Paediatric constipation and functional non-retentive faecal soiling
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Chapter 10

Summary & conclusions
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Childhood defecation disorders are common in general paediatric practice, and result in 3% of all consultations to a paediatrician (1). These disorders form the most common complaint in childhood gastrointestinal disease, and can make up to 25% of all consultations to a paediatric gastroenterologist (2). The two major entities within childhood defecation disorders are paediatric constipation (PC) and functional non-retentive faecal soiling (FNRFS). The most frequently presented symptom in children with PC and FNRFS is encopresis (3). Encopresis is defined as the (in-) voluntary faecal soiling of underwear in children older than 4 years (4). PC is characterised by a combination of (2 out of 4): a low defecation frequency, encopresis, the passage of large amounts of stool and the presence of faecal retention found at physical examination (4,5). On the other hand, FNRFS refers to encopresis as an isolated complaint in the absence of constipation (6). Although our understanding of the pathophysiology has grown in recent decades, the causes and pathophysiology underlying childhood defecation disorders remain largely obscure. Despite the prevalence of these symptom complexes, large randomised trials comparing treatment strategies are sparse (7). Consequently the management of these children is symptomatic and mainly based on clinical experience. This thesis describes the role of the rectum in paediatric defecation disorders. Furthermore, a health related quality of life questionnaire is developed to better understand the role of infrequent defecation and encopresis on the general well being of the child with defecation problems. Finally standard and newer treatment strategies are evaluated in children with constipation and FNRFS. These aims are described in more detail in chapter 1.

Chapter 2 provides a thorough and sometimes critical overview on the current diagnostic criteria, symptomatology, pathophysiology, diagnostic procedures, treatment and long-term follow-up in childhood constipation. Although constipation is the most prevalent gastrointestinal symptom in childhood, only little is known about the (patho-)physiology of defecation and the mechanisms involved in disturbed defecation. Moreover, and very disappointingly, only a few studies have been reported evaluating the efficacy of treatment regimens in this common childhood disorder. No well designed randomised trials with enough statistical power have been performed to provide thorough answers to relevant clinical questions. Paediatric defecation disorders deserve much more attention than they
currently do. Large double-blind, randomised controlled trials with well defined outcome measures should be performed. These studies are necessary to compare the safety and efficacy of different laxative regimens in children with constipation of varying severity. These trials should cover longer follow-up periods and include social outcomes (quality of life, school performance, and family history) as well as clinical relevant outcomes. Future international collaboration is necessary to develop and validate standard constipation-questionnaires in which difficult items as encopresis and soiling, large amounts of stool, consistency of stool, retentive posturing and faecal impaction are (re-)defined. These (validated) standard questionnaires might better recognise separate groups of children with different symptomatology within the broad symptom complex of constipation. This in turn might lead to different therapeutic approaches. Although there is 'some light at the end of the tunnel', the end of the tunnel is still a long way to go.

In chapter 3, the Rome II criteria for functional paediatric defecation disorders are evaluated. The prevalence of defecation disorders was assessed in 198 children attending our outpatient paediatric motility clinic using both the Rome II criteria (6) and the 'classic' (Iowa) diagnostic criteria (5;8). The prevalence of both criteria was compared. Surprisingly, our data show that not functional faecal retention (FFR) but functional constipation (FC) is the most prevalent disorder of defecation using the Rome II criteria. Evaluation of the total prevalence of constipation according to both criteria shows acceptable similarity. Despite this, 16% of the patients fulfilling the 'classic' criteria are not recognised as constipated using the Rome II criteria. On the other hand, 11% of the children with a positive Rome II diagnosis are not recognised by the 'classic' criteria. Good agreement is found on the prevalence of non-retentive faecal soiling. These patients, in contrast with children with retentive soiling, have no abnormalities on rectal examination. Therefore, it is essential to perform a rectal examination to differentiate between retentive and non-retentive soiling (i.e. constipation and FNRFS).

Using both Rome II and ‘classic’ criteria, encopresis is the most frequent accompanying symptom of childhood constipation (84%). It is essential to perform a rectal examination in children with defecation disorders to differentiate between retentive and non-retentive soiling.
Previously, rectal function (rectal sensitivity and rectal compliance) has been investigated using distension of the rectum with increasing volumes using anorectal manometry. To date, it however becomes increasingly clear that pressure/tension, and not volume mainly determines visceral perception. We designed a study evaluating rectal function using a pressure controlled distension protocol applied by a barostat in children with PC and FNRFS. The main finding described in chapter 4 is that not disturbed rectal sensitivity but increased rectal compliance is the major abnormality in constipated patients (58%). Due to the higher compliance these children require larger stool volumes to reach the intra-rectal pressure threshold triggering the sensation of urge to defecate. We also showed that FNRFS patients have a normal rectal function, underscoring the earlier clinical and manometric findings that FNRFS differs from constipation and constitutes a different clinical entity.

Increased rectal compliance and not decreased rectal sensitivity is the major pathophysiological mechanism in children with chronic constipation. Clinically, this means that these children, in contrast to those with a normal rectal function, will require a larger stool volume filling the rectum before the sensation of urge to defecate is triggered, leading to a lower defecation frequency.

Since long term outcome in PC is unfavourable, with 50% of patients still not successful after 5 years of treatment (9,10), it would be helpful to identify prognostic factors for successful outcome. We hypothesised that normalisation of rectal compliance is involved in accomplishing clinical success in PC. Chapter 5 describes a cross-sectional barostat study comparing rectal function (sensitivity and compliance) of children with PC compared with that of children recovered from constipation. We showed that rectal compliance is not normalised in 33% of clinically recovered patients, questioning rectal compliance as an important prognostic factor. These data suggest that other mechanisms may be more important determinants of recovery from childhood constipation.
Barostat studies could not identify rectal compliance as a prognostic factor for recovery from constipation. A total of 33% of the children successfully treated for constipation still had an increased rectal compliance. A prospective study evaluating the relation between rectal compliance, laxative treatment and the achievement of clinical success in paediatric constipation is needed.

Chapter 6 covers a case report in which an adolescent with longstanding, childhood onset FNRFS is described. Because he appeared resistant to all therapy (toilet-training, biofeedback-training and keeping a bowel diary), a trial with Loperamide suppositories was started. Rationale to use Loperamide is its inhibiting effect on colonic peristalsis and an increase in (internal) anal sphincter pressure. A dose of 5 mg 2 times daily resulted in a complete disappearance of encopresis with daily defecation on the toilet and no side effects. During follow-up the patient experienced a relapse of complaints when discontinuing Loperamide.

Loperamide might prove useful as new treatment modality in therapy resistant, functional non-retentive faecal soiling. A prospective trial evaluating the value of this opioid receptor agonist has to be performed.

To assess health related quality of life (HRQoL), many questionnaires have been developed so far. However, most of these questionnaires are generic and not disease-specific. The major disadvantage of generic instruments is their tendency not to be sensitive enough for measuring small changes or specific problems in patient groups. As a result, most generic instruments lack the sensitivity to measure small changes or specific problems (like encopresis) in patient groups. Therefore, we developed the first disease-specific health related quality of life questionnaire for patients with PC or FNRFS described in Chapter 7. The questionnaire was developed and validated using internationally accepted guidelines. The 'Disorder of Defecation List' (DDL) seems promising in measuring HRQoL in childhood defecation disorders.

Chapter 8 describes a long-term follow-up study of 114 FNRFS patients. All patients had taken part in two randomised trials in our department evaluating laxatives and/or biofeedback. This follow-up of 12 years shows that only 29% of
the patients with FNRFS are treated successfully after two years of intensive treatment. Thereafter, a steady increase in success is observed, resulting in a cumulative success percentage after 7 years of follow up of 80%. In other words: after a follow-up period of 7 years, 20% of all FNRFS patients did not once experience a successful outcome. Relapse is common (37%) and occurs most often within the first two years. This high percentage of relapse stresses the importance of intensive monitoring and follow-up of FNRFS patients. Our study also shows that 15% of young adults (18 years) still have encopresis, enervating the belief that children with non-retentive soiling will outgrow their symptoms during or after puberty.

At the age of 18 years, faecal soiling persists in 15% of the FNRFS patients seen in a tertiary clinic. Relapse after an initial period of success occurs frequently and most likely in the first two years after successful treatment. This stresses the importance of intensive monitoring and follow-up of these patients.

Chapter 9 describes the comparison of a polyethylene glycol (PEG 3350, Transipeg®) with lactulose in 100 constipated children. In this double blind, randomised controlled trial, we report a significant increase in defecation frequency and a significant decrease in encopresis frequency in both groups (PEG 3350 and Lactulose) after 8 weeks of study. However, success was significantly higher in the PEG group (56%) compared to lactulose (29%). The group treated with polyethylene glycol reported fewer side effects. For these two reasons, PEG 3350 should be the first choice laxative in childhood constipation. After 8 weeks of study, the dose of PEG in successful patients was: 0.26 ± 0.13 g/kg/day for children < 6 years and 0.26 ± 0.07 g/kg/day for children ≥ 6 years. The dose of lactulose in clinically successful patients < 6 years and ≥ 6 years was: 0.96 ± 0.45 g/kg/day and 0.45 ± 0.27 g/kg/day, respectively.

Polyethylene glycol (PEG 3350) when compared with lactulose, gives a higher success rate with fewer side effects. The PEG dose of successful patients was: 0.26 ± 0.11 g/kg. PEG 3350 should be the laxative of first choice in childhood constipation.
In conclusion, this thesis shows that the current Rome II criteria for functional defecation disorders are difficult to use in clinical practice. The next Rome criteria ('Rome III'), necessary to compare international studies, should include encopresis and rectal faecal impaction (assessed with rectal digital examination). Rectal function testing in patients with defecation disorders shows that increased rectal compliance and not a decreased rectal sensitivity is the major underlying abnormality in PC whereas FNRFS patients have a normal rectal function. Normalisation of rectal compliance was not shown in all subjects recovered from constipation, questioning its role in obtaining successful clinical outcome. In longstanding, therapy resistant FNRFS, loperamide may be an effective treatment option in these children. Furthermore, as 15% of FNRFS patients continue to have encopresis at the age of 18, we enervated the belief that these children will grow out of the encopresis. Finally, we show that the laxative polyethylene glycol 3350 is as effective as lactulose in increasing defecation frequency and decreasing encopresis frequency. However, it results in higher success rates with lower side effects. PEG 3350 should replace lactulose as first line treatment option in children with constipation.

**Future perspectives**

In this thesis, using rather sophisticated methods, we identified abnormalities in rectal function in children with constipation and confirmed normal rectal function in FNRFS patients. The question however remains whether this insight will contribute to better patient management. Indeed, in an ideal situation, we want to develop a treatment strategy targeting well defined abnormalities in rectal function or in the underlying pathophysiology, leading to clinical improvement.

Especially as we observed that rectal function is normal in a large population of constipated patients, and that clinical improvement occurs even in the presence of disturbed rectal compliance, suggests that other, so far unidentified factors must be involved. In view of the major impact of paediatric defecation disorders on quality of life of our patients and the high percentage of patients 'taking' their paediatric symptoms into adulthood, it is our duty to continue searching for new underlying mechanisms in order to improve treatment. In particular, studies trying to unravel neuromuscular mechanisms controlling colonic motility but also psychological components affecting colorectal function remain a challenge. Some
of these studies are currently in progress in our motility unit and will hopefully enhance our understanding of these common paediatric symptom complexes and boost treatment outcome.
References


