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Home-Based Hypnotherapy Self-exercises vs Individual Hypnotherapy With a Therapist for Treatment of Pediatric Irritable Bowel Syndrome, Functional Abdominal Pain, or Functional Abdominal Pain Syndrome

A Randomized Clinical Trial

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IMPORTANCE Individual gut-directed hypnotherapy (HT) is effective in pediatric irritable bowel syndrome (IBS) and functional abdominal pain or functional abdominal pain syndrome (FAP[S]). It is, however, unavailable to many children.

OBJECTIVE To compare the effectiveness of HT by means of home-based self-exercises using a CD with that of individual HT (iHT) performed by qualified therapists.

DESIGN, SETTING, AND PARTICIPANTS This noninferiority randomized clinical trial with a follow-up of 1 year after the end of treatment was conducted from July 15, 2011, through June 24, 2013, at 9 secondary and tertiary care centers throughout the Netherlands. A total of 303 children were eligible to participate. Of those, 260 children (aged 8-18 years) with IBS or FAP(S) were included in this study. Children were randomized (1:1 ratio) to home-based HT with a CD (CD group) or iHT performed by qualified therapists (iHT group). No children withdrew from the study because of adverse effects.

INTERVENTIONS The CD group was instructed to perform exercises 5 times per week or more for 3 months. The iHT group consisted of 6 sessions during 3 months.

MAIN OUTCOMES AND MEASURES Primary outcomes were treatment success directly after treatment and after 1-year follow-up. Treatment success was defined as a 50% or greater reduction in pain frequency and intensity scores. The noninferiority limit was set at 50% treatment success in the CD group, with a maximum of 25% difference in treatment success with the iHT group after 1-year follow-up. Modified intention-to-treat analyses were performed.

RESULTS A total of 132 children were assigned to the CD group and 128 to the iHT group; 250 children were analyzed (126 in the CD group and 124 in the iHT group) (mean [SD] age, 13.4 [2.9] years in the CD group and 13.3 [2.8] years in the iHT group; 94 female [74.6%] in the CD group and 85 [68.5%] in the iHT group). Directly after treatment, 46 children (36.8%) in the CD group and 62 (50.1%) in the iHT group were successfully treated. After 1-year follow-up, the 62.1% treatment success in the CD group was noninferior to the 71.0% in the iHT group (difference, −8.9%; 90% CI, −18.9% to 0.7%; P = .002).

CONCLUSIONS AND RELEVANCE Long-term effectiveness of home-based HT with a CD is noninferior to iHT performed by therapists in pediatric IBS or FAP(S). Treatment with hypnosis using a CD provides an attractive treatment option for these children.

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Irritable bowel syndrome (IBS) and functional abdominal pain (syndrome) (FAP[S]) are commonly diagnosed pediatric FAP disorders with a worldwide prevalence of 13.5%.[1] After appropriate medical evaluation, the symptoms cannot be attributed to another condition.[2,3]

Management of IBS and FAP(S) is challenging because pathophysiologic mechanisms are not elucidated.[4] Treatment is usually symptomatic, consisting of physician reassurance, dietary advice, education, and pharmacologic pain management.[4] If these interventions do not result in adequate relief, nonpharmacologic therapies are often prescribed. Success rates of gut-directed hypnotherapy vary from 49% to 100% in adults and children.[5-10] Three relatively small randomized clinical trials (RCTs), with sample sizes varying from 34 to 52 children, were conducted in children and compared hypnotherapy with supportive therapy,[5] usual care,[6] or waiting list.[8] All 3 trials[5,6,8] reported beneficial effects of hypnotherapy, with 1 study[11] reporting long-lasting beneficial effects up to 5 years after treatment. Despite its proven effectiveness, hypnotherapy (HT) is still unavailable to many children because individual HT (iHT) performed by therapists is costly and requires a significant time investment by children and parents. Hypnotherapy by self-exercises at home using a CD might also be effective in children with IBS and FAP(S).[6] In addition, the lack of well-trained child hypnotherapists compels for an alternative treatment of pediatric IBS and FAP(S). Hypnotherapy using CD-recorded self-exercises at home may be such an alternative. Before children are given access to this self-exercise alternative, however, it should first be proven to be at least as efficacious as face-to-face HT to avoid undertreatment. A noninferiority study design is suited to determine whether a new treatment is at least as efficacious as a reference treatment with predefined margin of noninferiority for the new treatment to be acceptable.[12] We therefore conducted a noninferiority RCT to compare the effectiveness of HT using CD-recorded self-exercises at home vs iHT performed by qualified therapists in children with IBS or FAP(S).

Key Points

Question What is the effectiveness of home-based hypnotherapy exercises compared with individual hypnotherapy performed by qualified therapists in children with functional abdominal pain?

Findings This noninferiority randomized clinical trial of 250 analyzed children found that the effectiveness of home-based treatment with hypnosis was noninferior to individual hypnotherapy performed by therapists 1 year after the end of treatment.

Meaning Hypnotherapy is a highly valuable treatment in children with functional abdominal pain and should be incorporated in national guidelines and reimbursed by health insurance companies. This study provides a rationale for the implementation of an easy-to-use home-based treatment in daily practice.

Methods

Study Design and Participants

A detailed description of the study protocol has been published elsewhere.[13] Two academic medical centers and 7 teaching hospitals throughout the Netherlands participated in this noninferiority RCT that was supported by the Netherlands Organisation for Health Research and Development. The study protocol was approved by the medical ethics committees of all participating hospitals (Medisch Ethische Commissie AMC, Medisch Ethische Toetsingscommissie Noord-Holland, Commissie LTME, St. Antonius Ziekenhuis, Medisch Ethische Toetsingscommissie Máxima Medisch Centrum, Medisch Ethische Toetsingscommissie Flevoziekenhuis, Medisch Ethische Toetsingscommisie Isala Klinieken Zwolle, Medisch Ethische Toetsingscommissie Amphia, Medisch Ethische Toetsingscommissie azM/UM, and Toetsingscommissie Onderzoek Rotterdam e.o. Maasstad Ziekenhuis). Children aged 8 to 18 years diagnosed with IBS or FAP(S) (Rome III criteria) were randomized from July 15, 2011, through June 24, 2013.[2] Before randomization, all patients underwent routine laboratory testing to exclude underlying organic disorders. Exclusion criteria were concomitant organic gastrointestinal disease, treatment by another health care professional for abdominal pain, previous HT, intellectual disability (mental retardation), and insufficient knowledge of the Dutch language.

Randomization and Masking

After patients and/or parents gave verbal and written informed consent, the child was randomly allocated to iHT performed by a therapist (iHT group) or home-based HT with exercises on audio CD (CD group). A central computerized random-number generator for concealment was used, performing randomization (1:1 ratio) with random permuted blocks of varying sizes of 2, 4, and 6. Randomization was stratified by hospital and school level (primary or secondary school). Outcomes were assessed using questionnaires, which were completed at home by the child and/or parents.

Interventions

The gut-directed HT protocol that we used is a combination of exercises from our previously used Manchester protocol[5,14] and the protocol of van Tilburg et al.[6] The HT protocol consisted of general relaxation exercises, exercises on control of abdominal pain and gut functioning, and ego-strengthening suggestions. The exact content of the iHT sessions and the exercises on the CD has been published in detail elsewhere.[13] Children in both groups were instructed to practice HT exercises daily.

CD Group

A specially trained research nurse visited all children randomized to the CD group. Children performed the first HT exercise to check whether the child understood the instructions. The CD contained 5 standard scripts of the HT exercises, which were identical to the exercises used in the iHT group. Distinct CDs for children who attended primary and secondary schools were used to ensure that the language used was adapted to the child's developmental age. The frequency of listening was re-

corded by participants. The research nurse called children after 4 and 8 weeks of treatment to stimulate treatment adherence.

iHT Group

Children in the iHT group received six 50- to 60-minute sessions during 3 months. The HT was performed by 11 qualified, experienced hypnotherapists (C.F.) affiliated with the recruiting hospitals. They were trained in working with the protocol and instructed to use the same scripts as used in the CD group. Therapists were, however, allowed to adapt the contents and order of the scripts to the child's interests and issues that arose during the sessions. Between sessions, children were stimulated to listen daily to the same CD as the CD group.

Outcome Measures

Outcomes were measured at baseline (T0), 3 months after treatment start (T1), and 6- and 12-month follow-up after the end of therapy (T2 and T3). eTable 1 in the Supplement lists the outcome measures used.[13]

Primary Outcomes

Children completed a standardized diary to assess abdominal pain frequency and pain intensity during 7 consecutive days, which were computed into a pain frequency score (PFS) (scale of 0-21, with 0 indicating no pain and 21 indicating abdominal pain lasting more than 120 minutes on 7 consecutive days) and pain intensity score (PIS) (scale of 0-21, with 0 indicating no pain at all and 21 indicating the most severe pain [facial scale] on 7 consecutive days), repectively.[5,11] Primary outcomes were the proportion of patients for whom treatment was successful at the end of treatment and the proportion of successfully treated patients after 1-year follow-up. Treatment success was defined as at least 50% reduction in the PFS and PIS.

Secondary Outcomes

Secondary outcomes included depression, anxiety, somatization, health-related quality of life (QoL), pain beliefs, coping strategies, and adequate relief. Details of the instruments used to assess these outcomes were published previously.[13]

Statistical Analysis

Primary analyses focused on the proportions of treatment success in treatment arms at T1 and T3. On the basis of previous trials,[5-7] we made a conservative estimate of 75% treatment success at T3 in the iHT group. We anticipated this percentage to be approximately 65% in the CD group. To be a reasonable alternative, this percentage should not become lower than 50% at T3.[13] This noninferiority limit should be viewed in relation to standard medical care success rates of approximately 30% to 40% in previous trials.[5-7] A total of 115 patients were needed per group to achieve a power of 80% with a 1-sided $P < .05$. Because a less than 10% dropout rate was expected, 130 patients were included per treatment arm. Because the sample size calculation was based on a 1-sided noninferiority hypothesis test at a 5% significance level, statistical uncertainty of the between-group differences in the primary outcome were expressed as 2-sided 90% CIs. Only the primary outcome was assessed in terms of non-inferiority. Analyses of secondary outcomes were exploratory using 2-sided 95% CIs. Modified intention-to-treat analyses were performed that included all patients who started study treatment. Differences between treatment groups at baseline were analyzed using the χ^2 test, unpaired 2-tailed *t* test, or Mann-Whitney test.

All patients had complete baseline PFSs and PISs. Missing PFSs and PISs at subsequent time points were imputed using multiple imputation by chained equations algorithm.[15] Multiple imputation was performed separately for both treatment groups, and 7 cycles of imputation were performed, with the assumption that unobserved measurements were missing at random.[15] Extensive exploration of missing data patterns confirmed this assumption. The 7 data sets were combined using Rubin's rules.[15]

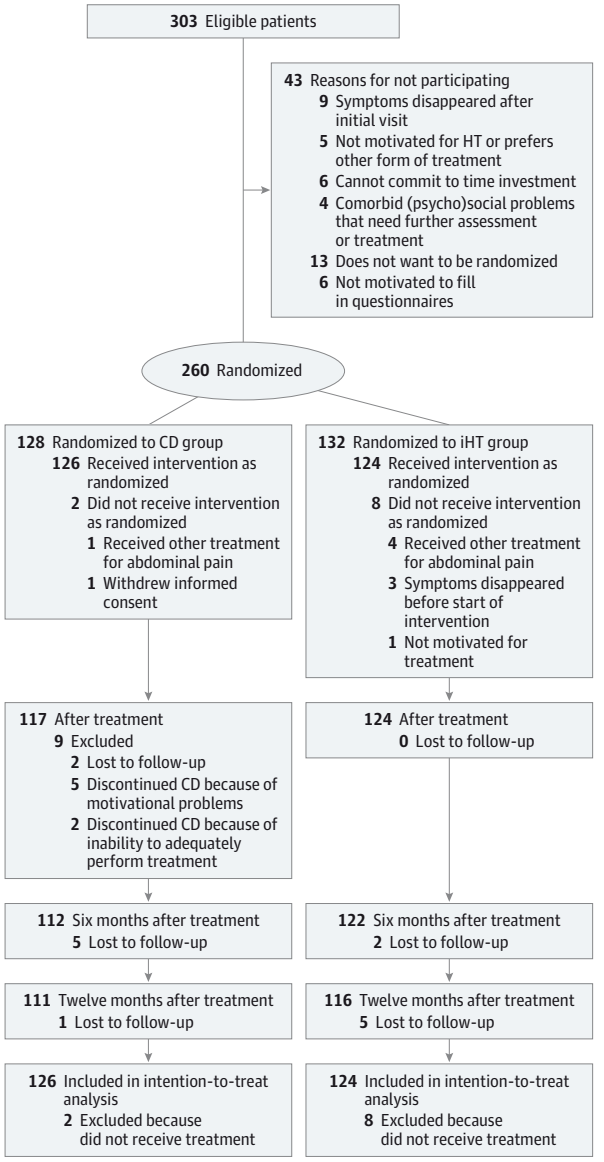
Two preplanned exploratory subgroup analyses (IBS vs FAP[S] and prepuberty [13 years or younger] vs older children) were performed and statistically tested with interaction effects in logistic regression analysis. In a secondary multivariable logistic regression analysis, baseline predictors for treatment success at T3 were identified out of a preselected set of candidate baseline predictors, similar to those used in multiple imputation. Variables univariately associated with treatment success ($P < .30$) were entered in a multivariable logistic regression model using backward elimination. In the iHT group, treatment success of different therapists at T3 was tested using a χ^2 test.

We compared the PFSs and PISs during the study (4 weeks, 8 weeks, T1, T2, T3) of both treatment groups by using marginal linear models adjusted for the baseline value and assuming an unstructured covariance structure among residuals observed at the 5 time points and based on restricted maximum likelihood estimation.[16] The course of the depression, anxiety, somatization, QoL, pain beliefs, and coping strategies scores was studied using marginal linear model analyses (eTable 2 in the Supplement). The binary outcome adequate relief over time was analyzed using a marginal model with a compound symmetry covariance structure for the residuals. The choices of covariance structures for all marginal models were based on the structure with the lowest Akaike information criterion value. Statistical analyses were performed using SPSS statistical software, version 20.0 (IBM Inc).

Results

A total of 303 children with IBS or FAP(S) were eligible to participate. A flowchart of study participants is presented in **Figure 1**. Of the 303 patients who fulfilled the inclusion criteria, 43 children (29 girls [67.4%]), with a mean (SD) age of 14.4 (2.9) years, declined participation. The most frequently reported reason for declining participation was unwillingness to be randomized (13 [30.2%]) because child and/or parents insisted on iHT performed by a hypnotherapist. A total of 260 children (85.8%) agreed to participate and were randomized to the CD group (n = 132) or the iHT group (n = 128). A total of

Figure 1. Flowchart of Study Participants



HT indicates hypnotherapy; iHT, individual hypnotherapy.

126 children started home-based treatment with the hypnosis CD, and 124 children started treatment in the iHT group and were included in the analyses (mean [SD] age, 13.4 [2.9] years in the CD group and 13.3 [2.8] years in the iHT group; 94 female [74.6%] in the CD group and 85 [68.5%] in the iHT group). Baseline characteristics of the 10 children not starting treatment did not differ from those who started treatment (eTable 3 in the Supplement). With the exception of the percentage of children with school absenteeism, no differences in baseline characteristics were observed between the groups (**Table 1**).

Primary Outcome

Children in the CD group listened to the CD a mean (SD) of 5.7 (1.4) times per week during the treatment period. Directly after treatment (T1), 46 children (36.8%) in the CD group were successfully treated compared with 62 (50.1%) in the iHT group (ie, a difference of −13.3%; 90% CI, −23.7% to −3.2%). At 6 months of follow-up after the end of treatment (T2), treatment success was 64 (51.1%) in the CD group and 81 (65.2%) in the iHT group (difference, −14.2%; 90% CI, −24.7% to −4.3%). One year after the end of treatment (T3), treatment success was 78 (62.1%) in the CD group and 88 (71.0%) in the iHT group (difference, −8.9%; 90% CI, −18.9% to 0.7%). The CD emerged as significantly noninferior to iHT because the lower limit of the 90% CI for this difference in success proportions was −18.9% (ie, lying above the noninferiority limit: 71.0%-18.9% = 52.1%; ie, >50% treatment success and −18.9% > −25% difference in treatment success; P = .002) (**Table 2**).

Exploratory subgroup analyses revealed no treatment effect modification by age (prepuberty or older age) or diagnosis (IBS or FAP[S]) at all time points (Table 2). In a secondary multivariable analysis of preselected candidate baseline predictors, male sex, shorter duration of symptoms, and having fewer negative beliefs about the abdominal pain were identified to have prognostic value for treatment success at T3 (eTable 4 in the Supplement). Neither expectations about treatment response of the child and both parents nor hypnotic susceptibility appeared to be associated with treatment success at T3 (eTable 4 in the Supplement). Whether the child still performed HT exercises at T1 was also not significantly associated with treatment success at T3 (odds ratio, 0.83; 95% CI, 0.34-3.80). In the iHT group, no therapist effect on treatment effect was observed (P = .80).

Secondary Outcomes

Mean PFSs and PISs with their corresponding 95% CIs in both treatment groups during treatment and follow-up are shown in **Figure 2**A and B. Adjusted for respective baseline pain scores, a significant improvement was seen in the PFSs and PISs in both treatment groups. Overall, the mean PFSs and PISs over time were on average 1.7 points higher in the CD group compared with the corresponding means in the iHT group (95% CIs, 0.4-3.0 for PFS and 0.4-2.9 for PIS; main treatment group effects). Exploratory analyses suggested improvement in time in both treatment groups for all secondary outcomes, with the exception of QoL self-perception (eTable 2 in the Supplement). No treatment differences were observed for these secondary outcomes except for negative pain beliefs and problem-focused coping potential, which favored the iHT group (eTable 2 in the Supplement). The proportion of parents reporting adequate relief directly after treatment was 82.7% in the iHT group and 70.2% in the CD group and increased to 87.0% in the iHT group and 75.9% in the CD group after 1-year follow-up (treatment group effect P = .002, no significant time P = .24, or time-treatment group interaction effect P = .74).

Discussion

This RCT confirms previously reported beneficial effects of gut-directed HT in children with IBS or FAP(S) and is the first, to our knowledge, to compare effectiveness of home-based treatment using a hypnosis CD with that of iHT performed by quali-

Table 1. Baseline Characteristics of Study Participants[a]

Characteristic	CD Group (n = 126)	iHT Group (n = 124)
Age, mean (SD), y	13.4 (2.9)	13.3 (2.8)
Female	94 (74.6)	85 (68.5)
IBS		
IBS-C	39 (60.0)	35 (57.4)
IBS-D	10 (15.4)	3 (4.9)
IBS-M	14 (21.5)	20 (32.8)
IBS-U	2 (3.1)	3 (4.9)
Total IBS	65 (51.6)	61 (49.2)
FAP(S)		
FAP	22 (36.1)	29 (46.0)
FAPS	39 (63.9)	34 (54.0)
Total FAP(S)	61 (48.4)	63 (50.8)
Duration of symptoms, median (IQR), y	2.3 (1.2-5.1)	2.7 (1.1-5.3)
School absenteeism	86 (68.3)	100 (80.6)
No. of school days missed in prior 6 mo, median (IQR)	14.0 (5.0-30.0)	21.1 (4.0-24.5)
Positive family history of abdominal pain	60 (47.6)	56 (45.2)
Prior psychological treatment	19 (15.2)	24 (19.4)
Hypnotic susceptibility, median (IQR)	6.0 (5.0-6.0)	6.0 (5.0-7.0)
Abdominal pain scores, mean (SD)		
Pain frequency score	15.1 (5.5)	14.6 (5.5)
Pain intensity score	15.1 (4.5)	14.6 (4.4)
Depression and anxiety scores, mean (SD)		
Depression	3.9 (2.4)	3.8 (2.5)
Anxiety, total score	10.9 (7.6)	11.8 (8.9)
Quality-of-life scores, mean (SD)		
Physical well-being	44.9 (10.3)	44.2 (9.7)
Psychological well-being	49.2 (9.9)	47.8 (9.6)
Moods and emotions	49.8 (10.8)	47.5 (11.4)
Self-perception	52.3 (10.4)	52.4 (10.4)
Social support and peers	50.7 (12.2)	49.2 (10.5)
School environment	53.1 (9.5)	51.9 (9.2)
Non-GI symptoms score, mean (SD)	14.1 (12.1)	14.9 (11.8)
Pain beliefs score, mean (SD)		
Negative pain beliefs	2.2 (0.6)	2.3 (0.6)
Problem-focused coping potential	1.4 (0.9)	1.3 (0.8)
Emotion-focused coping potential	2.2 (0.9)	2.3 (0.9)
Coping strategies score, mean (SD)		
Problem-focused coping	2.4 (0.5)	2.4 (0.5)
Positive cognitive reframing	2.1 (0.5)	2.1 (0.6)
Distraction strategies	1.7 (0.4)	1.8 (0.4)
Avoidance strategies	2.1 (0.4)	2.2 (0.5)
Support-seeking strategies	2.1 (0.7)	2.1 (0.6)

Abbreviations: FAP, functional abdominal pain; FAPS, functional abdominal pain syndrome; GI, gastrointestinal; IBS, irritable bowel syndrome; IBS-C, constipation predominant IBS; IBS-D, diarrhea predominant IBS; IBS-M, mixed type with alternating episodes of both constipation and diarrhea; IBS-U, unsubtyped IBS (abnormality in stool consistency is not sufficient to meet the criteria for IBS-C, IBS-D, or IBS-M); iHT, individual hypnotherapy.

[a] Data are presented as number (percentage) of patients unless otherwise indicated.

fied therapists. One year after the end of treatment, 62.1% of children in the CD group and 71.0% in the iHT group were successfully treated.

Despite a significant lower percentage of treatment success in the CD group, results fulfill the predetermined limit for noninferiority, and long-term effectiveness of treatment with a hypnosis CD is noninferior to that of iHT by therapists. In addition, both treatment groups had decreased depression, anxiety, and somatization scores and improvement of QoL and pain beliefs. Both treatment forms were well received, reflected by adequate relief after 1-year follow-up of 87.0% in the iHT group and 75.9% in the CD group.

The 62.1% response rate after CD treatment is comparable to the success rate reported in the trial performed by van Tilburg et al,[6] which used the same definition of treatment success. The 71.0% treatment success in the iHT group lies within the range of previously reported success percentages in adult and pediatric HT trials.[7-9] It is, however, lower than response rates reported in the previous Dutch RCT,[5] which used a more conservative definition of treatment success. This finding may be explained by the almost 5-fold higher sample size of the present study and by small adaptions of the HT protocol. In the previous trial, no fixed hypnotic scripts were used, and one additional exercise was included on visualizing the needs of the child's gut.[5] This exercise was excluded from the current HT protocol because it was difficult to standardize. Success rates in the current RCT, however, should be viewed in relation to markedly lower success percentages after standard medical care and a variety of pharmacologic and nonpharmacologic treatments.[17,18]

Subgroup analyses suggested that treatment effect did not vary for children of prepuberty age and older children. In addition, no indication was found for different treatment effects in children with IBS and FAP(S). Male sex was a significant predictor of treatment success 1 year after the end of treatment. One other pediatric HT trial[5] did not find sex differences in treatment response, whereas others[6-8] did not study sex differences because of small sample sizes; adult data are inconclusive.[19] Sex differences in treatment response may be attributable to neural processing of visceral stimuli, which was found to differ between male and female patients with IBS.[20] Furthermore, sex-specific differences in response to tasks on affect and emotion processing are shown in brain regions known to be involved in working mechanisms of HT, such as the anterior cingulate cortex.[21-23] Because the present RCT was only powered to evaluate treatment differences for the primary end point in the total study population, the results of subgroup and multivariable analyses should be interpreted with caution and considered to be hypothesis-generation analyses, which need to be established by future RCTs. Having fewer negative beliefs about the abdominal pain resulted in better treatment response. Negative beliefs are known to mediate outcomes of cognitive behavior therapy and may predict long-term outcome in children with IBS and FAP(S).[24-26] Our trial suggests that children with negative beliefs at baseline may benefit from combined gut-directed HT and cognitive restructuring.[27] Depression and/or anxiety scores at baseline

Table 2. Treatment Success

Variable	No. (%) of Patients[a] CD Group	iHT Group	Difference in Treatment Success (90% CI), %[b]
Primary analysis[c]			
Treatment success T1	46 (36.8)	62 (50.1)	−13.3 (−23.7 to −3.2)
Treatment success T2	64 (51.1)	81 (65.2)	−14.2 (−24.7 to −4.3)
Treatment success T3	78 (62.1)	88 (71.0)	−8.9 (−18.9 to 0.7)
Exploratory subgroup analysis (age <13 y)[d]			
Treatment success T1	23 (41.1)	35 (60.3)	−19.2 (−33.5 to −3.8)
Treatment success T2	32 (57.1)	42 (72.4)	−15.3 (−29.2 to −0.5)
Treatment success T3	38 (67.9)	45 (77.6)	−9.7 (−23.1 to 4.0)
Exploratory subgroup analysis (age ≥13 y)[e]			
Treatment success T1	24 (34.3)	27 (40.9)	−6.6 (−19.9 to 7.0)
Treatment success T2	33 (47.1)	39 (59.1)	−12.0 (−25.4 to 2.1)
Treatment success T3	39 (55.7)	43 (65.2)	−9.5 (−22.7 to 4.4)
Exploratory subgroup analysis (diagnosis of IBS)[f]			
Treatment success T1	24 (36.9)	33 (54.1)	−17.2 (−30.8 to −2.5)
Treatment success T2	31 (47.7)	41 (67.2)	−19.5 (−32.9 to −5.0)
Treatment success T3	37 (56.9)	43 (70.5)	−13.6 (−26.9 to 0.6)
Exploratory subgroup analysis (diagnosis of FAP[S])[g]			
Treatment success T1	22 (36.1)	29 (46.0)	−9.9 (−23.9 to 4.5)
Treatment success T2	33 (54.1)	40 (63.5)	−9.4 (−23.4 to 5.1)
Treatment success T3	40 (65.6)	45 (71.4)	−5.8 (−19.3 to 7.8)

Abbreviations: FAP, functional abdominal pain; FAPS, functional abdominal pain syndrome; iHT, individual hypnotherapy; T1, 3 months after treatment start; T2, 6-month follow-up after the end of therapy; T3, 12-month follow-up after the end of therapy.

[a] Rounded to whole integers.

[b] The difference in treatment success at each time was compared between subgroups by using interaction terms. No statistically significant differences were observed. Because the sample size calculation was based on a 1-sided noninferiority hypothesis test at a 5% significance level, statistical uncertainty of the between-group differences in the primary outcome were expressed as 2-sided 90% CIs. The lower limit of a 1-sided 95% CI equals the lower limit of a 2-sided 90% CI. See the Statistical Analysis subsection of the Methods section for further details on the definition of noninferiority.

[c] Includes 126 patients in the CD group and 124 in the iHT group.

[d] Includes 56 patients in the CD group and 58 in the iHT group.

[e] Includes 70 patients in the CD group and 66 in the iHT group.

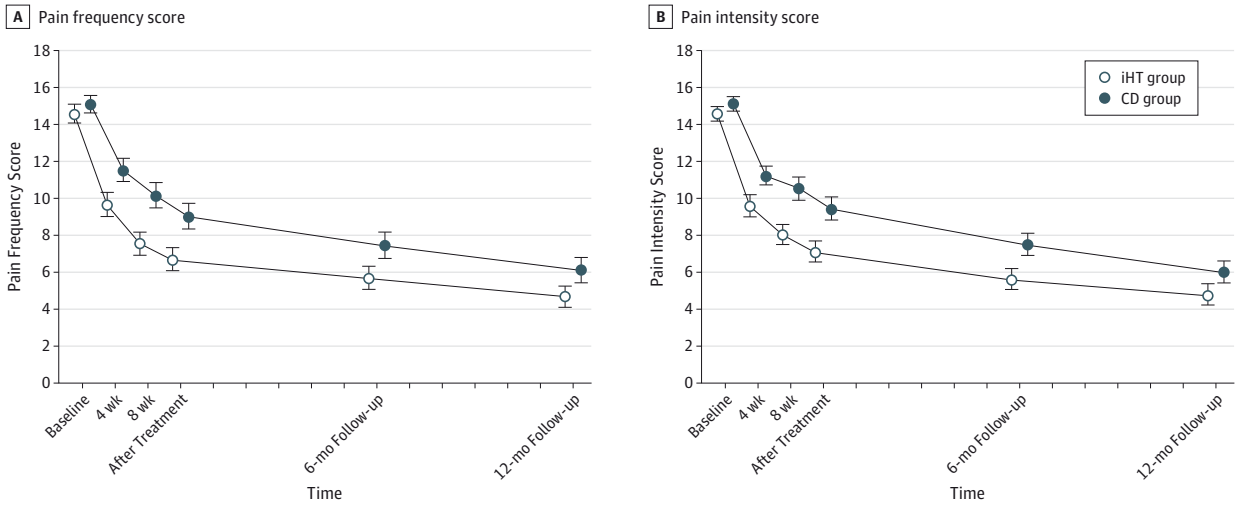
[f] Includes 65 patients in the CD group and 61 in the iHT group.

[g] Includes 61 patients in the CD group and 63 in the iHT group.

were not associated with treatment outcome, suggesting that HT is valuable, even for anxious or depressed children with IBS or FAP(S).

This is the largest RCT on HT in adults and children worldwide.[5-10] Previous pediatric HT trials included sample sizes of up to 52 children.[5-8] Generalizability of results is in-

Figure 2. Pain Frequency and Intensity Scores During Treatment and Follow-up



A, Mean pain frequency scores. B, Mean pain intensity scores. Error bars indicate 95% CIs. iHT indicates individual hypnotherapy.

creased by inclusion of children and adolescents recruited from secondary and tertiary care centers in rural and urban areas. Eleven therapists participated in the iHT group. No association between treatment success and the therapist performing the HT was found, which further strengthens results.

Limitations

The label *hypnosis* may increase beliefs and expectancies about treatment response, and expectancies are thought to (partly) mediate effects of psychological treatments.[28,29] The magnitude of this expectancy bias, however, appeared to be low in this RCT because treatment success was not predicted by treatment expectations of the child and both parents (eTable 4 in the Supplement). Hypnotic susceptibility also did not predict treatment success, which is in accordance with a large audit on HT for adults with IBS.[30] It could be hypothesized that the natural course of illness to some extent influenced response to treatment. Long-term follow-up studies in children with FAP disorders, however, found persisting symptoms in up to 45% of children after 5 years of follow-up,[31,32] and more than one-third of children still experienced symptoms after 10 years.[33] Children in this trial experienced abdominal symptoms for approximately 2.5 years before inclusion. Therefore, it is not likely that spontaneous remission contributed significantly to the proportions of treatment success. Inherent to the nature of HT, treatment masking is not possible. It could be hypothesized that this lack of masking is a limitation that may favor the iHT group because children might want to please their therapist. However, outcomes were recorded by children and parents at home and sent to the researchers without informing the therapist, which reduced the risk of socially desirable answers and detection bias. Individual variability of symptoms over time was corrected by recording abdominal pain at 7 consecutive days.

Conclusions

This study confirms earlier findings that HT is highly valuable in treating children with IBS or FAP(S), resulting in a significant decrease in pain scores and significant improvements in anxiety, depression, QoL, and pain beliefs. Therefore, HT should be incorporated in national guidelines on the treatment of pediatric IBS or FAP(S) and become reimbursed by health insurance companies. The noninferiority of home-based treatment with a hypnosis CD provides a rationale for implementation of this easy-to-use treatment in daily practice. Because the current generation of children and adolescents rarely uses CDs anymore, it would be preferable to implement the treatment as an application for a smartphone or tablet. Accessibility of HT will be improved because treatment with a CD can be started as soon as IBS or FAP(S) is diagnosed, without dealing with waiting lists caused by a shortage of qualified therapists.

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