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**TRANSANAL IRRIGATION IS A BETTER CHOICE FOR BOWEL DYSFUNCTION
IN ADULTS WITH SPINA BIFIDA: A RANDOMIZED CONTROLLED TRIAL**

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ABSTRACT

Aims: To compare transanal irrigation with conservative bowel management for the treatment of bowel dysfunction in Spina Bifida patients.

Methods: Patients with SB and bowel dysfunction were randomly assigned to receive either transanal irrigation or conservative bowel management. The effectiveness of the treatment was defined as a decrease of 4 points in the neurogenic bowel dysfunction (NBD) score at week 10. Data on incontinence (Cleveland scores (Jorge-Wexner (JW))) and constipation (Knowles-Eccersley-Scott Symptom Constipation Score (KESS)) were recorded at 10 and 24 weeks after inclusion. Data were analysed on an intention-to-treat basis.

Results: A total of 34 patients were randomised: 16 patients to conservative bowel management and 18 patients to transanal irrigation. A total of 19/31 (61%) patients improved at week 10, 13 (76%) in the transanal irrigation group vs. 6 (43%) in the conservative group ($p=0.056$). In the irrigation group, the decrease in NBD score was -6.9 [-9.9 - -4.02] versus -1.9 [-6.5 - -2.8] in the conservative group ($p=0.049$ in univariate and $p=0.004$ in multivariate analysis). The NBD, Cleveland (JW and KESS) and Rosenberg scores were significantly lower in the transanal irrigation group than in the conservative bowel management group at week 10.

Conclusions: This prospective, randomised, controlled, multicentre study in adult patients with SB suggests that transanal irrigation may be more effective than conservative bowel management.

Key Words: Spina Bifida, transanal irrigation, conservative treatment, randomised controlled trial, faecal incontinence, bowel dysfunction

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What does this paper add to the literature?'

Therapeutic management of bowel dysfunction in patients with Spina Bifida (SB) is poorly evaluated. Patients in the transanal irrigation group were 7 times more likely to improve after transanal irrigation compared to conservative management. Transanal irrigation is the treatment of choice in the management of SB patients with bowel dysfunction.

INTRODUCTION

Spina bifida (SB) is a congenital disease (1/10,000 live births in developed countries) (1) caused by abnormal closure of the neural tube. Bowel dysfunction is common in patients with SB (2) since 85% of patients are constipated and 70% have faecal incontinence (FI). These disorders severely affect their quality of life (3). Therapeutic management of these disorders is relatively well established in spinal cord injury patients (4), but there is only scant evidence in the field for rare SB patients (5).

The pathophysiological basis of the neurogenic bowel dysfunction experienced by SB patients has not been clearly established and is probably different from that of spinal cord injury patients. We recently showed the absence of an association between the neurological level and severe FI (6,7), and FI in patients with SB is mainly associated with rectal abnormalities (8).

Based on data from the spinal cord injury literature, bowel management in SB patients is based on the use of dietary plans, oral and/or local laxatives, digital evacuation/stimulation and colonic irrigation. The more pragmatic aims of transanal irrigation are to prevent FI and treat constipation. Systems for transanal irrigation have evolved in past decades to allow easier use (9). A randomised trial conducted in patients with spinal cord injury showed that this method improved continence and defecation disorders and their impact on quality of life compared to conservative management (10).

However, in adults with SB suffering from bowel dysfunction, this approach has never been specifically evaluated. Moreover, SB can be associated with both intellectual disability and cognitive impairment that may affect both defecation function and therapeutics. To date, there is limited evidence in the literature supporting any bowel management program in SB adults

in favour of another, and controlled trials are still lacking since this is a rare condition. Therefore, the present study aims to compare transanal irrigation with conservative bowel management in a prospective, randomised, controlled, multicentre study among SB patients with neurogenic bowel dysfunction.

MATERIALS AND METHODS

Patients

Between March 2015 and March 2019, 34 patients (**Figure 1**) with SB and bowel dysfunction were randomly assigned to receive either transanal irrigation or conservative bowel management. Patients were recruited from 5 French centres (Rennes, Lille, Nantes, Kerpape and Rouen). The diagnosis of spinal dysraphism was based on previous spine imaging and operative reports, as well as magnetic resonance imaging (MRI) of the spine for every patient. For the present study, the inclusion criteria were as follows (all criteria were required): (i) age over 15 years; (ii) pelvic-perineal neurological consequences of SB as evidenced by clinical neurological examination, urinary and/or anorectal functional data and/or neurophysiological data; and (iii) moderate to severe anorectal functional disorders defined by a neurogenic bowel dysfunction (NBD) (11) score greater than 9. The exclusion criteria were as follows: psychiatric, cognitive or intellectual disorders that compromised the assessment of the primary endpoint; performance of transanal irrigation on a regular basis; functional colostomy; anal or colorectal stricture; colorectal cancer; acute or chronic inflammatory bowel disease; recent anal or colorectal surgery < 3 months; polyp removal < 4 weeks; ischaemic colitis; urinary or orthopaedic surgery planned during the follow-up period; active anal pathology such as suppuration, haemorrhoids or rectal prolapse; and pregnancy or lactation.

Study design

The study was a prospective, controlled, randomised study aiming to compare transanal irrigation with conservative bowel management in patients suffering from continence and/or defecation disorders related to the pelvic neurological sequelae of SB. Patients who contacted the centres and met the inclusion criteria were approached and informed both in writing and orally about the study. On the day of the inclusion consultation, the patient signed the consent

form. The medical interview and a detailed clinical examination verified the eligibility criteria and the modalities of participation in the trial. Randomisation was then performed via a WEB interface (electronic observation book created using Clinsight software). Patients were block randomised across centres. The study was without blinding procedures. Indeed, blinding is difficult for several reasons: (i) during the telephone interview, it cannot be ensured that the patient does not give the nurse information about the nature of the treatment allocated; (ii) the nature of the treatments; and (iii) some tolerance assessment criteria are specific to colonic irrigation. The study was approved by the research ethics committees (*ID-RCB 2013-A01520-45 and ANSM DMTCOS/DMCOSM/SV/2013-A01520-45*). All authors had access to the study data and reviewed and approved the final manuscript.

Endpoints and assessments during the study

The primary endpoint was the measurement of the neurogenic bowel dysfunction score (NBD score) (11) 10 weeks after inclusion. Taking into account the data available in patients with spinal cord injury (10), the effectiveness of the treatment was defined as a decrease of 4 points in the NBD score compared to the score at inclusion. The NBD score was also analysed as a continuous variable.

Secondary endpoints were (i) data from the incontinence (Cleveland scores (Jorge & Wexner (JW))) (12) and constipation (Knowles-Eccersley-Scott Symptom Constipation Score (KESS)) (13) questionnaires 10 and 24 weeks after inclusion; (ii) the levels of tolerance, feasibility, satisfaction, and improvement of the quality of life evaluated and quantified by semi quantified scales 10 and 24 weeks after inclusion; (iii) self-esteem (Rosenberg scale) (14) 10 weeks after inclusion; and (iv) the digestive function score (NBD) 24 weeks after inclusion. As described previously (15–17), FI was defined by a Cleveland score (JW) ≥ 5 , and severe incontinence was defined by a JW score ≥ 9 . Constipation was defined by a KESS score ≥ 10 (13). Clinically relevant improvements in continence and constipation were defined as an improvement in the JW and KESS scores of at least 50% (18).

In the absence of a specific scale available and validated, we chose to evaluate tolerance, feasibility, satisfaction and improvement of the quality of life in a semiquantitative way. The remaining secondary endpoints were assessed during the week preceding each evaluation at 10 and 24 weeks using a stool calendar: cumulative duration of time spent on the toilet, number of incontinence accidents, number and nature of diapers or pads, number of bowel movements and the consistency of the stool, symptoms experienced at the time of defecation

(abdominal pain, anal pain, nausea, discomfort, headache), and anal digitation to defecate. Loose stools were defined by Bristol stool scores of 5, 6 or 7; normal stools were defined by Bristol scores of 3 or 4; and hard stools were defined by Bristol stool scores of 1 or 2 (19).

Baseline demographic data and baseline values of primary and secondary end points were recorded. The baseline characteristics recorded were sex, age at referral, height, weight, type of SB (open/closed/myelomeningocele), neurological level, mobility, school level, professional status, urinary status, main anorectal complaints using a short questionnaire, Bristol stool score (19), gaping anus, anal hypotonia, and perianal anaesthesia.

Primary and secondary end points were recorded 10 and 24 weeks after inclusion. During the follow-up, patients were contacted for the 10- and 24-week assessments by the education nurse. Any changes in concomitant treatment and the occurrence or modification of adverse events were collected. In addition, weekly transit data sheets (stool calendar) were sent to each patient. These sheets were to be completed by the patient the week before each assessment and returned to each centre. The patient was also asked to complete the self-esteem scale for the 10-week assessment and return it.

Sample Size

In patients with spinal cord injury, a study quantifying the NBD mean value before (14.8 ± 4.6) and after retrograde colonic irrigation (10.4 ± 6.8) is available (10). In this study, drug treatment alone did not induce any variation in the score (13.0 ± 6.5 before and 13.3 ± 6.4 after treatment). Comparing means for this score, based on the hypothesis to obtain a 4-point difference of NBD score between the two groups (14.4 vs. 10.4) with a standard deviation of 6.4, at 5% alpha and 10% beta risks, the proposed sample size would be 54 for each group.

Statistical Analysis

Categorical variables were expressed as numbers and percentages; quantitative data were expressed as the means \pm standard deviations (SD) if normally distributed and medians (Q1–Q3) if not normally distributed. Comparisons of descriptive characteristics were performed with the chi-squared test or Fisher's exact test if necessary. Comparisons of quantitative variables were performed with Student's t test or the Mann–Whitney test if necessary.

To detect heterogeneity at inclusion, baseline values were compared between irrigation and conservative bowel management. Then, multivariate analyses were performed using logistics

or linear regression models to estimate relationships with primary and secondary endpoints. Variables with $p < 0.2$ in the univariate analyses were introduced into the multivariate models. Data were analysed on an intention-to-treat basis. For each analysis, two-sided tests were used and considered statistically significant for p values less than 0.05. All statistical analyses were performed with SAS statistical software, V9.4 (SAS Institute, Cary, NC, USA).

To assess the impact of missing values, multiple imputation was performed. The datasets were generated ($n=100$) with fully conditional specification imputation methods for missing values, by using MI procedure from SAS 9.4. The 100 complete data sets were then analyzed by using the Generalized linear regression procedure with the previously defined model for each dataset, and results from these sets were combined for the inference study, by using the MIANALYZE procedure from SAS 9.4, using Rubin's rule.

Interventions

Two types of interventions are differentiated: "transanal irrigation + conservative bowel management" and "conservative bowel management".

Patients randomised to the "transanal irrigation + conservative bowel management" arm used an integrated system for transanal irrigation, the Peristeen Anal Irrigation system (Coloplast A/S, Denmark). This system has been specifically developed to ease bowel irrigation in spinal cord injury patients (10,20). It is an integrated system consisting of a coated rectal balloon catheter, a control unit including a manual pump, and a water container, thereby making it possible to handle the irrigation procedure without assistance from another person. Physicians, nurses and patients were trained in the correct use of the medical device using educational tools common to the participating centres. The volume of water used, the degree of balloon inflation, and the frequency of enema administration were determined during the first weeks of treatment. The usual start volume was 750 mL of tepid tap water administered once a day.

Conservative bowel management was defined as best supportive bowel care without using irrigation. A patient education protocol was set up based on the understanding of anorectal physiology, the description of the level of disability (sensitivity disorders, dyssynergia), the identification of indirect signs (dysautonomia, spasticity), the proposal of a strategy for evacuating rectal contents based on anal digitation to defecate and defecation time.

Depending on the consistency of the stool (assessment by Bristol scale) and the dominant complaint, dietary advice and transit-modifying drugs (transit inhibitors, mild laxatives) were proposed on request.

A specialist nurse conducted training of patients in transanal irrigation and/or conservative bowel management. Patients were encouraged to contact the specialist nurse for advice, especially at the initiation of treatment.

RESULTS

Baseline

Overall, 34 patients were included. According to the CCIS, 32 patients (94%) suffered from FI (CCIS ≥ 5), with mainly severe complaints (24 (71%) had a CCIS ≥ 9). Constipation (KESS score ≥ 10) was present in all patients. Most of the patients (24/34, 71%) had very low/low self-esteem at inclusion. Overall, 19 patients suffered from abdominal pain, 6 from anal pain, 4 from nausea, 5 from discomfort and 4 from headaches during defecation. The repartition between the centres was as follows: 2 in Kerpape, 3 in Lille, 2 in Nantes, 26 in Rennes and 1 in Rouen ($p=0.79$). The demographic data of the patients are detailed in **Table 1**.

The patients were randomly assigned to the 2 groups: 16 patients to conservative bowel management and 18 patients to transanal irrigation (**Figure 1**). The 2 groups were comparable except for sex and the NBD score: male gender was predominant in the transanal irrigation group, and the mean value of the NBD score tended to be slightly lower in patients allocated to the irrigation group (**Tables 1 & 2**).

Follow-up

Overall, 19/31 (61%) patients had a decrease of at least 4 points in NBD score at week 10. Regarding the primary endpoint, 13 (76%) and 6 (43%) patients experienced a benefit in the irrigation and conservative groups, respectively ($p=0.056$), at week 10. In the irrigation group, the decrease in NBD score was -6.9 [-9.9- -4.02] versus -1.9 [-6.5- -2.8] in the conservative group ($p=0.049$). Multivariate analysis including NBD score as continuous variable was performed and the decrease in NBD score was significantly higher in the irrigation group than in the conservative group ($p=0.004$). According to the percentage of variation of the scores,

the NBD score and KESS decreased significantly at week 10 ($p=0.001$ and $p=0.003$). The NBD, Cleveland (JW and KESS) and Rosenberg scores were significantly lower in the transanal irrigation group than in the conservative bowel management group (**Table 3**) at week 10. The number of incontinence accidents per week was significantly lower in the irrigation group at week 10. To investigate whether an apparent imbalance of gender and the NBD score at inclusion between the 2 groups affected the primary outcome (decrease of at least 4 points in NBD score at week 10), multivariate analysis was performed: patients in the transanal irrigation group were 7 times more likely to improve than patients in the conservative management group (OR= 6.99 [1.18-41.25]) adjusted for NBD value at inclusion. The proportion of patients with NBD score <9 , JW <9 and KESS <10 at week 10 are described in Figure 2 (**Figure 2A, 2B and 2C**, respectively). After multiple imputation analysis, the results were comparable regarding initial NBD score ($p=0.004$) and randomization group ($p=0.002$). Overall, 21 patients (62%) reported a significant improvement of at least one score (19 for NBD score, 2 for KESS and 12 for JW score) (14 (78%) in transanal irrigation vs. 7 (44%) in conservative bowel management, $p=0.04$). At week 10, 21/28 (75%) patients had very low/low self-esteem.

At week 24, the Cleveland (JW and KESS) scores were significantly lower in the transanal irrigation group than in the conservative bowel management group (**Table 3**). The improvement in the NBD score between inclusion and week 10 was significantly associated with the improvement in NBD score at week 24 (OR= 50.3 [2.27-115.53], $p=0.0132$) adjusted for BMI and stool consistency. Among the 19/31 patients with improvement in NBD score at week 10, 18 patients were evaluated at week 24. Among them, 14/18 (78%) were still improved at week 24.

Stool consistency, anal digitation to defecate, and time spent on the toilet were not significantly different between the 2 groups at week 10 and week 24.

The patient's perceptions of improvement in well-being, satisfaction and feasibility of treatment at week 10 and week 24 are described in **Figure 3**. At week 10, compared with patients in the conservative bowel management group, patients in the transanal irrigation group considered the treatment better for general well-being ($p=0.005$), and they were more satisfied with the treatment overall ($p=0.003$), finding the treatment acceptable ($p=0.03$).

Of the 18 patients in the transanal irrigation group, 17 patients were followed up to week 10 and week 24. Of the patients in the transanal irrigation group, 10/17 (59%) had no other medical digestive treatment and 6/17 (41%) had oral laxatives; of the 15 patients in conservative bowel management group, 13/15 (87%) had oral laxatives and 2/15 (13%) had both oral laxatives and local laxatives ($p=0.001$). The duration of calls, the number of calls, and the number of consultations at week 2, week 10 and week 24 were comparable between the 2 groups (**Supplementary material**). Of the 17 patients in the transanal irrigation group, none had complementary training at week 10, and one had complementary training between week 10 and week 24. Compared with patients in the conservative bowel management group, patients in the transanal irrigation group reported half as many concomitant treatments (**Supplementary material**). During follow-up, 10 patients in the transanal irrigation group reported 17 adverse events. Of these, 11 adverse events were device-related: device leakage was reported in 3 patients and device rupture in 7 patients. Four patients reported abdominal discomfort and 4 patients reported headache.

DISCUSSION

The present study is the first prospective, randomised, controlled, multicentre study addressing bowel management exclusively in an adult population with SB. The aim was to compare transanal irrigation with conservative bowel management. The present work highlights the fact that transanal irrigation improves the bowel function of SB patients, as assessed by different outcome measures. Transanal irrigation is tolerable and not very time-consuming. The effect of transanal irrigation is perceived at week 10 and is predictive of effectiveness at week 24.

The main strengths of this work are that the population was homogeneous and composed of adult SB patients, and few patients were lost to follow-up. The assessment of bowel function was carried out using scales validated in SB patients (11) and refined using validated scales already used in SB patients (6,18,21). Finally, some factors that could potentially impact the effectiveness of the treatment were taken into account, such as level of education, autonomy, and self-esteem.

However, our study results should be interpreted with caution for several reasons. The recruiting centres were expert centres, which explains the bias of recruitment. It is possible

that treatment in expert centres has an impact on the treatment modalities and on patient compliance. Furthermore, as blinding was not possible due to the type of treatment proposed, this included a bias. As described, the number of included patients was smaller than expected, with only 34 patients available for evaluation (vs. 104 expected). This is an important limitation of this work. Indeed, the low statistical power reduces the chance of detecting a true effect and also reduced the likelihood that a statistically significant result reflects a true effect (22). Several hypotheses can be put forward to explain this: (i) it is a rare disease, and recruitment may be difficult due to geographical dispersion; (ii) it is a congenital disease, and patients have often tried different treatments in childhood and have been disappointed ; (iii) the device was already marketed before the start of the study, as it had shown efficacy in neurological patients (10), and some SB patients have already had this treatment. A feasibility study was performed and suggested difficulties for inclusion. However, the project leaders wanted to perform this study because treatments for digestive disorders are few and often not evaluated in rare and congenital diseases such as SB. However, it was decided to stop the inclusions due to the long inclusion period already achieved, the decline in the inclusion curve and the recruitment difficulties. Finally, research methodology on rare diseases is challenging (23). The methodological approaches need to be adapted in these particular situations, and design variations, including N-of-1 trials, could be proposed.

The primary endpoint was the measurement of the neurogenic bowel dysfunction score (NBD score (11)) 10 weeks after inclusion, and the effectiveness of the management was defined as a decrease of 4 points in the NBD score compared to the score at inclusion. The choice to use a binary endpoint is questionable because it may decrease the power of the study. However, using NBD score as continuous variable, results were equivalent. The choice of a primary endpoint is often difficult when designing a trial because it conditions the results of the study and the take-home message. When designing the study, the NBD score was a recently validated score and had not yet been used as a primary endpoint to assess the effectiveness of a treatment in bowel dysfunction. It seems important to use this score systematically to assess bowel dysfunction in SB patients. The NBD score is a composite score that takes into account data on FI and constipation. Validated scores on FI and constipation were assessed in this study and thus allowed for a more refined analysis. Thus, both scores were significantly lower in the transanal irrigation group than in the conservative bowel management group at week 10. This highlighted that transanal irrigation is effective for both continence disorders and constipation symptoms, as suggested in the literature (10,24–26).

Importantly, transanal irrigation does not consume more medical or paramedical time than conventional management, and the adverse events are not serious. First, we would assume that because of the cognitive impairment of SB patients (27), the time spent explaining the use of the equipment would be significant. These are probably indirect criteria showing that this treatment is simple to use and effective. Second, the adverse events reported here are not serious, and importantly, these adverse events did not lead to withdrawal from the study. Finally, these events are foreseeable and mentioned in the device's instructions. These data add to the benefits of transanal irrigation.

In conclusion, this first prospective, randomised, controlled, multicentre study in an adult population with SB suggests that transanal irrigation may be more effective than conservative bowel management. Transanal irrigation improves the bowel function of SB patients, both constipation and continence. Transanal irrigation is tolerable and safe. Thus, transanal irrigation is probably the treatment of choice in the management of adult SB patients with bowel dysfunction.

Table 1: Demographic data at baseline

	All	Transanal irrigation	Conservative bowel management	p-value
Age (y), mean (SD)	35.8 (9.6)	34.8 (8.5)	36.9 (10.9)	0.54
Sex				0.0021
Female	16	4	12	
Male	18	14	4	
BMI, mean (SD)	29.9 (7.0)	28.9 (6.0)	31.1 (8.0)	0.38
Type of spinal dysraphism				0.85
Open	24	14	10	
Closed	4	2	2	
Myelomeningocele	5	2	3	
Neurological level of injury				0.12
T12 and above	2	0	2	
L1-L3	11	7	4	
L4-L5	12	4	8	
Sacral	8	6	2	
Mobility				0.25
Walking	16	11	5	
Waking with canes >200m	8	3	5	
Walking with canes <200	3	2	1	
Wheelchair	7	2	5	
School level				0.52
Level 1 (<CEP)	3	1	2	
Level 2 (<= Bac)	18	11	7	
Level 3 (>Bac)	13	6	7	
Professional insertion				0.16
Full time activity	10	8	2	
Part-time activity	8	4	4	
No activity	6	3	3	
Disability	10	3	7	

Abbreviations: BMI= Body Mass Index; SD= Standard deviation

Table 2: Characteristics and outcome measures at baseline**Abbreviations:** SD= Standard deviation, NBD= Neurogenic Bowel Dysfunction; JW=Jorge Wexner ;

	All	Transanal irrigation	Conservative bowel management	p-value
Gaping anus	3	2	1	1.00
Low anal tone	16	10	6	0.29
Perianal anesthesia	29	14	15	0.34
Number of stool/week, mean (SD)	9.4 (8.2)	9.3 (8.1)	9.5 (8.4)	0.95
Time spent on the toilet , mean (SD)	65.7(58.8)	70.0 (75.2)	61.4 (38.6)	0.71
Bristol stool				0.35
Hard stools	10	6	4	
Normal stools	5	3	2	
Liquid stools	17	7	10	
Number of incontinence accidents/week, mean (SD)	2.6 (6.1)	1.6 (2.0)	3.8 (8.7)	0.31
Number pads/week, mean (SD)	13.6 (13.5)	18.5 (14.8)	8.7 (11.2)	0.22
Number anal digitation/week, mean (SD)	1.0 (1.5)	0.9 (1.6)	1.1 (1.4)	0.73
NBD score, mean (SD)	16.6 (4.3)	15.2 (3.5)	18.3 (4.7)	0.04
Incontinence Cleveland score (JW), mean (SD)	11.1 (4.0)	10.7 (4.8)	11.7 (3.0)	0.46
Constipation Cleveland score (KESS), mean (SD)	19.9 (5.5)	18.6 (5.0)	21.4 (5.7)	0.13
Rosenberg score, mean (SD)	27.8 (6.3)	28.9 (6.8)	26.6 (5.6)	0.27

KESS= Knowles-Eccersley-Scott Symptom Constipation Score

Table 3: Outcome measures at weeks 10 and 24

		Transanal irrigation		Conservative bowel management	p-value
Week 10					
NBD score, mean (SD)	17	8.5 (5.6)	14	16.5 (6.7)	0.0010
Incontinence Cleveland score (JW), mean (SD)	17	5.6 (3.0)	13	10.8 (4.6)	0.0009
Constipation Cleveland score (KESS), mean (SD)	16	13.7(3.6)	13	20.5 (7.3)	0.0028
Rosenberg score, mean (SD)	15	29.9 (5.3)	13	25.3 (5.3)	0.0288
Number of incontinence accidents/week, mean (SD)	17	0.5 (0.9)	17	3.5 (4.9)	0.0305
Week 24					
NBD score, mean (SD)	17	9.4 (6.0)	13	13.7 (6.3)	0.0645
Cleveland score (JW), mean (SD)	17	5.5 (3.4)	13	10.9 (4.2)	0.0005
Cleveland score (KESS), mean (SD)	17	15.9 (3.6)	13	22.2 (6.2)	0.0018

Number of incontinence accidents/week, mean (SD)	18	0.4 (0.9)	15	2.3 (3.6)	0.07
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Abbreviations: SD= Standard deviation, NBD= Neurogenic Bowel Dysfunction; JW=Jorge Wexner ; KESS= Knowles-Eccersley-Scott Symptom Constipation Score

Figure Legends:

Figure 1

Flow chart

Figure 2

(2A) At week 10, 11 patients (35%) had NBD scores <9 (10 in the transanal irrigation group vs. 1 in the conservative bowel management group, $p=0.007$). At week 24, 12 patients (40%) had NBD scores <9 (10 in the transanal irrigation group vs. 2 in the conservative bowel management group, $p=0.016$).

* $p < 0.005$

(2B) At week 10, 17 patients had Jorge-Wexner scores < 9 (13 in the transanal irrigation group vs. 4 in the conservative bowel management group). At week 24, 16 patients had Jorge-Wexner scores <9 (13 in the transanal irrigation group vs. 3 in the conservative bowel management group).

(2C) At week 10, 3 patients (10%) had KESS < 10 (2 in the transanal irrigation group vs. 1 in the conservative bowel management group, $p=1.00$). At week 24, twelve patients (40%) had NBD scores <9 (10 in the transanal irrigation group vs. 2 in the conservative bowel management group, $p=0.016$).

* $p= 0.016$

Figure 3: Patient perceptions

At week 10, compared with patients in the conservative bowel management group, patients in the transanal irrigation group considered the treatment better for general well-being ($p=0.005$) (3A), and they were more satisfied with the treatment overall ($p=0.003$) (3B), finding the treatment acceptable ($p=0.03$) (3C).

REFERENCES:

1. Mitchell LE, Adzick NS, Melchionne J, Pasquariello PS, Sutton LN, Whitehead AS. Spina bifida. *Lancet Lond Engl.* 20 nov 2004;364(9448):1885-95.
2. Brochard C, Peyronnet B, Dariel A, Ménard H, Manunta A, Ropert A, et al. Bowel Dysfunction Related to Spina Bifida: Keep It Simple. *Dis Colon Rectum.* nov 2017;60(11):1209-14.
3. Krogh K, Lie HR, Bilenberg N, Laurberg S. Bowel function in Danish children with myelomeningocele. *APMIS Suppl.* 2003;(109):81-5.
4. Coggrave M, Wiesel PH, Norton C. Management of faecal incontinence and constipation in adults with central neurological diseases. *Cochrane Database Syst Rev.* 19 avr 2006;(2):CD002115.
5. Brochard C, Peyronnet B, Hascoet J, Olivier R, Manunta A, Jezequel M, et al. Defecation disorders in Spina Bifida: Realistic goals and best therapeutic approaches. *Neurourol Urodyn.* févr 2019;38(2):719-25.
6. Brochard C, Peyronnet B, Dariel A, Ménard H, Manunta A, Ropert A, et al. Bowel Dysfunction Related to Spina Bifida: Keep It Simple. *Dis Colon Rectum.* nov 2017;60(11):1209-14.
7. Brochard C, Bouguen G, Olivier R, Durand T, Henno S, Peyronnet B, et al. Altered epithelial barrier functions in the colon of patients with spina bifida. *Sci Rep.* 3 mai 2022;12(1):7196.
8. Brochard C, Ropert A, Peyronnet B, Ménard H, Manunta A, Neunlist M, et al. Fecal incontinence in patients with spina bifida: The target is the rectum. *Neurourol Urodyn.* mars 2018;37(3):1082-7.
9. Shandling B, Gilmour RF. The enema continence catheter in spina bifida: successful bowel management. *J Pediatr Surg.* mars 1987;22(3):271-3.
10. Christensen P, Bazzocchi G, Coggrave M, Abel R, Hultling C, Krogh K, et al. A randomized, controlled trial of transanal irrigation versus conservative bowel management in spinal cord-injured patients. *Gastroenterology.* sept 2006;131(3):738-47.
11. Krogh K, Christensen P, Sabroe S, Laurberg S. Neurogenic bowel dysfunction score. *Spinal Cord.* oct 2006;44(10):625-31.
12. Jorge JM, Wexner SD. Etiology and management of fecal incontinence. *Dis Colon Rectum.* janv 1993;36(1):77-97.
13. Knowles CH, Eccersley AJ, Scott SM, Walker SM, Reeves B, Luniss PJ. Linear discriminant analysis of symptoms in patients with chronic constipation: validation of a new scoring system (KESS). *Dis Colon Rectum.* oct 2000;43(10):1419-26.
14. Rosenberg M. *Society and the adolescent self-image.* Princeton university press; 2015.
15. Brochard C, Bouguen G, Bodère A, Ropert A, Mallet AL, Morcet J, et al. Prospective cohort study of phenotypic variation based on an anal sphincter function in adults with fecal incontinence. *Neurogastroenterol Motil Off J Eur Gastrointest Motil Soc.* oct 2016;28(10):1554-60.
16. Brochard C, Vénara A, Bodère A, Ropert A, Bouguen G, Siproudhis L. Pathophysiology of fecal incontinence in obese patients: A prospective case-matched study of 201 patients. *Neurogastroenterol Motil Off J Eur Gastrointest Motil Soc.* août 2017;29(8).
17. Rothbarth J, Bemelman WA, Meijerink WJ, Stiggelbout AM, Zwinderman AH, Buyze-Westerweel ME, et al. What is the impact of fecal incontinence on quality of life? *Dis Colon Rectum.* janv 2001;44(1):67-71.
18. Brochard C, Peyronnet B, Hascoet J, Olivier R, Manunta A, Jezequel M, et al.

Defecation disorders in Spina Bifida: Realistic goals and best therapeutic approaches. *Neurourol Urodyn.* 2019;38(2):719-25.

19. Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. *Scand J Gastroenterol.* sept 1997;32(9):920-4.

20. Faaborg PM, Christensen P, Kvitsau B, Buntzen S, Laurberg S, Krogh K. Long-term outcome and safety of transanal colonic irrigation for neurogenic bowel dysfunction. *Spinal Cord.* juill 2009;47(7):545-9.

21. Brochard C, Ropert A, Peyronnet B, Ménard H, Manunta A, Neunlist M, et al. Fecal incontinence in patients with spina bifida: The target is the rectum. *Neurourol Urodyn.* 2018;37(3):1082-7.

22. Button KS, Ioannidis JP, Mokrysz C, Nosek BA, Flint J, Robinson ES, Munafò MR. Power failure: why small sample size undermines the reliability of neuroscience. *Nat Rev Neurosci.* 2013;14(5):365-76.

23. Whicher D, Philbin S, Aronson N. An overview of the impact of rare disease characteristics on research methodology. *Orphanet J Rare Dis.* 19 janv 2018;13(1):14.

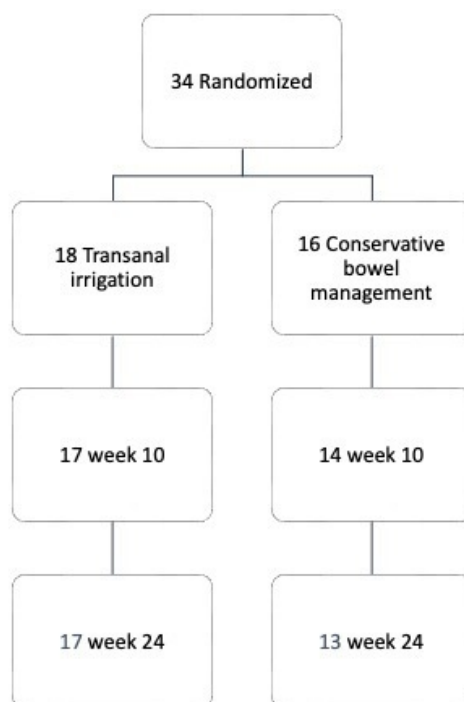
24. Christensen P, Krogh K. Transanal irrigation for disordered defecation: a systematic review. *Scand J Gastroenterol.* mai 2010;45(5):517-27.

25. Christensen P, Krogh K, Buntzen S, Payandeh F, Laurberg S. Long-term outcome and safety of transanal irrigation for constipation and fecal incontinence. *Dis Colon Rectum.* févr 2009;52(2):286-92.

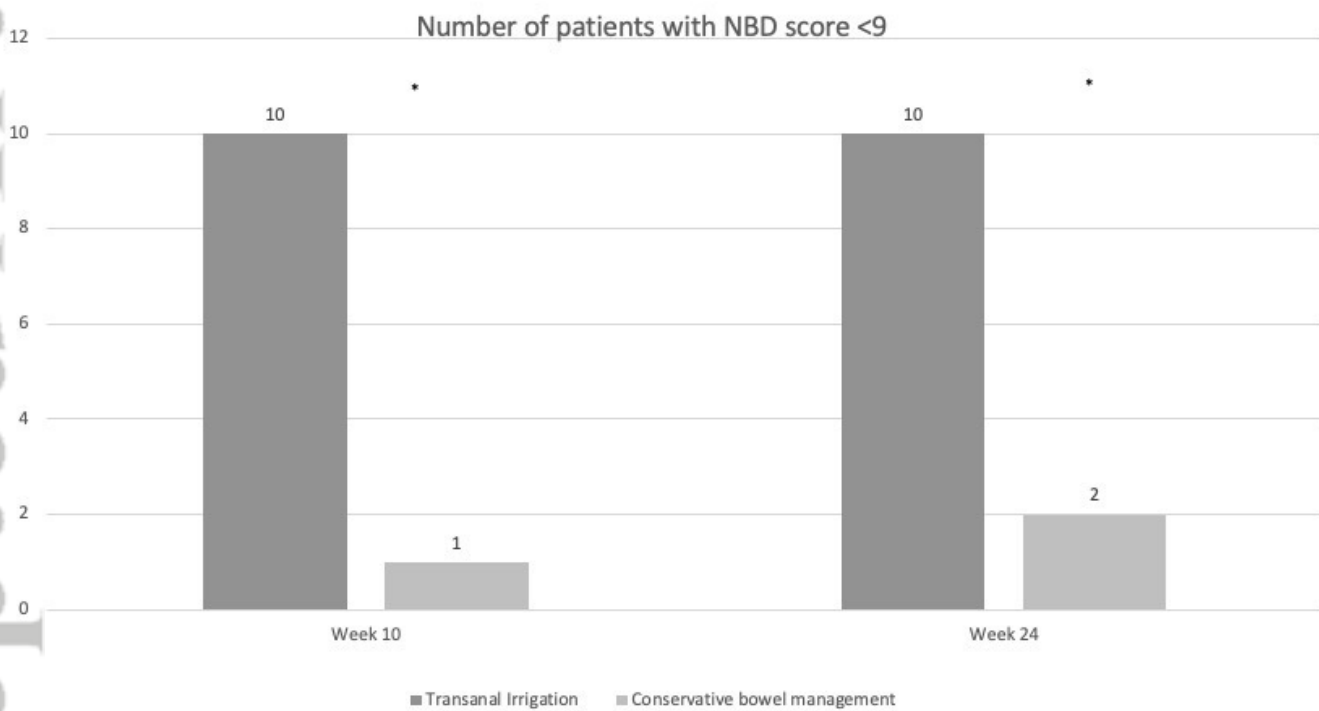
26. Faaborg PM, Christensen P, Kvitsau B, Buntzen S, Laurberg S, Krogh K. Long-term outcome and safety of transanal colonic irrigation for neurogenic bowel dysfunction. *Spinal Cord.* juill 2009;47(7):545-9.

27. Riedel D, Hagman G, Green D, Fristedt S. Cognitive function and performance of everyday activities in adults with spina bifida. *J Rehabil Med.* 9 sept 2021;53(9):jrm00225.

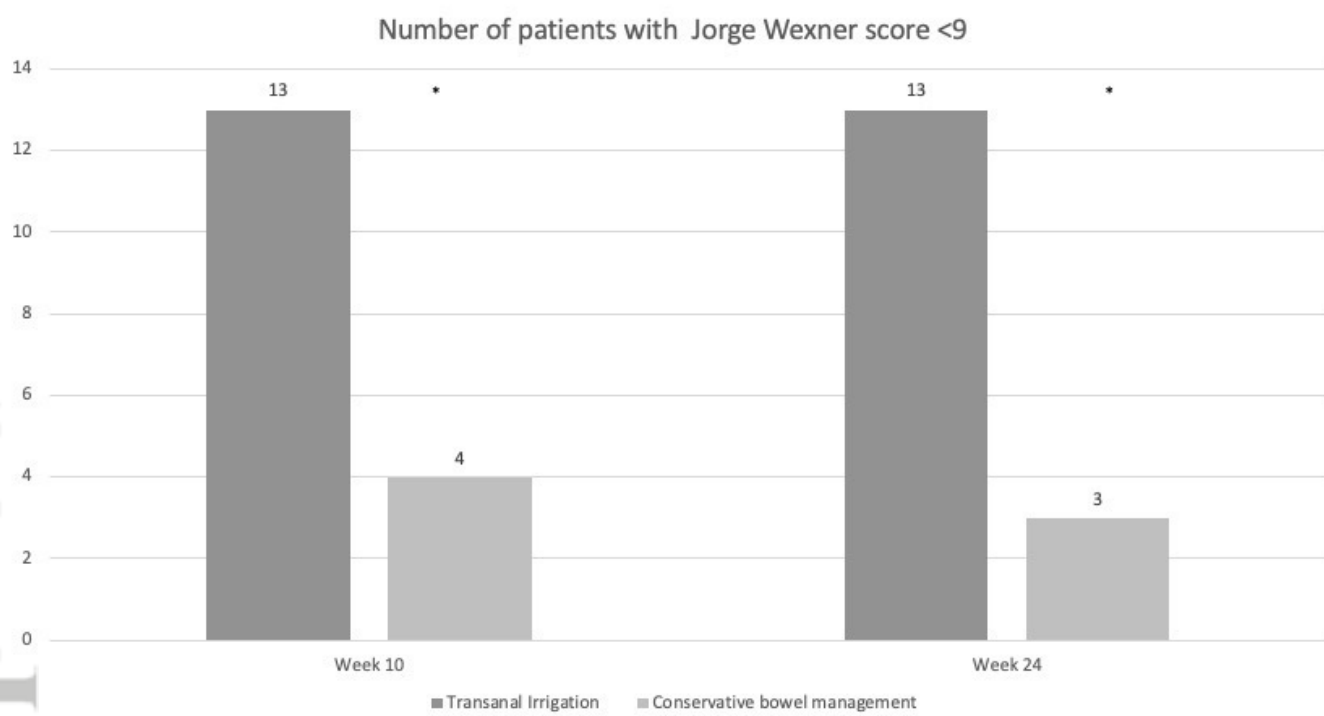
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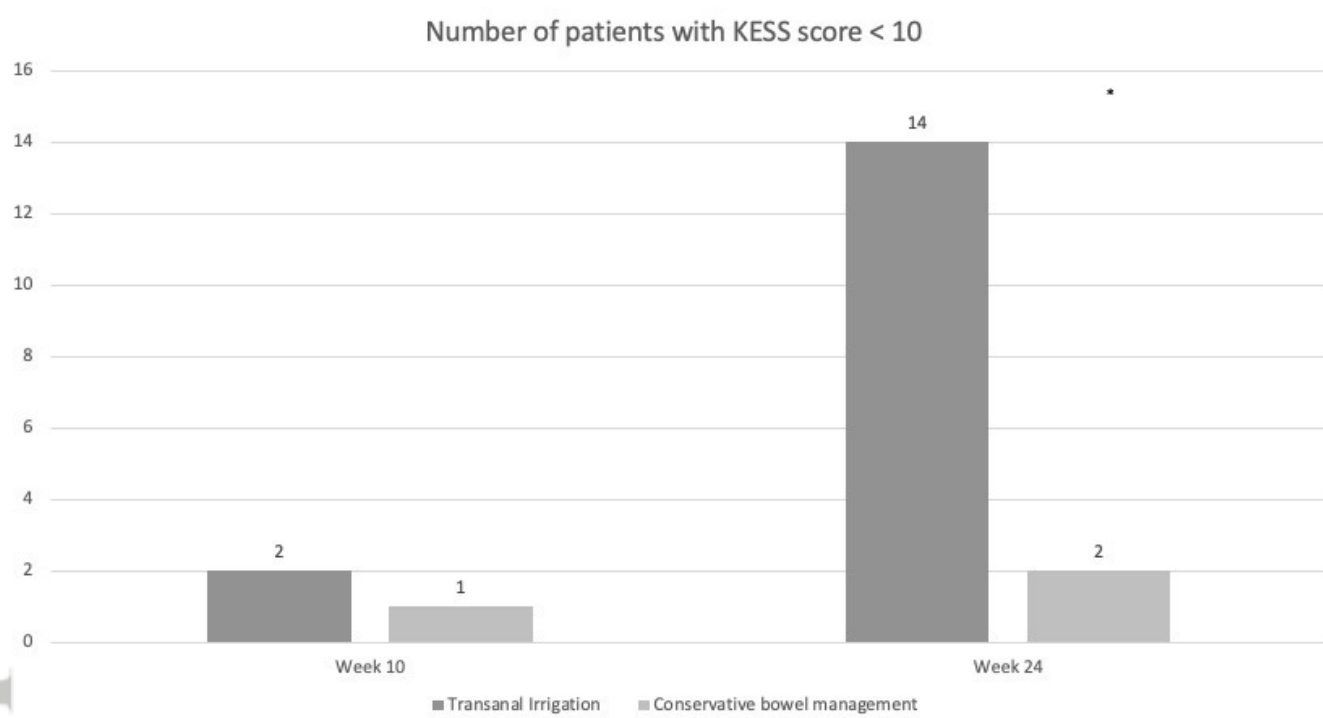
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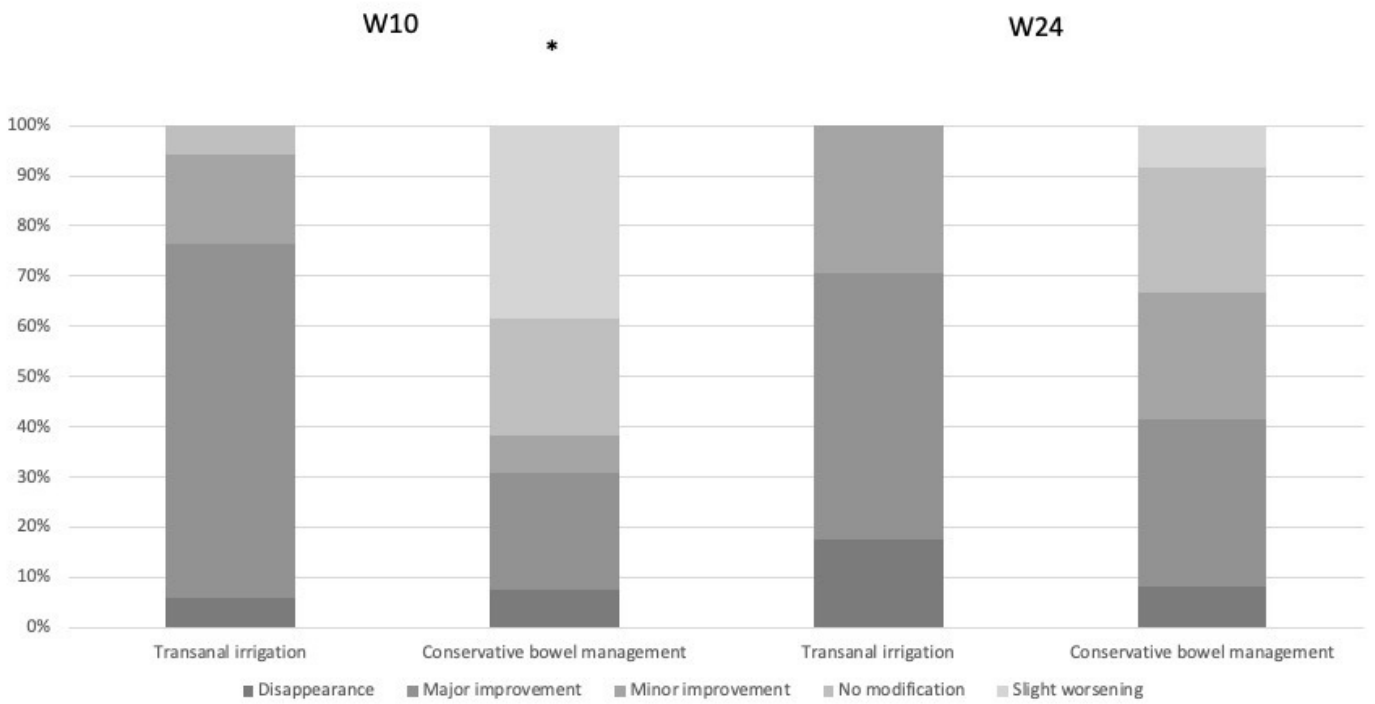
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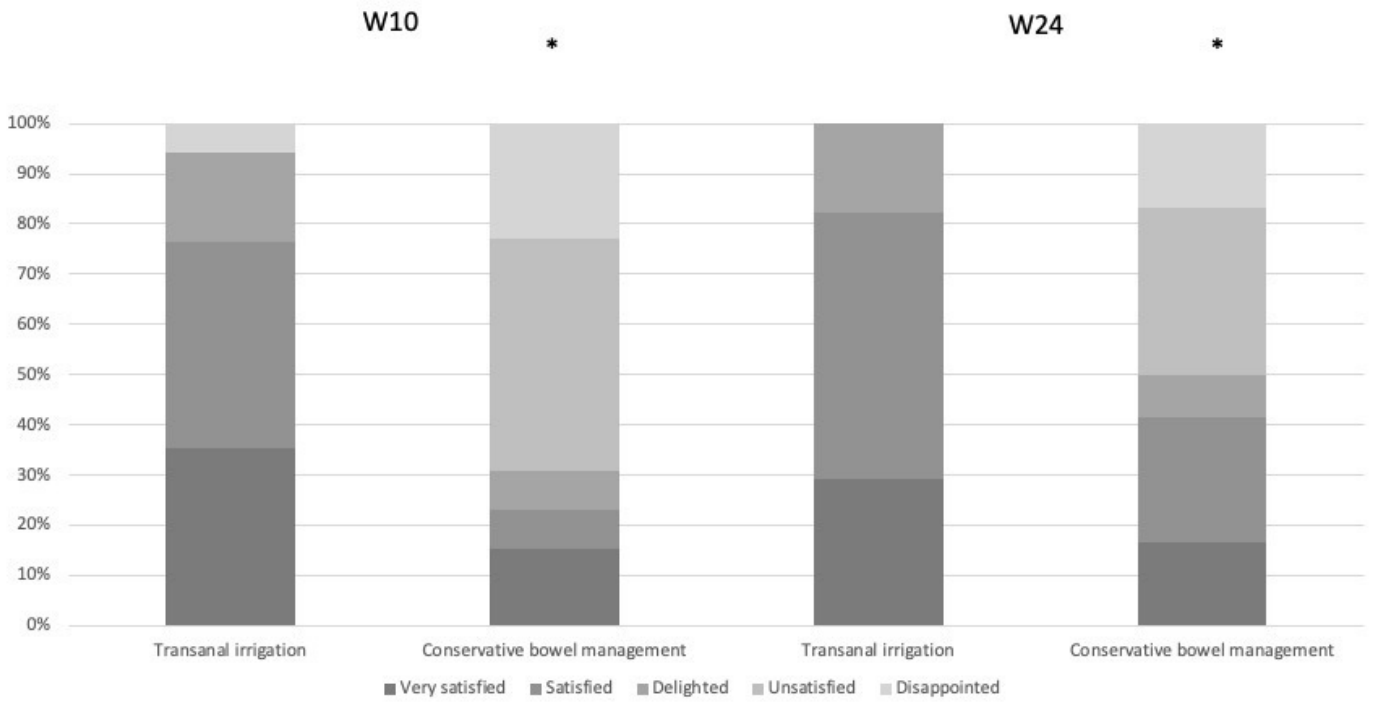
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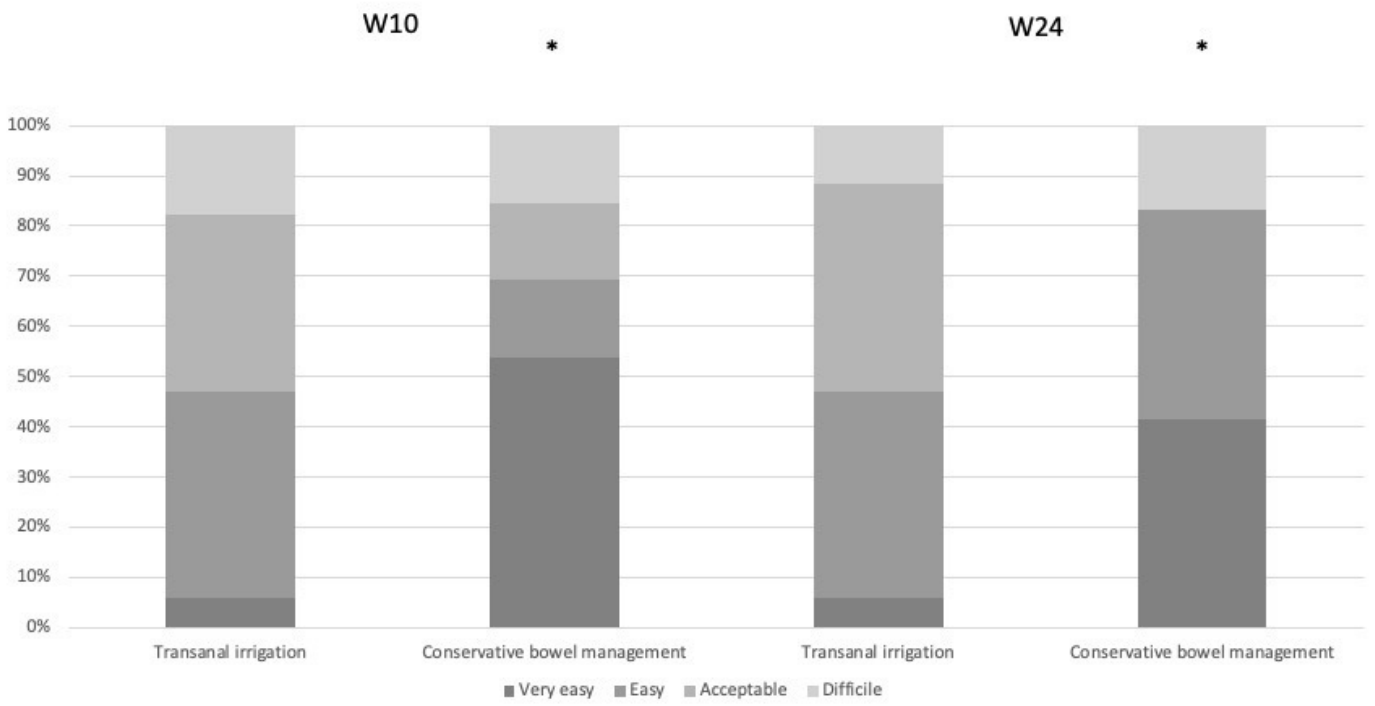
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