Abdominal massage plus advice, compared with advice only, for neurogenic bowel dysfunction in MS: a RCT

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Scientific summary

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Background

Multiple sclerosis (MS) has an increasing prevalence in the UK and is the most common neurological condition in young adults, affecting > 100,000 people at present. It is estimated that 60% of people with multiple sclerosis (PwMS) have problematic neurogenic bowel dysfunction (NBD). NBD is rated as one of the most devastating scenarios affecting these people and includes symptoms of constipation, faecal incontinence (FI), bowel evacuation difficulties or a combination of these. Constipation can lead to the individual becoming housebound, spending hours trying to empty their bowels and limiting their ability to work, whereas FI is often described as the most devastating event imaginable, leading to social and emotional issues. Management of NBD in PwMS has been underexplored and lacks supporting evidence. It is costly both in terms of carer and patient time and to the NHS. PwMS have two or three times more admissions to hospital for bowel complications than people without MS. PwMS use laxatives, suppositories, prolonged digital rectal stimulation and/or rectal irrigation but often these interventions have inconsistent results. Abdominal massage is a minimally invasive modality potentially stimulating gut motility. A Cochrane review (McClurg D, Hagen S, Dickinson L and Campbell P, Glasgow Caledonian University, 2018) reported significant benefits in the reduction of the symptoms of constipation in several small trials with heterogeneous populations. Abdominal massage may offer a new option in the pathway to treat NBD.

Objectives

The aim of this study was to assess the clinical effectiveness and cost-effectiveness of adding abdominal massage to the provision of advice calls compared with advice only, with both groups being supported by weekly telephone calls. We also aimed to identify and investigate, via a process evaluation substudy, pilot transit and anorectal physiological substudy, the mediating factors that affected the clinical effectiveness and possible implementation to identify possible mechanisms of action.

All outcomes were undertaken at baseline, weeks 6 and 24.

Primary outcome

The primary outcome was the difference in change between the intervention and control groups in the Neurogenic Bowel Dysfunction Score (NBDS) from baseline to week 24.

Secondary outcomes

- Change in the Constipation Scoring System (CSS) from baseline to weeks 6 and 24.
- Information from the study trial-specific 7-day bowel diary (recorded at baseline, weekly during the 6 weeks of intervention, and during week 23).
- Bladder dysfunction, as measured by the Short Form (SF)-Qualiveen.
- Quality of life as measured by the EuroQol-5 Dimensions, five-level version (EQ-5D-5L), and by a novel NBD questionnaire.
- Resource use as collected by a patient resource questionnaire.
- Bowel transit and anorectal physiological tests (one centre only) undertaken pre intervention and at week 24.

Other outcomes recorded at each telephone conversation

- Change in medication.
- Adverse events.

Process evaluation outcomes

- Qualitative interviews with 20 participants were conducted before and after undertaking the intervention ($n = 40$).
- Interviews with health-care professionals (HCPs) ($n = 25$) involved in the delivery of the trial were conducted shortly after starting the study and/or at the end of the study ($n = 42$).
- Interviews with six key stakeholders involved with incontinence policy or services for PwMS were conducted at only one stage of the study ($n = 6$).

Methods

The study was a UK-based, multicentre, pragmatic, parallel-group randomised controlled trial (RCT). There was 1 : 1 allocation between the groups, with stratification by site and minimisation on level of disability.

Eligibility was being 'bothered' by bowel symptoms.

Inclusion criteria

- Males or females aged ≥ 18 years.
- A diagnosis of MS (no MS relapse in the previous 3 months).
- No major change of medication in the previous 1 month.
- Not used abdominal massage in the previous 2 months.

Exclusion criteria

- Being unable to undertake the massage themselves and did not have a carer willing to do it.
- Being unable to understand the study processes in order to give informed consent.
- Contraindications to abdominal massage, for example abdominal/pelvic cancer, hiatus, inguinal or umbilical hernia, rectal prolapse, inflammatory bowel disease or abdominal scars, abdominal wounds or skin disorders.
- Being pregnant.

After assessment for eligibility and completion of informed consent, each participant was scheduled for one study visit for collection of baseline data. Details were entered into a bespoke database held at Dundee Clinical Trials Unit, which facilitated immediate on-screen randomisation with allocation concealment. All participants were provided with the MS Society Booklet on bowel management. Those in the intervention group additionally received instruction in undertaking the massage (to be given by self or carer), had the massage demonstrated on them and they or their carer were given the opportunity to ask questions and undertake supervised practice. A digital versatile disc (DVD) showing the massage and two leaflets outlining it were also provided. Participants were recommended to undertake the massage daily for ≈10 minutes.

Sample size for the RCT was based on the NBD score using data from a pilot study. To detect a difference between groups of 4.21 [standard deviation (SD) 7.02] at a 5% level of significance with 90% power, 60 participants per group were needed. Thus, for a fully powered study the total sample size, allowing for a 20% dropout rate, was 150 participants. However, in response to suggestions from the funding body, the sample size was increased to 200 participants (100 per group), which allowed for greater attrition.

Ethics approval for the study was granted by the West of Scotland Research Ethics Committee 4, on 11 June 2014 (reference number 14/WS/0111). A total of 11 NHS trusts/health boards granted 12 local NHS site recruitment approvals (two different hospitals belonged to one trust). The study sponsor was Glasgow Caledonian University (GCU) and the Abdominal Massage for Bowel Dysfunction Effectiveness Research (AMBER) trial office was based in the Nursing, Midwifery and Allied Health Professions Research Unit (NMAHP RU) at GCU.

Statistical analysis

Categorical data are presented using counts and percentages; continuous variables are presented using mean (SD) and absolute differences are presented with 95% confidence intervals (CIs). Data for continuous outcome measures (both primary and secondary) were assessed for normality before analysis. Transformations of the outcome variables were used when necessary, if these were not normally distributed.

If data were normally distributed, outcome measures were assessed by multiple linear regression. The primary analysis consisted of comparisons between treatment groups (bowel massage vs. no massage) at the final visit (week 24), adjusted for site, minimisation on level of mobility (walking unaided, aided or wheelchair bound) as well as baseline measure of the outcome and sex.

In a secondary analysis of the primary outcome, the baseline variables of age, sex, body mass index (BMI), type of MS, number of years since diagnosis, cognitive symptoms of MS and minimisation variable on level of mobility (walking unaided, aided or wheelchair bound) were included in the model.

When data were not normally distributed and could not be transformed into a normal distribution, data were analysed using non-parametric methods in addition to multiple linear regression.

In addition to the comparison of baseline data with week 24 outcomes, a repeated measures analysis was performed on the outcomes using all available visits.

Data for categorical outcome measures were assessed by logistic regression in the same way as described for continuous outcome measures.

Statistical significance was taken as two-sided p-value of ≤ 0.05.

Results

Information about the study was given to 389 patients; of these, 273 (60.9%) patients were screened and 191 (48.1%) were randomised: 90 (47.1%) were allocated to the intervention group and 100 (51.8%) to the control group. The number of participants per site ranged from 9 to 26 (median 16 participants). Of the randomised participants, 22 did not complete the study. Two of these were post-randomisation exclusions (essentially randomised in error) from whom data were not collected, leaving 189 for analysis. Fifteen participants in the intervention group and five in the control group withdrew or were lost to follow-up. The missingness of any data appeared to be at random with no obvious bias.

Baseline

Women constituted 81% (154/189) of participants and the mean age of all participants was 53 years (range 26–79 years). The mean time since diagnosis of MS was 14.3 years (range 0–51 years). Demographics and clinical symptom profiles of the two groups were evenly matched. Bowel symptoms had commenced > 10 years previously in 37% of participants and < 1 year previously in 4% of participants. The main bowel

symptoms reported by participants at baseline were feelings of incomplete emptying, straining to pass stool and bloating.

Primary outcome

At baseline, for the intervention group, the mean total NBDS was 7.6 points (SD 5.31 points) and for the control group it was 8.6 points (SD 5.08 points). At week 24, the mean total NBDS was 7.4 points (SD 5.23 points) for the intervention group and 8.7 points (SD 5.70 points) for the control group. The mean difference in change of NBDS between groups was not statistically significantly different for the total score in our primary outcome measure at 24 weeks (–1.61 points, 95% CI –3.32 to 0.04 points; $p = 0.0558$).

Secondary outcomes (primary analysis)

At baseline, the intervention group had a total mean CSS score of 11.7 points (SD 4.05 points) and the control group had a total mean CSS score of 11.5 points (SD 3.77 points). At week 24, the intervention group had a mean CSS score of 10.1 points (SD 4.10 points) and control group had a mean CSS score of 11.1 points (SD 3.91 points). There was no significant mean difference in change of CSS score between groups at week 24 (–0.88 points, 95% CI –2.03 to 0.27 points; $p = 0.1308$).

There were virtually no differences between the two groups, either at baseline or at post treatment, in the SF-Qualiveen or in the EQ-5D-5L.

In our feasibility study on mechanistic evaluation, the low number of participants (11/23) that completed the transit study and anorectal physiology tests make it impossible to undertake meaningful analysis on differences between groups. However, just over 60% of all participants demonstrated slow colonic transit at baseline.

Bowel diary

The mean frequency of stools passed per week at baseline in the intervention group was 3.9 (SD 1.68), and for the control group it was 4.0 (SD 1.74) stools passed per week. At week 24, the frequency of stools passed per week for the intervention group was 4.3 (SD 1.88) and for the control group it was 3.9 (SD 1.89). This was a significant mean difference in change between the groups of 0.62 stools per week (95% CI 0.03 to 1.21 stools per week; $p = 0.039$).

There was no significant difference in the mean change between groups in time spent on the toilet or the number of attempts to pass stool at week 24: –3.35 minutes (95% CI –23.1 to 16.4 minutes; $p = 0.7377$) and 1.14 attempts (95% CI 0.92 to 3.19 attempts; $p = 0.2770$).

There was a significant difference in the mean change between groups in the number of times the participants felt that they had successfully emptied their bowel at week 24 (1.08 times, 95% CI 0.41 to 1.76 times; $p = 0.002$), with the intervention group showing greater effect.

Using repeated measures analysis, statistically significant results were also found at week 6 for the number of stools passed per week [odds ratio (OR) 0.98, 95% CI 0.36 to 1.61; $p = 0.039$] and the number of times participants felt that their bowels were emptied (OR 0.56, 95% CI 0.03 to 1.10; $p = 0.039$), with the intervention group showing greater effect. However, this effect decreased for both outcomes at week 24.

There is also some evidence that the laxative use at week 24 was twice as likely to be lower in the intervention group than the control group (OR 2.37, 95% CI 0.87 to 6.46; $p = 0.092$).

Other outcomes

Regression analysis indicated a greater response in the intervention group for participants walking unaided or aided than for those using a wheelchair. Older participants and those with a higher BMI also did slightly better. The time since diagnosis of MS did not seem to be important, but those with relapsing–remitting MS responded better than those with primary or secondary progressive MS. Cognition severity indicated that those with mild cognitive impairment did better than those with more severe impairment. Consistent with other findings, the outcomes for males were significantly better than the outcomes for women (OR –2.789, 95 % CI –5.179 to –0.399; $p = 0.0226$).

Serious adverse events

There were nine serious adverse events (SAEs); none was related to the trial and all were resolved.

Process evaluation

From the intervention group, 20 participants were interviewed twice: at baseline and at the end of the intervention period. The recordings were transcribed and then supported by NVivo, version 10 (QSR International, Warrington, UK). All 20 completed the study, with 15 reporting benefits such as increased frequency of stools and feeling complete evacuation more often. Other benefits not recorded by trial measures represented important improvements in quality of life for participants, including increased appetite, greater energy, better sleep and greater control over bowel function. Participants shared their experiences of administering the massage, including solutions that they had devised to manage any difficulties. Comparison with change in our primary outcome measure identified inconsistencies in what a participant was saying in the interviews and change in total score. For the five interviewees who felt that there was no change in their bowel habits, analysis of their bowel diaries and interviews gave some indication as to why the treatment may not have worked for them – they had an ideal stool type at baseline and they struggled to administer the massage because of poor dexterity, fatigue and weakness. Eighteen interview participants reported that they would continue with the massage beyond 24 weeks. The HCP interviewees ($n = 25$) were involved with recruitment and had been trained in delivering the massage intervention. Most reported that recruitment of study participants was aided by the fact that this was a non-pharmacy intervention and could be performed by the participant themselves. The six stakeholders identified that there was a lack of evidence-based interventions for patients with NBD and, potentially, abdominal massage could offer a safe, non-expensive additional option for managing bowel problems.

Economic evaluation

A cost–utility analysis was conducted from a NHS and patient cost perspective. The mean incremental cost for the intervention group compared with the control group was £56.50 (95% CI –£372.62 to £415.68). The incremental gain in quality-adjusted life-years (QALYs) was –0.002 QALYs (95% CI –0.029 to 0.027 QALYs). Given these results, the intervention appears to be dominated by the control group.

Conclusions

Abdominal massage is a non-invasive, non-pharmacological intervention. Although the increment in the primary outcome favoured the intervention group, it was small and not statistically significant, and the economic analysis identified that the intervention was dominated by the control group. Given the small improvement in the primary outcome, but not in terms of QALYs, a low-cost version of the intervention, for example as part of a self-management pathway, might be considered worthwhile by some patients. Some secondary outcomes were in favour of the intervention and reached statistical significance with 15 out of 20 interviewees reporting improvements.

Additional research is required to further establish validated outcome measures in this population, as well as further mechanistic investigations.

Trial registration

The trial is registered as ISRCTN85007023, and on ClinicalTrials.gov as NCT03166007.

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