Complementary therapies in paediatric gastroenterology: prevalence, safety and efficacy studies
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Chapter 5

No change in rectal sensitivity after gut-directed hypnotherapy in children with functional abdominal pain and irritable bowel syndrome

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Submitted
Abstract

**Objective:** Gut-directed hypnotherapy has recently been shown to be highly effective in treating children with functional abdominal pain (FAP) and irritable bowel syndrome (IBS). This study was conducted to determine to what extent this treatment success is due to improvement of rectal sensitivity.

**Design:** 46 patients (8-18 years) with FAP (n=28) and IBS (n=18), were randomized to either 12 weeks of standard medical therapy (SMT) or gut-directed hypnotherapy (HT). To assess rectal sensitivity a pressure-controlled intermittent distension protocol (barostat) was performed before and after therapy.

**Results:** Rectal sensitivity scores changed in SMT patients from 15.1 ± 7.3 mmHg at baseline to 18.6 ± 8.5 mmHg after 12 weeks of treatment (p=0.09) and in HT patients from 17.0 ± 9.2 mmHg to 22.5 ± 10.1 mmHg (p=0.09). The number of patients with rectal hypersensitivity decreased from 6/18 to 0/18 in the HT group versus 6/20 to 4/20 in the SMT group (p=0.1). No relation was found between treatment success and rectal pain thresholds. Rectal sensitivity scores at baseline were not correlated to intensity, frequency or duration of abdominal pain.

**Conclusion:** Clinical success achieved with HT can not be explained by improvement of rectal sensitivity. Furthermore, no association exists between rectal barostat findings and clinical symptoms in children with FAP and IBS. Further studies are necessary to shed more light on both the role of rectal sensitivity in pediatric FAP and IBS and the mechanisms by which hypnotherapy results in improvement of clinical symptoms.
Introduction

Functional abdominal pain (FAP) and irritable bowel syndrome (IBS) in childhood are two of the most common pediatric functional gastrointestinal disorders with prevalence’s up to 19%. These disorders are characterized by recurrent or chronic abdominal pain and by disturbed defecation in case of IBS. There is no objective evidence of an underlying organic disease. The pathogenesis of pediatric functional abdominal pain and irritable bowel syndrome is still under debate, but it is generally accepted that these disorders are a result of disordered brain-gut interaction. Visceral hypersensitivity, a heightened sensitivity of the gut for stimuli, is thought to play a central role in the pathogenesis. Several studies using rectal or gastric barostat have confirmed visceral hypersensitivity by demonstrating lower pain thresholds in children with FAP and IBS compared to healthy controls.

Gut-directed hypnotherapy (HT) has been shown to be very effective in the treatment of adult patients with IBS, with the majority of patients showing long-term improvement of symptoms and quality of life. The mechanisms by which hypnosis produces these therapeutic effects are not completely elucidated. It has been suggested that gut-directed hypnotherapy impacts IBS by improvement of visceral hypersensitivity. However, results have been conflicting with two studies demonstrating a reduction in rectal sensitivity after hypnosis whereas two others failed to find such an effect. Recently we have shown that gut-directed hypnotherapy is very effective in the treatment of children with FAP and IBS. After 3 months of therapy, 59% of the patients in the HT group were in clinical remission with another 26% significantly improved. In the control group, receiving standard medical treatment (SMT), only 12% was in remission and 32% improved. One year after treatment, 85% of the patients treated with HT was asymptomatic versus 25% of the children who received SMT. The present study was conducted to determine to what extend treatment success of hypnotherapy in children with FAP and IBS is due to improvement of rectal sensitivity.

In adult literature, controversy exists regarding the relation between symptom severity and altered visceral sensitivity in IBS, with some studies reporting that RHS is correlated with severe symptoms in IBS, and others not finding such an association. In children with FAP or IBS, only one small study has been performed, showing that rectal hypersensitivity was not proportional to the severity of symptoms in children with FAP and IBS. Therefore, a second goal of our study was to analyze the correlation between rectal barostat findings and clinical symptoms in children with long lasting FAP and IBS.
Patients and Methods

Study participants

This study was part of a randomized controlled trial of hypnotherapy versus standard medical care in the treatment of children with FAP and IBS. Children were recruited from the department of pediatric gastroenterology of the Emma Children’s Hospital / Academic Medical Centre Amsterdam, the Netherlands. All children between 8 and 18 years who were diagnosed with either FAP or IBS according to the Rome II criteria and with a history of abdominal complaints of at least 12 months were invited to participate. Exclusion criteria were the use of medication influencing gastrointestinal functions; a concomitant organic gastrointestinal disease; functional constipation; treatment by another health care professional for abdominal symptoms; mental retardation; neurological or psychiatric problems and insufficient knowledge of the Dutch language. All patients and/or parents gave written informed consent. The study protocol was approved by the medical ethics committee of the hospital.

Design

Patients were randomly allocated using a computerized random-number generator for concealment to either hypnotherapy or standard medical care. Hypnotherapy was carried out by C.M. and consisted of 6 sessions of 50 minutes over a 3-month period. The Manchester protocol of gut-directed hypnotherapy was used, adapted for children. Patients in the standard medical treatment group received standard care consisting of education, dietary advice, extra fibers and pain medication or proton-pump inhibitors if considered necessary. Moreover they received 6 half hour sessions of supportive therapy over a three month period with M.A.B. or A.M.V. In these sessions symptoms of the previous weeks were discussed with an exploration of possible contributory triggers like dietary products, emotional problems and stressful events.

Abdominal pain and rectal sensitivity were measured at baseline and shortly after therapy. Participants were asked to keep a 7-day pain diary card, on which they recorded daily the intensity and frequency of abdominal pain. Pain intensity was scored using an affective facial pain scale with faces showing no pain at all (face A) to faces showing severe pain (face I). Afterwards, these scores were transposed to a daily score of 0 = no pain, 1 = faces A-C, 2 = faces D-F and 3 = faces G-I. The data for 7 days were totaled, giving a maximum pain intensity score of 21. Pain frequency was daily scored as follows: 0 = no pain, 1 = 1 to 30 minutes pain, 2 = 31 to 120 minutes of pain, 3 = > 120 minutes pain per day. Again, the data for 7 days were totaled, giving a pain frequency score. Pain diaries were analyzed by a medical student, who was blinded for the treatment arm. Clinical remission was defined as a decrease of the pain intensity and frequency scores of > 80%; significant improvement was defined as a decrease of these scores between
30 and 80% and treatment was considered unsuccessful if the scores improved < 30% or got worse.

Rectal barostat
In patients, at baseline and after 12 weeks of therapy a rectal barostat test was performed as previously reported. Pain medications and all medications known to affect gastrointestinal motility were discontinued 48 hours prior to the test. A non-compliant polyethylene balloon with a maximum volume of 500 ml was connected to a computer-driven barostat device (Synectics Visceral Stimulator; Synectics, Netherlands). The balloon was fixed on a silicone catheter with an outside diameter of 4 mm and an inside diameter of 3 mm, allowing a flow of air of 38 ml/sec. Before and after each study, the balloon was checked for leakage. The subjects were placed in the left lateral position. Before insertion of the balloon, rectal digital examination was performed to check if the rectum was empty. The lubricated balloon was introduced manually into the rectum. Prior to the pressure-controlled distension protocol, the balloon was unfolded by stepwise volume increase (30 ml per step) until a volume of 150 ml was reached. The inflated balloon was then pulled back against the pelvic floor. After deflation and a 15 minute period of equilibration, the minimal distension pressure (MDP) was determined by stepwise increasing the intra-balloon pressure (1 mmHg steps of 1 minute). MDP was defined as the pressure resulting in an intra-balloon volume of at least 30 ml at which volume changes to breathing could be identified. Another 15 minute period with a deflated balloon was added to allow for rectal adaptation. Rectal sensation was determined from an intermittent distension protocol with step-wise increases of 3 mmHg to a maximum of 39 mmHg above MDP, lasting 1 minute with intervals of 1 minute at MDP. When pain occurred during the protocol or when maximal balloon volume (500 ml) was reached, the balloon was immediately deflated and the study ended.

At every pressure step the child was asked to score sensation when the selected pressure was reached and after 30 seconds. An ordinal scale from 0-5 was used to score sensation: 0=no sensation, 1=first sensation, 2=urge to defecate, 3=moderate urge to defecate, 4=severe urge to defecate, 5=pain. Thresholds for sensation were expressed as pressure above MDP. When individuals did not report urge or pain during the protocol, or the maximal balloon volume was reached before the end of the study, the highest pressure value was assigned (i.e. 39 mmHg above MDP). Rectal hypersensitivity was defined as a pain threshold below the 5th percentile of healthy controls (≤ 9 mmHg above MDP).

Data Analysis
Baseline characteristics of study subjects were analyzed in a descriptive way. Potential differences in baseline characteristics between therapy groups were assessed by
Chi-square, Fisher’s exact, and Mann-Whitney U tests. Pearson correlations were calculated to examine the relation between pressure thresholds for pain and predefined baseline factors (duration of symptoms, pain intensity scores, pain frequency scores). Wilcoxon signed rank tests were used to evaluate the change of pressure thresholds for pain from baseline to 12 weeks. For all statistical analyses, statistical significance was set at the .05 level, and all tests were 2-tailed. Statistical analysis was performed using SPSS version 16.0. This trial is registered as an International Standard Randomized Clinical Trial, number ISRCTN 26628553. There was no external funding source.

Results

A total of fifty-three children fulfilled the ROME II criteria for FAP or IBS and were recruited for the study: 28 patients were allocated to the HT group and 25 to the SMT group (Figure 1). Of the HT group, one patient was lost to follow-up and 4 refused to undergo a rectal barostat. In the SMT group, 2 children refused the barostat. Therefore, 23 patients in each group were included in the data analysis prior to therapy. After 3 months of treatment, a follow-up barostat was performed in 18 patients of the HT group and 20 patients in the SMT group; in 5 versus 3 children no second barostat was performed, because they refused to undergo a second test. Demographic characteristics, disease variables and rectal barostat results of all participating patients are provided in Table 1: no significant differences were found between the two treatment groups.

Rectal sensitivity in relation to treatment outcome

Change in pain thresholds was analyzed in those patients, in whom two barostat exams had been performed. In both treatment groups a trend was observed towards

<table>
<thead>
<tr>
<th>Table 1: Baseline characteristics of participants, by treatment group.</th>
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<tr>
<td><strong>Standard Therapy</strong> (n = 23)</td>
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<tr>
<td>Age, yrs *</td>
</tr>
<tr>
<td>Girls (%)</td>
</tr>
<tr>
<td>FAP (%)</td>
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<tr>
<td>IBS (%)</td>
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<td>Duration of symptoms, yrs *</td>
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<tr>
<td>Pain intensity score*</td>
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<td>Pain frequency score*</td>
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<tr>
<td>Pain threshold - mmHg</td>
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<td>Patients with RHS (%)</td>
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FAP = functional abdominal pain; IBS = irritable bowel syndrome; RHS = rectal hypersensitivity. * Data are mean (SD).
improvement of rectal sensitivity: in SMT patients pain thresholds changed from 15.1 ± 7.3 mmHg at baseline to 18.6 ± 8.5 mmHg at 12 weeks (p=0.09) and in HT patients from 17.0 ± 9.2 mmHg to 22.5 ± 10.1 mmHg (p=0.09). The number of patients with rectal hypersensitivity decreased from 6/18 to 0/18 in the HT group versus 6/20 to 4/20 in the SMT group (p=0.1). We then analyzed if this trend towards improvement in rectal sensitivity was related to clinical outcome. Figure 2 shows that outcome, defined as clinical remission, significantly improvement or treatment failure, was unrelated to rectal sensitivity with similar thresholds in patients of different outcome categories.

Rectal sensitivity at baseline in relation to symptoms.

The second goal of our study was to analyze the correlation between rectal barostat findings and clinical symptoms. No relation was found between pain threshold at baseline and pain intensity score (r=0.102; p=0.50), pain frequency scores (r=0.06; p=0.70) and duration of symptoms (r=-0.09; p=0.60) in patients with FAP and IBS (figures 3a, 3b and 3c).
Discussion

This study clearly shows that in children with functional abdominal pain or irritable bowel syndrome, resolution of abdominal pain, either due to hypnotherapy or standard medical treatment, is not related to a change in rectal sensitivity. Our observations are consistent with some findings in adult IBS patients, treated with gut-directed hypnotherapy. However, results on this issue are divergent with two other adult studies demonstrating significant changes of rectal pain thresholds after HT. It has been suggested that improvement of rectal hypersensitivity and hyposensitivity, found in those latter studies, was not due to hypnotherapy, but simply represented a regression to the mean; i.e. high values tend to decrease and low values to increase on repeated testing. This could also explain the trends we found towards an increase in pain thresholds after therapy in both patient groups and the decrease in the number of patients with RHS. Another explanation is that rectal responses in hypersensitive patients normalize due to habituation followed repeated testing, but this is a debated issue.

To our surprise, we found rectal hypersensitivity in only 23% of the patients. A recent study by Faure et al., using a similar barostat protocol and measuring rectal pain thresholds in children with FGIDs, found much higher percentages of children with RHS when compared to our study: 85% of 21 IBS patients and 88% of 8 FAP patients had rectal hypersensitivity. This difference was probably caused by the fact that the cut-off value for RHS was 30.8 mm Hg in the latter study compared to 9 mmHg in our study (both 5th percentile of control children). When we used the same criteria as the group of Faure to define visceral hypersensitivity, 41 of 46 (89%) patients could be classified as hypersensitive. It is unclear why 9 mm Hg was the 5th percentile of rectal pain threshold in our group of 22 healthy children versus 30.8 mm Hg in the study of Faure, who examined 8 healthy volunteers. It is reasonable to assume that the low number of control children in both studies has attributed to this difference. A larger cohort of healthy pediatric volunteers should therefore be examined to establish a reliable cut-off value for defining rectal hypersensitivity in children, making comparison between studies.
No change in rectal sensitivity after hypnotherapy

**Figure 3a.** Relation between pain intensity scores at baseline and rectal barostats, including a regression line ($r=0.102; p=0.50$).

**Figure 3b.** Relation between pain frequency scores at baseline and rectal barostats, including a regression line ($r=0.06; p=0.70$).

**Figure 3c.** Relation between duration of abdominal symptoms in years and rectal barostats, including a regression line ($r= -0.09; p=0.60$).
possible. Ethical issues have prevented us thus far to study a larger cohort of HV. In adult literature, similar differences in the proportion of IBS patients with hypersensitivity have been reported; again the difference in definition of hypersensitivity has been considered as one of the factors contributing to those discrepancies.15,17,26

No relation was found between rectal sensitivity scores and duration of symptoms, pain intensity and pain frequency, suggesting that rectal barostat is not an adequate tool to distinguish pediatric FAP and IBS patients with mild symptoms from those with severe symptoms. This is in agreement with a similar study among 47 pediatric patients with FAP and IBS, showing that rectal hypersensitivity was not proportional to the severity of abdominal symptoms.18 There is no clear-cut explanation for these findings. It has been suggested that rectal barostat is not an adequate tool to investigate visceral hypersensitivity, because FAP and IBS symptoms originate predominantly from the colon or small intestine. Measuring thresholds in the colon instead of the rectum27, or using the recently introduced water load symptom provocation test28 might proof to be more reliable methods to study pain thresholds. Another explanation for the lack of correlation between pain thresholds and symptoms can be that visceral hypersensitivity plays only a minor role in the etiology of abdominal pain in children and that other factors, like parental attention, concomitant anxiety or depression, or an increased tendency to report pain, are more important.29-31

Several limitations should be kept in mind when interpreting these data. First, our ability to draw robust conclusions may be hampered by the relatively small number of patients, which caused limited statistical power and small effects of the intervention may therefore not have been detected. Furthermore, some confounding might have occurred with the high number of children who withdrew their consent to undergo a barostat exam. We cannot exclude the possibility that children with RHS are more likely to fear a barostat exam than children with a normal sensitivity, thereby lowering the percentage of children with RHS in our study at baseline. Interestingly, however, 5 of the 8 children who refused a second barostat had a pain threshold ≥ 30 mmHg at baseline, suggesting that RHS was not a reason for refusing a barostat. Thirdly, a significant proportion of the patients in this study showed a continuing improvement in symptoms in the year after hypnotic treatment, probably due to post-hypnotic suggestions.14 One can imagine that also rectal sensitivity continued to improve, but because the second barostat was already performed in the first month after the last treatment session, we may have missed long-term improvement in rectal sensitivity.

These caveats not withstanding, some conclusions can be drawn from this study. Rectal sensitivity scores are not correlated with symptom severity, and the response to either gut-directed hypnotherapy or standard medical treatment in these patients is not associated with improvement of rectal sensitivity. Our findings question the central
role of rectal hypersensitivity in the pathogenesis of pediatric functional gastrointestinal disorders. We hypothesize that other factors like anxiety and depression, parental attention to pain, and an altered cerebral perception of pain stimuli are more important in the etiology of symptoms in FAP and IBS. Further studies are necessary to shed more light on both the pathogenesis of FAP and IBS in children and the mechanisms by which hypnotherapy results in improvement of clinical symptoms.
Reference List


