Transanal Irrigation for Neurogenic Bowel Dysfunction in Multiple Sclerosis: A Retrospective Study

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Background/Aims
Sixty percent of multiple sclerosis (MS) patients suffer from neurogenic bowel dysfunction (NBD). Transanal irrigation (TAI) is part of the therapeutic strategy. This retrospective study aims to assess the efficacy of TAI in MS population.

Methods
Twenty-eight MS patients who underwent TAI after a learning period were included. We collected several demographic data: MS disease characteristics, treatments, urinary and bowel dysfunction characteristics, urodynamic parameters, results of the NBD score, the Urinary Symptom Profile (USP) score, and the Patient Global Impression of Severity score, completed by patients before the learning and during the follow-up consultation. We defined 4 specific groups depending on the NBD score severity: very minor, minor, moderate, and severe.

Results
Mean follow-up was 124 days, 85.0% were initially constipated and 36% had fecal incontinence. After TAI, improvement of NBD score was higher in initial Moderate NBD score group with 75.0% of patients decreasing their NBD score into lower severity categories. Few modifications were observed for baseline Very minor and Severe NBD score groups with 60.0% and 87.5% of patients staying in the same category. Statistical improvement of USP voiding dysfunction score was observed (95% CI, −6.13−−1.19; \( P = 0.005 \)) without improvement of overactive bladder USP sub-score.

Conclusions
TAI is effective in NBD, especially in MS patients with initial Moderate NBD score. Improvement of voiding dysfunction following TAI confirms the pelvic organ cross-talk and the need to systematically consider and treat bowel dysfunction in MS to also improve urinary symptoms.

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Key Words
Lower urinary tract symptoms; Multiple sclerosis; Neurogenic bowel; Therapeutic irrigation
Introduction

Multiple sclerosis (MS) is an immune-mediated process causing an abnormal inflammatory response of the immune system directed against the central nervous system. This reaction leads to a demyelination of the insulating covers of nerve cells in the brain and the spinal cord. Various neurologic symptoms could be observed (sensory and motor impairment, ataxia, cognitive dysfunction, urinary, and bowel dysfunction), depending on the localization of the demyelination patch.

Although sensory-motor dysfunction, ataxia or cognitive impairment can lead to obvious disability and dependence, urinary and bowel dysfunctions also have a great impact in the patient quality of life.

In primary intention, conservative strategies of constipation and fecal incontinence (FI) are widely used (diet habits, rectal suppositories, and laxatives). In case of failure of all these therapeutics, transanal irrigation (TAI) can be proposed as a second line therapy.

The aim of this study is to assess the efficacy of TAI on NBD in MS population.

Materials and Methods

This was a retrospective study on 76 patients with MS who learned the TAI technique at the Neuro-Urology Department of a tertiary university hospital between January 2010 and December 2017. TAI was proposed to these patients with MS, as a first line therapy if they had fecal incontinence, or as a second line therapy of digital stimulation or evacuation, frequency of fecal incontinence, drops against constipation, time used for each defecation, frequency and perspiration or discomfort before or during defecation, tablets and medication against fecal incontinence, flatus incontinence, and perianal skin problems. The USP is a valid and reliable questionnaire providing comprehensive evaluation of all urinary disorders and their severity in both men and women with stress urinary incontinence, overactive bladder, and perianal skin problems. The PGI-S was used to analyze and quantify patient impression. It is a 1-item questionnaire (absent, mild, moderate, and severe) to evaluate the severity of the bowel symptoms.

For the statistical analysis, we considered an improvement of these scores if they shifted towards a better score (absolute value change). For the NBD score, we also considered in the analysis an improvement of this score if it shifted towards a better sub-group category.

Statistical analyses were realized with R 3.2.3 (R Development Core Team, http://www.R-project.org) and R studio version 1.0.136 software programs. Baseline characteristics were described with the absolute percentage considering the missing data as an absence of the parameter collected. Normality test was done for each variable. Continuous variables were expressed as mean ± SD, if they passed normality tests, and as median with interquartile range (first quartile-third quartile) if they did not. Categorical variables such as EDSS were expressed as median with interquartile range. Significance was set at the 95% level (P = 0.050). Comparison between pre-TAI and post-TAI scores were analyzed with Student’s t test.
for quantitative variables and Fisher’s exact test for categorical variables, since the expected number was less than 5. Statistical association between the various studied variables and the improvement of the NBD score in absolute value or its shift to a better sub-group category were realized with Fisher’s test for qualitative variables and Student’s t test for quantitative variables.

### Results

Between January 2010 and December 2017, 76 MS patients learned how to perform TAI, but only 51 went to the follow-up consultation. Since our primary outcome was the evolution of NBD score before and after TAI, we only included and analyzed the 28 patients with pre- and post-TAI NBD score (Fig. 1).

At baseline, there were 22 women (78.6%), and mean age was 45 ± 8 years. TAI was mainly proposed to patients with constipation (25 patients [89.2%]), with or without associated FI. Only 3 patients (10.7%) had an isolated FI. 22 patients used laxatives (78.6%), 17 patients used rectal suppositories (60.7%), and 11 patients (39.3%) did digital evacuation. All patients’ baseline characteristics are summarized in Table 1.

The mean follow-up consultation was at 124 days since the start of TAI. At this consultation 21 patients (75.0%) still continued this therapy, 5 patients (17.8%) interrupted it, and we had missing information for only 2 patients. The majority used the TAI system 2 times a week (11 patients, 39.0%) and 4 patients (14.3%) used it 1 or 3 times a week (Table 1).
The NBD score improved statistically in absolute value after TAI, $P = 0.005$ (Table 2). Moreover, if the improvement was considered as a shifted change towards a better sub-group category, the improvement of NBD score was the highest in the Moderate NBD group at baseline, with 75.0% of patients decreasing their NBD score and shifting to Minor or Very minor NBD categories. In the Minor NBD group at baseline, the patients either stayed in the same NBD category or they shifted towards Very minor category, in the same proportions, after TAI. Only 1 person worsened in bowel dysfunction even if he did not interrupt TAI. In the Very minor NBD group at baseline, patients either improved their NBD score or remained in the same category after TAI. However, in the Severe NBD group at baseline, all patients except 1 remained with a Severe NBD score after TAI (Fig. 2).

No significant association were found between baseline characteristics and the improvement of the NBD score neither in absolute value nor towards a better sub-group category. Hence, the improvement of the NBD score was not associated to the initial USP score or the initial NBD score (Table 3).

Thus, surprisingly, USP voiding dysfunction score statistically improved after TAI (95% CI, $–6.13––1.19; P = 0.005$; Student’s t test) (Table 2).

**Discussion**

The NBD score improved after TAI, especially in MS patients
who were in the Moderate sub-group at baseline. The improvement of the voiding function following TAI highlights the importance of bowel dysfunction treatment in urinary dysfunction cares. Due to the multiple neurological pathways that can be affected in MS, there are various clinical presentations of bowel dysfunction in this population. Constipation is due to pelvic floor dyssynergia and slow bowel transit either caused by an autonomic nervous system alteration or a lack of mobility due to motor impairment often observed in these patients. FI is usually associated with constipation but can also be isolated, and caused by an anal sphincter weakness secondary to a pyramidal tract lesion and loss of rectal sensitivity caused by somesthetic pathways alterations. Among patients with MS, 68.0% has NBD. Prevalence is heterogeneous according to previous studies, but although remains high. Indeed, Hinds found 43.0% of constipation and 53.0% of incontinence in his 280 patients among 30 MS patients who learnt TAI, found 55.0% with constipation and 37.0% with FI.

Table 3. Correlation Between the Improvement of the Neurogenic Bowel Dysfunction Score and Baseline Characteristics

| Baseline characteristics | Improvement of NBD score in absolute value | Improvement of NBD score by shifting into a lower category |
|--------------------------|-------------------------------------------|----------------------------------------------------------|
| EDSS                     | $P = 0.278$                                | $P = 0.250$                                               |
| EDSS form                | $P = 0.682$                                | $P = 0.561$                                               |
| Age                      | $P = 0.974$                                | $P = 0.444$                                               |
| Gender                   | $P = 0.467$                                | $P = 0.999$                                               |
| BMI                      | $P = 0.628$                                | $P = 0.711$                                               |
| Fecal incontinence       | $P = 0.311$                                | $P = 0.653$                                               |
| Constipation             | $P = 0.355$                                | $P = 0.999$                                               |
| Stress urinary incontinence | $P = 0.999$                            | $P = 0.191$                                               |
| Detrusor overactivity    | $P = 0.294$                                | $P = 0.862$                                               |
| Vesico-sphincteric dyssynergia | $P = 0.056$                     | $P = 0.272$                                               |
| Urinary leakage          | $P = 0.410$                                | $P = 0.999$                                               |
| Laxative                 | $P = 0.999$                                | $P = 0.653$                                               |
| Rectal suppository       | $P = 0.199$                                | $P = 0.999$                                               |
| Digital extraction       | $P = 0.999$                                | $P = 0.999$                                               |
| NBD score pre-TAI        | $P = 0.873$                                | $P = 0.335$                                               |
| USP score pre-TAI        | $P = 0.524$                                | $P = 0.622$                                               |

NDB, neurogenic bowel dysfunction; EDSS, Expanded Disability Status Scale; BMI, body mass index; TAI, transanal irrigation; USP, Urinary Symptom Profile.

In first line therapy, conservative strategies of constipation and FI are used. Indeed, diet habits such as eating fibers, vegetables, fruits and drinking enough water are recommended, and are generally associated with laxatives to modulate the consistency of stools. Rectal suppositories and digital evacuation can also be used to empty the bowel regularly to avoid FI accidents. Biofeedback has also been shown to be efficient in NBD. In cases of all these therapeutics inefficiency, TAI can be proposed as a second line therapy. Previous studies have related the TAI efficacy in NBD.

Christensen et al., in a multicenter controlled trial, randomized 87 spinal cord injury (SCI) patients: 42 in the TAI arm and 45 in conservative managements (diets, fluids, regular physical activity, and laxatives) arm. After a 10-week trial period, results showed benefits of TAI over conservative managements in several scores of bowel symptoms severity and quality of life (Cleveland Clinic constipation scoring system, St Mark’s FI grading system, NBD score, and the modified American Society of Colorectal Surgeon fecal incontinence score).

In his review on the efficacy and safety of TAI for NBD (23 studies), Emmanuel et al., reported benefits of this technique in SCI population but also suggested the positive impact in other neurologic populations (spina bifida and MS). However, further investigations were still needed in these populations because data were only extracted from observational studies or analyzed overall in mixed neurologic patient populations and not separately. Same conclusions were shared in a Christensen and Krogh et al. systematic review (23 studies of mixed etiologies, spina bifida population, SCI population, and failed perineal and rectal surgeries).

In the MS population, Preziosi et al. included in a prospective observational study 30 MS patients with bowel dysfunction (constipation and/or fecal incontinence) who underwent Wexner Constipation and Wexner Incontinence scoring (primary outcomes), and the 36-item Short Form (SF-36) health survey (secondary outcome) before and after 6 weeks of TAI. Sixteen patients were responders with at least 50.0% improvement in bowel symptoms. The Wexner Constipation score significantly improved ($P = 0.001$), as well the Wexner Incontinence score ($P < 0.001$). However, SF-36 scores did not improve significantly ($P = 0.051$).

Passananti et al. also assessed the long-term efficacy and safety of TAI in MS patients. They included 49 patients who underwent anorectal physiology testing, NBD score, and EQ-5D questionnaires at baseline and annual follow-up. Mean follow-up was 40 months, and by then, all patients who did not interrupt the therapy improved their NBD scores. Among patients with fecal incon-

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the NBD score was the highest in baseline Moderate NBD category. Indeed, treating bowel dysfunction also improves bladder dysfunc-
tion on bowel dysfunction treatment on urinary symptoms. The NBD score improved significantly after TAI, while no urinary treatment
due to inefficiency (50.0%) and only 20.0% stopped it because of dislikes.
TAI seems to be efficient in NBD in MS population too.

Unlike Passananti et al\textsuperscript{11} who found an improvement on the NBD score for all MS patients who continued the therapy (i.e., all NBD scores reduced shifting mainly to the Very minor category during the follow-up),\textsuperscript{1,11,14} in our study however, the improvement of the NBD score was the highest in baseline Moderate NBD category. Thus, 40.0% patients of baseline Very minor category worsened their score, and almost all of baseline Severe NBD score category remained with severe bowel dysfunction after introduction of TAI. Poor compliance could possibly explain the failure of TAI but only 5 patients (17.0%) had interrupted TAI in our study, versus 45.0% in Passananti’s study. Therefore, it must have been other explanations to this incomplete success. Our first hypothesis is the possible lack of conservative bowel management associated with TAI. Indeed, diet habits and laxatives are sometimes needed to modulate the stools’ consistency to improve the efficacy of TAI. However, we did not have the information at the follow-up consultation. The second hypothesis could be the disparity of TAI frequency. In the consensus review of best practice of TAI in adults, TAI should be performed daily in the beginning (approximately the 10-14 first days) and then reduced to alternate days.\textsuperscript{15} To our knowledge, there is no study analyzing the best frequency of TAI requested for better efficacy, but in clinical practice, TAI is usually done every 2 or 3 days. Indeed, most of our patients did it less than twice a week (53.0%).

Moreover, in previous studies, observance of TAI technique tends to decline gradually. Even if we still had 75.0% patients who continued TAI at 124 days (mean follow-up in our study), generally, within 1 year of follow-up only 40.0% still pursue TAI.\textsuperscript{16,17} In the Juul and Christensen study,\textsuperscript{17} interruption of using TAI was mainly due to inefficiency (50.0%) and only 20.0% stopped it because of dislike.

Furthermore, in our study, the USP voiding dysfunction subscore improved significantly after TAI, while no urinary treatment modification was done during the follow-up period, which suggests the impact on bowel dysfunction treatment on urinary symptoms. Indeed, treating bowel dysfunction also improves bladder dysfunction since bladder and rectal functions are intimately linked by a real pelvic organ cross-talk.

In animal experiments (forty-six male Sprague–Dawley rats), responses of superficial and deeper lumbosacral spinal neurons to convergent inputs from the urinary bladder and colon suggested that these neurons might contribute to the cross-talk that occurs between these 2 visceral organs.\textsuperscript{18} Minagawa et al\textsuperscript{19} showed that continuous colorectal distension increased the bladder single unit afferent activity of C and A delta fibers in a pressure dependent manner. Rapid colorectal distension increases the response in the afferent bladder pathways conducted by the C fibers only, which suggests that the convergence of bladder and colorectal peripheral nerves is conducted by mechanosensitive convergent C fibers. In clinical studies, colorectal distension and constipation alter bladder sensation.\textsuperscript{20,21} Inversely, when the bladder is full, sensation of rectal filling is decreased,\textsuperscript{22} confirming this bi-directional pelvic organ cross-talk.

Besides the observational retrospective design of this study some other limitations should be considered.

Firstly, among the 54 MS patients who underwent the follow-up consultation, only 28 MS patients had an objective assessment before and after TAI with the NBD score evaluation. Since the aim was to assess the efficacy of TAI on NBD, we chose to analyze only those who had this objective assessment. This choice could be criticized, especially because it leads to a very small sample-sized study and potential selection bias. Thus, there is no controlled group study.

Secondly, the efficacy of TAI was assessed on the improvement of the NBD score. The sub-analysis of the 10 items in the NBD response after TAI was not performed because some items of the NBD score may not be relevant (for instance, none of our patients took constipation pills, so no improvement of the amount of constipation pills taken can be reported) and also because there was missing information due to the retrospective design of the study.

Thirdly, safety could not be strictly assessed in our study. Even if inefficiency of TAI was the main reason of stopping it before the follow-up consultation, no other complications were self-reported by the patients or systematically asked and reported.

Fourthly, no correlation between the improvement of the NBD score and baseline characteristics were found. It is possibly explained by insufficient statistical power (small sample size of patients) or by a non-validated severity bowel dysfunction score for this specific neurologic population (the NBD score is only validated in SCI population and some items was irrelevant), questioning the relevance of NBD score in MS population to quantify the severity of bowel dysfunctions.

Nevertheless, this study contributes to enhance the fact that the TAI may be effective for NBD in the MS population, and despite its small-size, it confirms the pelvic organ cross-talk concept with the improvement of the voiding function while treating bowel dysfunction.
Further randomized studies are needed to validate this therapeutic strategy in MS bowel dysfunction.

**Supplementary Material**

Note: To access the supplementary figure mentioned in this article, visit the online version of *Journal of Neurogastroenterology and Motility* at [http://www.jnmjournal.org/](http://www.jnmjournal.org/) and at [https://doi.org/10.5056/jnm19040](https://doi.org/10.5056/jnm19040).

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