a compliance rate of 100% throughout the study period. Although this may have meant that not all participants received the full dose, our study provides significant, real-life information regarding the feasibility and practicality of the use of abdominal FES in people with MS. The reasons cited for the discontinuation of treatment were device related (three participants), return to work (one participant), medical complications (one participant) and the loss of caregiver support (one participant).

Finally, entry of the smart pill into the ileo-caecal junction was at times difficult to identify. A similar phenomenon involving the identification of the ileo-caecal junction was previously noted by Wang et al.[32] and this was attributed to possible incompetence of the ileocaecal valve or altered pH levels in the ascending colon due to increased bacterial fermentation. As the analysis of regional gut transit times from the SmartPill device was originally based on parameters of healthy individuals, it may be that additional parameters and data will need to be recorded in order to obtain a more clear and more accurate measurement of regional gut transit times in individuals with disease. Finally, we observed seven cases of device failure out of 42 SmartPill capsules administrated, giving us a relatively high equipment failure rate of 16.7%.

Conclusion

Our study found that home-based abdominal FES training did not significantly alter WGTTs and CTTs in people with MS. However, participants reported an improvement in constipation and incontinence-related quality of life post-intervention, which suggests that there might be a role for abdominal FES in the management of bowel problems in people with MS. Larger randomised controlled trials in a more controlled environment will be useful in ascertaining the efficacy of abdominal FES in improving bowel function in MS.

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Conflicting of Interests

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