

## Functional Nonretentive Fecal Incontinence: Do Enemas Help?

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**Objective** To assess the current treatment of functional nonretentive fecal incontinence, which consists of education, toilet training, and positive motivation.

**Study design** Patients, age 6 years and older, referred for fecal incontinence (FI) and diagnosed with functional nonretentive fecal incontinence were eligible candidates. Seventy-one children (76% boys, median age 9.3 years) were randomized to receive conventional therapy (control group) or conventional therapy in addition to daily enemas during 2 weeks. Treatment success was defined as <2 episodes of FI/month without use of enemas.

**Results** At intake, the median FI frequency was 6.1 per week, whereas the median defecation frequency was 7.0 per week. At the end of the treatment period, the median number of FI episodes was significantly decreased in both groups: from 7.0 (IQR 4.0-11.5) to 1.0 (IQR 0.5-2.0) in the intervention group and from 6.0 (IQR 4.0-10) to 2.0 (IQR 0.5-3.5) in the control group. No statistical difference was found between the groups at the end of the treatment period ( $P = .08$ ) nor during additional follow-up (average success rate 17% for both groups,  $P = .99$ ).

**Conclusion** Temporarily application of additional rectal enemas did not significantly improve treatment success compared with conventional therapy alone. (*J Pediatr* 2013;162:1023-7).

Fecal incontinence (FI) represents an upsetting and psychologically distressing problem in children and results in lower health-related quality of life.<sup>1</sup> In approximately 95% of children with FI, no organic cause can be identified; these children are considered to have a functional defecation disorder. In approximately 90% of these children, FI is the result of constipation, and children are treated with laxatives (oral and enemas).<sup>2,4</sup> The remaining 10% of patients present with FI as a single symptom without any organic cause or sign of constipation and is currently classified as functional nonretentive fecal incontinence (FNRFI).<sup>2,4,5</sup>

The current cornerstones for treatment of FNRFI are education, toilet training, and a daily bowel diary with reward system. A randomized controlled trial in children with FNRFI showed that oral laxatives are not helpful and even increase the number of FI episodes.<sup>6</sup> In another randomized controlled trial using behavioral techniques (such as biofeedback training), we were able to change abnormal defecation dynamics but this had no effect on treatment success.<sup>7</sup> Anecdotal success has been described using loperamide in childhood-onset, long-standing FNRFI.<sup>8</sup>

Despite intensive treatment programs, success rates after 2 years of medical and/or behavioral treatment were only 29% in children with FNRFI. Moreover, at the age of 12 years, almost 50% of the children still suffered from FI.<sup>9</sup> It has been suggested that children with FNRFI deny or neglect normal physiological stimuli to defecate and contract the external anal sphincter to retain stool in the rectum.<sup>2</sup> We hypothesized that the daily use of rectal enemas, which results in clean underwear, can lead to motivation to (re)gain normal toilet skills. Therefore, the purpose of our randomized controlled trial was to investigate whether daily enemas in addition to conventional therapy would increase the number of patients with treatment success compared with conventional therapy alone.

### Methods

To be eligible for the trial, patients had to fulfill all of the following criteria: presence of FI with >1 episode of FI per week during the preceding 3 months, a defecation frequency of  $\geq 3$  times per week, no large stools, no palpable abdominal mass or large stool in the rectum at physical examination, and age between 4 and 17 years.<sup>6,7</sup> Children with stool withholding behavior were considered as eligible candidates for this study. Children with a delayed colonic transit time (CTT) and organic causes of FI such as muscle disorders, spina bifida, and children operated for anal atresia or Hirschsprung's disease, and those children with mental retardation were excluded.

All children were referred for functional defecation disorders by general practitioners, school doctors, and pediatricians to a tertiary hospital (Emma Children's Hospital/AMC, Amsterdam, The Netherlands). All parents and

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CTT	Colonic transit time
FI	Fecal incontinence
FNRFI	Functional nonretentive fecal incontinence
GEE	Generalized estimating equations model

children >12 years gave written informed consent. The study protocol was approved by the medical ethics committee of the hospital.

Children were randomized on a 1:1 basis to one of the following treatment groups: conventional treatment (control group) or conventional treatment combined with regular application of rectal enemas (intervention group). Randomization was carried out with the help of a specialized program on a central computer. The randomization was stratified by sex.

To obtain baseline data assessment, children were asked to record, with assistance from their parents, their defecation pattern (defecation frequency and episodes of FI) in a daily diary a week before randomization ( $t = -1$  until  $t = 0$ ). In all patients, medication influencing motility was discontinued during this week.

Before randomization, each child underwent a complete investigation including a detailed medical history, abdominal and rectal examination, and CTT measurement. A standardized interview was conducted to determine whether children fulfilled the criteria for FNRFI.<sup>10</sup> The child and parents were asked about bowel function, frequency of defecation and FI, consistency and size of stool, pain during defecation, and associated symptoms such as abdominal pain, appetite, and urinary incontinence. The standardized questionnaire at intake also included questions regarding medical history, age at onset of defecation problems, and laxative use.

Abdominal examination focused on distension and the presence of an abdominal fecal mass. Rectal examination included inspection for fissures, hemorrhoids, scars, gluteal cleft deviation, or dimples. Digital examination was performed to provide information about anal tone and the presence of a rectal fecal mass.

CTT was determined by using the method described by Arhan et al.<sup>12</sup> A single abdominal radiograph was taken following ingestion of capsules, each containing 10 radio-opaque markers (Sitzmarks; BioPharma, Weesp, The Netherlands), on 6 consecutive days.<sup>11</sup> This procedure was performed without bowel preparation. Calculation of CTT was performed according to a previously described formula (CTT in hours = number of markers  $\times$  2.4). When the total CTT exceeded 62 hours, it was considered to be delayed, indicating constipation.<sup>12</sup> Subsequently, the patient was excluded from the study.

### Treatment Strategies

Patients were randomized to 1 of the 2 treatment groups. The control group was treated according to conventional therapy; education, toilet training, behavioral strategies, bowel diary, and a reward system. The child and the parents were educated about the different aspects of FI, with an explicit effort to alleviate guilt and to be nonaccusatory. All children were instructed to try to defecate on the toilet for 5 minutes after each meal. Motivation was enhanced by praises and small gifts. After the 6-week active treatment period, patients in the control group were allowed to start the use of enemas. The intervention group was treated with rectal enemas in addition to the conventional therapy as described above.

Standardized instructions were given to the parents and child regarding the administration of the rectal enemas. Children were instructed to bend their knees while lying sideways on their bed and attempt to defecate during introduction of the enema. Furthermore, we recommended to heat the enema towards body temperature before administration and try to retain the fluid until strong urge to defecate was felt.

During the first 2 weeks of the 6-week active treatment period, patients were instructed to use daily enemas (dioctyl-sulfosuccinate sodium, Klyx; [Pharmachemie, Haarlem, The Netherlands] 120 mL for children  $\geq 6$  years of age or natriumfosfaat; Colex Klysma; [Tramedico BV] 133 mL for children  $\geq 6$  years of age) at home. Thereafter, this frequency was reduced stepwise by 1-2 per week every week if the physician considered treatment successful. Success was defined as a 50% reduction in the number of FI episodes compared with number of FI episodes occurring the week before.

### Measurements of Outcome

All patients had outpatient visits/telephone contacts during which therapy compliance and defecation frequency and FI episodes (information from bowel diary) were discussed at 1, 2, 4, and 6 weeks after the start of the treatment. Children receiving conventional therapy with persistence of episodes of FI were able to start with rectal enemas after the 6-week active treatment period. Two more assessments were performed at 6 months and 1 year after randomization to evaluate defecation pattern and use of medication during additional follow-up. Follow-up was performed either during a clinical visit or by phone with a standard questionnaire.

The primary outcome measures were FI frequency per week and treatment success during active treatment and additional follow-up. Treatment was considered successful if the child had less than 2 episodes of FI/month without use of enemas. Secondary outcome measures were defecation frequency per week, painful defecation, and abdominal pain during defecation. Clinical improvement was defined as  $\leq 1$  FI/week regardless the use of enemas.

To study outcome measures over time, we differentiated the series of visits in 2 periods; the first 6 weeks after randomization; the 'active treatment period' ( $t = 1$  until  $t = 6$ ) and the visits performed at 12 weeks, 6 months, and 1 year after randomization considered as the 'additional follow-up period'.

### Sample Size Consideration

Before start of the study, a sample size calculation was made, expecting a 30% difference in the proportion of success between the control and intervention treatment. To detect such a difference using a 2-sided significance level of 0.05 with a power of 0.80 would require a sample size of 39 children in each group.

### Safety

The incidence of adverse events during the weeks of treatment with enemas was also documented. Both the incidence and severity of gastrointestinal adverse events (abdominal pain, painful defecation) were recorded in the diary and

assessed at weeks 1, 2, 4, and 6 of the period of the trial on a 3-point scale: 0 = no gastrointestinal symptoms present, 1 = symptoms present to some extent, and 2 = gastrointestinal symptoms present.

## Data Analyses

Demographic and clinical characteristics at baseline were analyzed in a descriptive way. Data for all patients were analyzed according to an intention-to-treat approach. Outcome data consisted of repeated measurements over time in the same patient; therefore, we applied models that explicitly take into account the correlation that is likely to exist between measurements within the same individual. To study the success rates over time, we used the generalized estimating equations (GEE) model. GEE models are used to analyze trends over time in binary outcomes (for this study; treatment success). GEE models are an extension of generalized linear models to deal with correlated outcomes.<sup>13</sup> Within the GEE framework, a working correlation matrix is estimated to adjust the standard parameters for the correlation that is present. The working correlation matrix was considered exchangeable. The GEE models contained the following variables: treatment given, time as a categorical variable, and the interaction between treatment and time. Results are presented as OR together with 95% CIs.

Statistical analyses were performed by using SPSS Windows v. 16.0 (SPSS Inc, Chicago, Illinois). Statistical significance was accepted at  $P < .05$ .

## Results

Between November 2000 and December 2009, a total of 71 children were enrolled fulfilling the Rome II criteria for FNRFI. Of these children, 17% had been seen only by their general practitioner, 62% visited a general pediatrician, and 39% had visited a psychologist or psychiatrist. A total of 36 patients were allocated to the intervention group and 35 to the control group. Unfortunately, enrollment of 39 children per group, as aimed based on the sample size calculation, was not reached in 10 years. The baseline characteristics per treatment group are presented in Table I. None of the patients in the control group used enemas during the 6-week active treatment period.

There were 4 protocol violations in the intervention group; these children decreased the use of rectal enemas in advance of the predetermined scheme. At the end of the 6-week treatment period, 47% of the children in the intervention group still used 5 enemas/week, whereas 42% of the children used 2-4 enemas per week. Only 2 children were successfully treated at the end of the 6-week treatment period. These children had no FI without the use of enemas.

## Main Outcome Measures

The results of the intention-to-treat analysis, based on all 71 patients, with regards to the FI frequency per week and treatment success (defined as successful if the child had less than 2 episodes of FI/month without use of enemas) are shown in

**Table I.** Demographic and clinical characteristics at baseline\*

	Intervention group	Control group
Number of patients	36	35
Boys	75 (n = 27)	77 (n = 27)
Median age in y (range)	9.0 (8.1-10.3)	9.3 (8.3-10.4)
Median defecation frequency/wk	7.0 (6.3-11.1)	7.0 (5.0-12.5)
Median FI episodes/wk	7.0 (4.0-11.5)	6.0 (4.0-10)
Pain during defecation	33 (n = 12)	29 (n = 10)
Hard stools	2.8 (n = 1)	8.6 (n = 3)
Abdominal pain	70 (n = 25)	60 (n = 21)
Passage of large stools	28 (n = 10)	23 (n = 8)
Withholding behavior	86 (n = 31)	74 (n = 26)
Use of laxatives	2.8 (n = 1)	0
Urinary incontinence (day)	25 (n = 9)	37 (n = 13)
Urinary incontinence (night)	36 (n = 13)	34 (n = 12)
CTT (h)	31.2 (24.0-45.6)	28.8 (14.4-45.6)

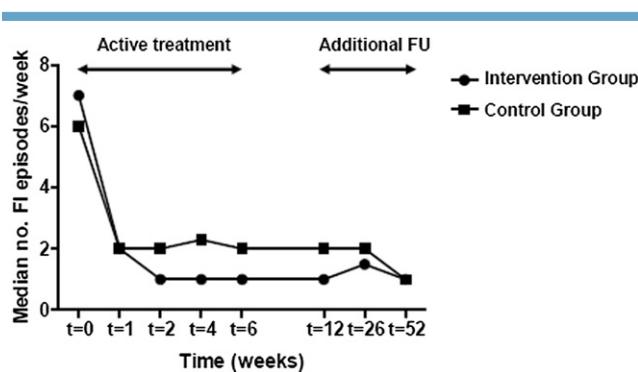
\*Depicted as proportion (%) or median (IQR).

**Table II** and the **Figure**. From baseline to the end of the treatment period, the median number of FI episodes significantly decreased from 7.0 (IQR 4.0-11.5) to 1.0 (IQR 0.5-2.0) in the intervention group and from 6.0 (IQR 4.0-10) to 2.0 (IQR 0.5-3.5) in the control group. No statistical difference was found between the 2 groups at the end of the active treatment period ( $t = 6$ ,  $P = .08$ ) (Figure). No significant difference ( $P = .3$ ) was found in the number of FI episodes at additional follow-up between the intervention group and control group (median 1.6 [IQR 0.6-2.8] and 2.1 [IQR 1.1-3.1]), respectively. The number of FI episodes during additional follow-up were statistically significantly lower compared with the start of the treatment period in both study groups ( $P < .001$ ). The treatment success was not significantly different between the groups during additional follow-up (summary OR across all time points 1.0 [95% CI 0.4-2.4];  $P = .99$ ) with a mean success rate of 17% for both groups (Table II). The number of patients fulfilling the criteria for clinical improvement was significantly higher in the intervention group compared with the control group during the active treatment period (OR 2.1 [95% CI 1.1-3.9],  $P = .02$ ) but not during additional follow-up (OR 1.3 [95% CI 0.64-2.43],  $P = .51$ ) (Table II).

In the intervention group 50%, 25%, and 2.9% of the children were still using enemas at 12, 26, and 52 weeks, respectively. One patient in the control group used enemas at  $t = 12$ , which resulted in disappearance of FI, whereas 1 control patient used enemas at  $t = 52$ , which resulted in a decrease

**Table II.** Treatment success and clinical improvement

	Success		OR (95% CI)	<i>P</i> value
	Intervention group	Control group		
Treatment success				
Additional FU	17%	17%	1.0 (0.4-2.4)	.99
Clinical improvement				
Active treatment	53%	35%	2.1 (1.1-3.9)	.02
Additional FU	54%	49%	1.3 (0.6-2.4)	.5



**Figure.** Median FI episodes per week.

in the number of FI episodes from 5 at intake to 1 FI episode/week at the end of the follow-up period.

### Clinical Characteristics

During the active treatment period, the defecation frequency per week was 9.5 (IQR 8.4-14.3) in the intervention group and 11.3 (IQR 7.2-14) in the control group ( $P = .5$ ). During additional follow-up the defecation frequency per week was 8.0 (IQR 6.5-11) in the intervention group and 8.9 (IQR 6.7-15) in the control group ( $P = .6$ ).

At intake, 3 children in the control group (8.6%) and 1 child in the enema group reported hard stools ( $P = .5$ ). The consistency of stools did not change during the intervention period in both groups.

Abdominal pain during defecation was reported by only a minority (2.8%-8.3%) of the children in the intervention group during the active treatment period at different visits. None of the patients in the control group reported abdominal pain during defecation. Urinary incontinence during day and night decreased from 31% and 35% at intake to 27% and 7.0%, respectively, at the end of the intervention/active treatment period ( $t = 6$ ), and 9.8% and 17%, respectively, at 1-year follow-up in the entire study cohort.

### Side Effects

Pain during defecation in the anorectal region was reported by 8.3%-17% in the intervention group during the active treatment period, and in 5.6%-8.3% during additional follow-up. In the control group, pain during defecation was reported by 2.9%-17% during active treatment, and by 0%-8.6% during additional follow-up. None of the children in the intervention group stopped the use of enemas because of water and electrolyte disturbances.

### Discussion

This randomized controlled trial investigated the role of rectal enemas in the treatment of children with FNRFI. A significant decrease in the number of FI episodes was found in both the intervention group and control group after the active treatment period and during follow-up. However, rectal enemas were not more effective than conventional therapy

in these children. Using strict success criteria, low success rates were found in both treatment groups during follow-up.

The median number of FI episodes at intake and the decrease of the number of FI episodes after active treatment in our current study is in line with our former randomized controlled trial evaluating the effect of biofeedback training in children with FNRFI.<sup>6</sup> It is noteworthy, however, that in other randomized controlled trials in children with functional gastrointestinal disorders, a significant improvement in symptoms is observed during the first weeks of treatment.<sup>14,15</sup> Most of these large clinical trials are performed in tertiary centers. One might speculate that these experienced academic pediatric gastroenterologists in the field of functional gastrointestinal disorders are well aware of the importance of education, reassurance, and allocation of time to the initial consultation to validate the patients' symptoms and respond to the patient's specific needs and fears, might influence the initial treatment effect. During follow-up, the number of FI episodes were still significantly lower compared with intake in both groups, underlining the importance of long-term follow-up of these patients. During the frequent outpatient visits, we enhance motivation and stress the importance of adherence to the treatment strategies.

Clinical improvement, defined as  $\leq 1$  FI/week regardless the use of enemas, was observed significantly more frequently in the intervention group compared with the control group during the active treatment period but this difference is not expanding throughout additional follow-up (OR 1.3). We hypothesize that the fast reduction in the number of rectal enemas per week, as put forward in the treatment protocol, was too optimistic. These children might be better treated when the frequency of enema application is maintained for a period of at least 3 months and not reduced within the first weeks. The extension of the treatment period with rectal enemas seems suitable because we have shown that children tolerate rectal therapy surprisingly well without any side effects.<sup>16,17</sup> A recent systematic review described the adverse effects of sodium phosphate enema in adults and children.<sup>18</sup> All side effects described were due to water and electrolyte disturbances. The main risk factors were children younger than 2 years of age and associated comorbidity.

Another explanation is that children are obliged to stick to the toilet training and behavioral strategies with frequent use of rectal enemas and tend to lose interest, trust, and compliance when enemas are reduced. This seems plausible because children with constipation considered rectal enemas important to solve their defecation disorders.<sup>16</sup>

A high percentage of children was found with daytime and night time urinary incontinence.<sup>6</sup> These rates, 31% for daytime urinary incontinence and 35% for night-time urinary incontinence, were much higher than reported in children with constipation with or without FI seen in primary pediatric clinics. In this group of constipated patients, only 3.3% exhibited daytime, 1.8% day and night-time, and 5.4% night-time urinary incontinence respectively.<sup>19</sup> It has been suggested that early intervention with laxatives may prevent fecal and/or urinary incontinence.<sup>19</sup> Nevertheless, the exact

mechanism(s) underlying the relationship between defecation disorders and lower urinary tract symptoms remain unclear. We hypothesize that children with FNRFI not only deny or neglect their urge to defecate but exhibit the same behavior towards micturition.<sup>2</sup>

In accordance with our earlier randomized controlled trial, strict toilet training, with or without rectal enemas resulted in a significant and sustained decrease in the occurrence of urinary incontinence.<sup>6</sup> This supports the idea that a strict regimen of toilet training together with demystification and motivation is able to improve both urine and FI.<sup>20,21</sup>

A limitation of this study is that no questionnaires were used to evaluate subjective feelings about and experience with the application of rectal enemas for a longer period of time. A recent study, however, showed that the prolonged use of enemas in children with long-lasting constipation was well tolerated.<sup>16</sup> The majority of these children (76%) never/seldom felt worse after application of an enema, whereas 15% perceived them as extremely terrible. Another drawback of this study is that we did not succeed in including the 78 patients, as was based on sample size calculation before start of the study, despite our 10-year period of inclusion. However, the identical success rate of 17% in both treatment arms during additional follow-up makes it highly unlikely that further inclusion of patients would have generated clinically relevant differences.

In summary, temporary use of daily rectal enemas in addition to conventional therapy is not more effective than conventional therapy alone in children with FNRFI. More importantly, low success percentages were found after 1 year follow-up. Because the use of enemas is not more effective than conventional treatment, new treatment strategies are necessary to successfully treat this group of children. ■

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