Yoga Therapy for Abdominal Pain-Related Functional Gastrointestinal Disorders in Children: A Randomized Controlled Trial

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See ''Placebo Effect or Not: Yoga Therapy in Children With Functional Abdominal Pain'' by Vandenplas on page 451.

ABSTRACT

Objectives: The aim of the present study was to compare effects of 10 weeks of yoga therapy (YT) and standard medical care (SMC) on abdominal pain and quality of life (QoL) in children with abdominal pain–related functional gastrointestinal disorders (AP-FGIDs).

Methods: Sixty-nine patients, ages 8 to 18 years, with AP-FGIDs, were randomized to SMC complemented with YT or SMC alone. YT is a mixture of yoga poses, meditation, and relaxation exercises and was given once a week in group sessions. SMC consisted of education, reassurance, dietary advice, and fibers/mebeverine, if necessary. Pain intensity (pain intensity score [PIS] 0–5) and frequency (pain frequency score [PFS] 0–4) were scored in a pain diary, and QoL was measured with KIDSCREEN-27. Follow-up was 12 months. Treatment response was defined as $\geq$50% reduction of weekly pain scores.

Results: At 1-year follow-up, treatment response was accomplished in 58% of the YT group and in 29% of the control group ($P = 0.01$); no significant differences for other time points were found. YT, and not SMC, resulted in a significant reduction of PIS ($P < 0.01$) and PFS ($P < 0.01$) after 12 months. During the study, however, YT was not significantly superior compared with SMC. Subanalyses for time points demonstrated a significant greater reduction of PIS at 12 months in favor of YT. No differences were found for QoL. YT was more effective in the reduction of reported monthly school absence ($P = 0.03$).

Conclusion: At 1-year follow-up, YT in addition to standard care was superior compared with SMC according to treatment success, PIS, and reduction of school absence. YT, however, was not significantly more effective in improving PFS or QoL, compared with SMC.

Key Words: children, functional abdominal pain, functional gastrointestinal disorders, irritable bowel syndrome, quality of life, yoga

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What Is Known

- Psychological distress is strongly associated with abdominal pain in children.
- Yoga therapy has shown its efficacy in stress management and has been recommended as intervention in adults with irritable bowel syndrome.

What Is New

- Yoga is an effective intervention for abdominal pain–related functional gastrointestinal disorders in childhood.
- It is safe and easy to implement.
- Ten weeks of yoga intervention resulted in a significant reduction of school absence and improved abdominal pain at 12-months follow-up.

Functional abdominal pain (FAP) is a common problem worldwide, with a prevalence of 13.5% (1). No organic cause can be identified to explain these symptoms (2). The Rome III criteria are currently used to determine the type of abdominal pain–related functional gastrointestinal disorder (AP-FGID); AP-FGIDs include functional dyspepsia, irritable bowel syndrome (IBS), abdominal migraine (AM), FAP, and FAP syndrome (3).

Abdominal pain can markedly interfere with the quality of life (QoL) and ranks second in causes of school absence (4). Benefits of standard treatment (reassurance and dietary alteration) and pharmacologic therapy are limited, and patients are often referred for additional psychological or behavioral therapy (5,6). In 29.1% of patients with FAP, pain persists for >5 years, despite frequent medical attention and interventions (7).

Several studies showed that psychological distress is strongly associated with abdominal pain in children, not just as a consequence of pain, but probably also as predictor of symptoms (8). This explains why relaxation-based therapy results in improved QoL and fewer complaints. Behavioral interventions, that is, based

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on relaxation, such as hypnotherapy (HT) and cognitive behavioral therapy (CBT) have shown to be more effective than standard medical therapy in children with FAP or IBS (9,10).

Another type of relaxation-based therapy is yoga therapy (YT) (11,12). Originating in India >4000 years ago (13), this mind–body exercise has been widely used to reduce stress and anxiety in patients with chronic conditions (eg, cancer patients, postmenopausal women with rheumatic arthritis, Crohn disease, and hypertension) and in healthy adults (14). Moreover, yoga is simple and can be easily applied at home. In Western civilization, yoga is most often associated with physical postures, breathing techniques, and meditation to promote physical and mental wellbeing (15). Limited research has shown that YT decreases stress in children, including psychological and physical symptoms (16,17). Furthermore, stress reduction as a result of compassion-based meditation has been correlated to structural changes in stress-responding brain areas (18,19). A pilot study showed promising results for the efficacy of yoga for children with FAP (20). There is, however, a clear need to further investigate and confirm effects of yoga on children with AP-FGIDs. This study aims to compare the effect of YT complementary to standard medical care (SMC) and SMC alone on pain frequency, pain intensity, and QoL in children with AP-FGIDs.

METHODS

Study Population

This randomized controlled trial (RCT) was performed at a nontertiary center, the Jeroen Bosch Hospital in The Netherlands. Between February 2012 and August 2013, all the patients visiting the outpatient clinic, ages 8 to 18 years, with abdominal pain fulfilling Rome III criteria for AP-FGIDs were eligible for inclusion (3). Children who already participated in any form of relaxation therapy (eg, HT, CBT, mindfulness, and meditation) for AP-FGIDs in the past and children with mental retardation were excluded. The study protocol was approved by the medical ethical committee of the hospital and was carried out in accordance with the Declaration of Helsinki. All the children and/or their legal guardians gave written informed consent.

Yoga Sessions

Weekly yoga sessions of 1.5 hour each were provided by certified children's yoga teachers (NvE/HD) for 10 weeks. Children ages 8 to 12 years and 13 to 18 years were divided into 2 groups of 5 to 10 children, with an approach conforming to their age. Sessions were based on classic Hatha yoga principles in combination with specialized yoga exercises for children (21,22), including classical yoga poses, meditation and breathing techniques, and relaxation exercises. Patients were taught to relax the abdomen and to focus their thoughts on a single positive topic or good experience instead of random wandering of thoughts or thinking about negative experiences, as described in compassion-based meditation (23). In doing this, the yoga teacher used standard practices using several animations: for example, dog, snake, and sun. Overall goals were to achieve balance, flexibility, concentration, and relaxation, and to improve positive self-awareness in breathing. Participants received a workbook with yoga exercises and were encouraged to practice on a daily basis at home.

Design

Eligible patients were randomly assigned to either YT and SMC or SMC alone by the physician. Random numbers were generated by a computer program with an allocation ratio of 1:1 and well-balanced blocks. A stratification scheme was used to assure balance between groups with respect to age (8–12 and 13–18 years). Before enrollment, all the children had received SMC, that is, education about their diagnosis, reassurance, dietary advice, extra fibers, and mebeverine, if considered necessary.

Outcomes were assessed at baseline, directly after finishing treatment, and at 6 and 12 months after baseline. All the participants visited the clinician at these time points. During the trial, the clinician was easily available for consultation by telephone or e-mail for both groups. Participants were asked to keep a 4-week abdominal pain diary, in which they recorded intensity and frequency of abdominal pain daily. Pain intensity was scored using the validated 6-face Faces Pain Scale-Revised (24), ranging from 0 (no pain) to 5 (very much pain). Pain frequency was scored as 0 = no daily pain, 1 = 0–20 minutes of daily pain, 2 = 20–40 minutes of daily pain, 3 = 40–90 minutes of daily pain, and 4 = >90 minutes of daily pain. The daily scores were added up, and mean week scores were used to obtain a pain intensity score (PIS) and a pain frequency score (PFS) for these different time points. In case of missing values, data of the available weeks were used for the mean weekly pain scores.

At the same time points, the KIDSCREEN-27 QoL questionnaire was administered (25). KIDSCREEN-27 is a validated screening instrument for children of ≥8 years and their parents, which encompasses physical wellbeing (5 items), psychological wellbeing (7 items), autonomy and parents (7 items), social support and peers (4 items), and school functioning (4 items). A 5-point response scale was used. Higher scores indicate a better QoL. Furthermore, school absenteeism related to abdominal pain was scored, defined as school absence at least once a month. Adverse events were inventoried during clinician visits.

Patients completed questionnaires online at home, using a data managing system (Research Manager; Nova Business Software, Zwolle, The Netherlands). If necessary, reminders were sent via e-mail. All the fields were mandatory; therefore, we had no missing data of the KIDSCREEN-27. Rasch scores and t values were calculated according to the KIDSCREEN-27 manual, and T values for children and their parents were compared between the intervention and the control groups.

Primary outcome measure was treatment response, defined as a decrease of combined abdominal pain scores (PIS and PFS) of ≥50%, during 1-year follow-up. Secondary outcome measures were the improvement of PIS, PFS, QoL, and school absenteeism.

Statistical Analysis

Sample size was based on the treatment response in both groups. The trial was designed to detect a minimal intervention-induced difference between both groups of 35% at 1-year follow-up: a treatment response of ≥50% was anticipated in >35% of the patients in the SMC group and in ≥70% of the patients in the intervention group. Under the assumption of a within subject correlation of 0.7 and using the formulas provided by Twisk (26), a total of 52 children would be needed ($\alpha = 0.05$, $\beta = 0.80$). To allow for a dropout rate of ≥20% because of withdrawal, a total number of 69 subjects were randomly assigned. Descriptive statistics were used to characterize the study sample and to document information for all variables measured within the present study. Between-group differences of treatment response, PIS, PFS, QoL and school absence were analyzed with generalized estimating equations (GEEs). GEE takes into account that the observations within each subject are correlated. This longitudinal data analysis technique is suitable to investigate the course over time of the outcome variables and to compare this overall effect between study arms. In all the models, the outcome variable was analyzed as a dependent variable using study group as the key independent variable adjusted for the baseline measurement. Adjustment for baseline leads to equal starting points for both groups, and therefore, the intervention effect is presented by the coefficient on the study group. The group-time interaction provides information about whether the observed effect is stronger at the beginning or at the end of the study (27). Possible effect modification was analyzed for the following variables: sex and age. Subgroup analyses were performed in cases where significant effect modification ($P < 0.10$ for the interaction term) was detected. An exchangeable correlation structure was assumed in all the GEE analyses. All the analyses were on intention-to-treat basis, and variability in the number of subjects in the analysis is because of incomplete data sets. The criterion $P < 0.05$ was applied to indicate statistical significance. All the analyses were conducted using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp, Armonk, NY).

RESULTS

Between February 2012 and August 2013, a total of 105 children with AP-FGIDs were eligible for inclusion. Of these, 69 agreed to participate in the study, of whom 35 patients were allocated to YT complemented to SMC and 34 patients to SMC alone (Fig. 1). No children with AM were included. Four children from the YT group and 16 children from the SMC group withdrew from the study before starting the intervention or discontinued treatment during follow-up; data of all children were used for analyses. Baseline characteristics of participants in both groups were similar, only constipation was more common in family members of the YT group (Table 1).

Treatment Response and Abdominal Pain Scores

Treatment response was defined as a decrease in the combined abdominal pain scores of $\geq$50%; therefore, mean week scores of PIS and PFS were added up. An increase was shown after YT and SMC during the time of follow-up; 21.2%, 32.2%, and 58.1%, and 20%, 26.9%, and 28.9%, respectively, at post intervention, 6 months, and 12 months follow-up. Only at 12 months after baseline, YT was significantly more effective than SMC ($P = 0.01$).

Figure 2 displays the progression of child-reported abdominal pain scores throughout the study. Mean scores for each time point and the results of the GEE investigating differences between

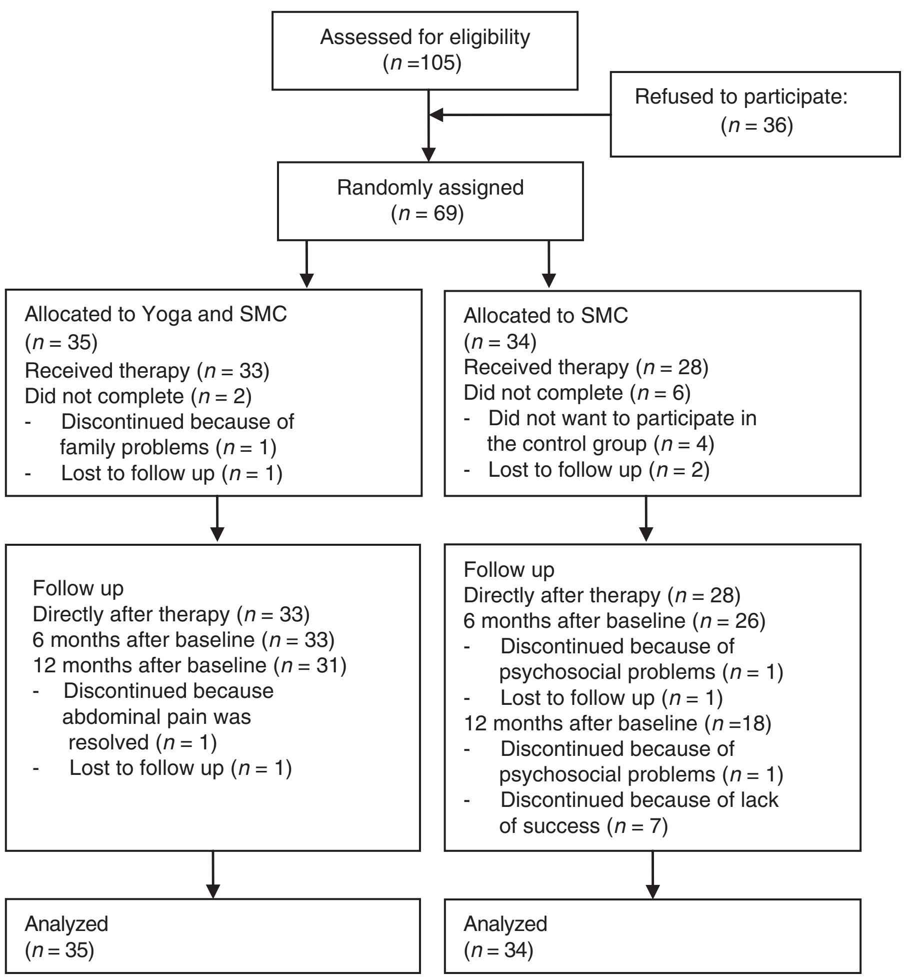

FIGURE 1. Flow diagram of trial progress. SMC = standard medical care.

TABLE 1. Baseline characteristics

	Yoga, N = 35	SMC, N = 34
Demography		
Age, y*	12.2 (2.9)	12.1 (2.7)
Girls, %	29 (83)	25 (74)
Rome III diagnosis, %		
IBS	12 (34)	14 (41)
FAP (S)	18 (51)	17 (50)
FD	5 (14)	3 (9)
Duration of symptoms, %		
<1 y	8 (23)	9 (27)
1–2 y	7 (20)	5 (15)
2–5 y	12 (34)	10 (29)
>5 y	8 (23)	10 (29)
Other functional symptoms, %		
Headache	20 (57)	20 (59)
Back pain	7 (21)	11 (32)
Neck pain	7 (21)	8 (24)
Tiredness	14 (46)	15 (56)
Family member with functional symptoms, %		
FAP/IBS	21 (60)	16 (47)
Constipation	18 (51)	11 (32)
Headache	13 (38)	16 (47)
Back pain	16 (52)	8 (25)
School absenteeism, %		
<Monthly	15 (45)	12 (35)
Monthly	18 (55)	15 (65)

FAP = functional abdominal pain; FAP(S) = FAP (syndrome); FD = functional dyspepsia; IBS = irritable bowel syndrome; SMC = standard medical care.

*Data are mean (SD).

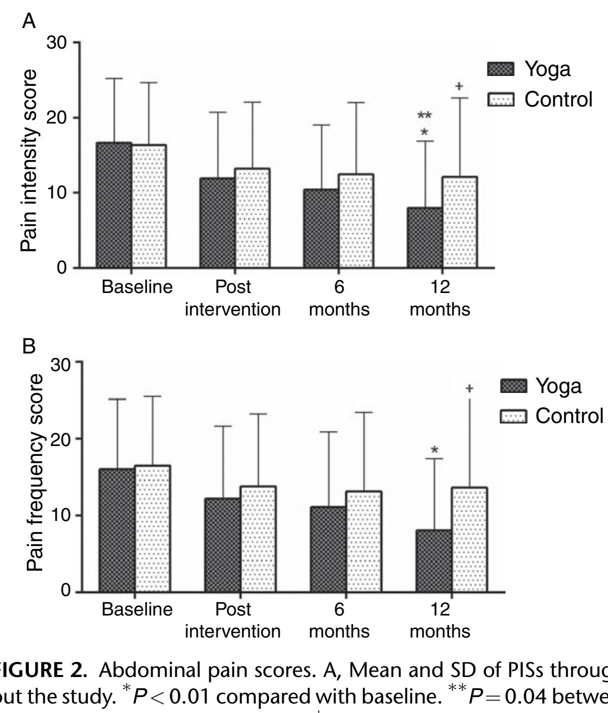

FIGURE 2. Abdominal pain scores. A, Mean and SD of PISs throughout the study. $^{*}P < 0.01$ compared with baseline. $^{**}P = 0.04$ between groups at 12 months (subanalysis). $^{\dagger}P = 0.83$ compared with baseline. B, Mean and SD of PFSs throughout the study. $^{*}P < 0.01$ compared with baseline. $^{\dagger}P = 0.40$ compared with baseline. PFS = pain frequency score; PIS = pain intensity score.

the 2 treatments are displayed in Table 2. The PIS decreased from 17 to 8 at the final end point 12 months after baseline in the yoga group ($P < 0.01$) and from 16 to 12 in the SMC group ($P = 0.83$). The PFS decreased from 16 to 8 ($P < 0.01$) in the YT group and from 16 to 14 in the SMC group ($P = 0.40$). The overall effect measured with GEE showed no significant differences between the study groups for PIS or PFS alone.

No significant ($P < 0.10$) interaction between time, sex, and age on the one hand and PIS and PFS on the other hand was found in any of the analyses. Subanalysis, however, showed a significant lower PIS in favor of YT compared with SMC, at 12 months follow-up ($P = 0.04$); this was not found directly after therapy or at 6 months follow-up. Children ages 13 to 18 years were more likely to report a decrease in PIS after YT compared with SMC, but this did not reach significance ($P = 0.06$).

Quality of Life

Compared with baseline, after YT, QoL scores increased at each time point for 4 of the 5 QoL subscales, except for ''autonomy and parents' relation.'' Yoga was not more effective than SMC for any of the subscales (Table 2). A trend was shown for better psychological wellbeing reported by children receiving YT ($P = 0.06$).

School Absenteeism

GEE analysis showed an overall significant effect in favor of YT ($P = 0.03$). Subanalysis for time points showed, however, that this significant difference was only present at 12 months follow-up. Directly after YT and SMC, school absenteeism decreased from 55% to 12.5% and from 65% to 36%, respectively ($P = 0.06$). Improvement continued at 1-year follow-up; 7% of children in the YT group and 33% in the SMC group reported school absenteeism ($P = 0.03$) (Fig. 3).

Adverse Events

No serious adverse events were reported.

DISCUSSION

This RCT shows that YT in addition to standard care is significantly more effective in reaching treatment response at 1-year follow-up and in decreasing school absence than standard care alone. A total of 58% of children in the yoga group reached an improvement of abdominal pain of $\geq$50%, whereas this was only 29% after SMC. Moreover, YT significantly reduced pain intensity and frequency, which was not reported after SMC. Only at 12 months follow-up, however, YT was superior to SMC regarding PIS. No effects were found in improving QoL. No adverse events were reported after YT.

In accordance with earlier studies, yoga was shown to be a safe and feasible intervention for children and adolescents with IBS (11,28). Two RCTs were conducted evaluating effects on YT in childhood IBS compared with waitlist controls (11,28). In line with our results, no significant effects on abdominal pain were reported directly after YT. In our study, however, significant effects for YT on pain scores were found at 12 months follow-up. Other data reporting the long-term efficacy of yoga are currently not available. It is difficult to explain why effects were noted only at 12-months follow-up. Improvement of abdominal pain was found in both groups, but only YT showed a further improvement at long-term follow-up. Similar posttreatment effects were reported after HT and CBT in children with IBS and FAP (29,30). This effect could be

TABLE 2. Mean scores of outcome measures at all time points and overall effect tested with GEE

	Before treatment		Directly after treatment		6 Mo after baseline		12 Mo after baseline			
	YT	SMC	YT	SMC	YT	SMC	YT	SMC	β	*P*
Abdominal pain scores										
PIS	16.65	16.39	11.91	13.18	10.42	12.47	7.99	12.14	−2.676	0.09
PFS	16.04	16.49	12.23	13.83	11.15	13.15	8.06	13.66	−1.899	0.20
QoL scores										
KIDSCREEN child										
Physical wellbeing	44.2	44.5	46.2	45.8	46.7	46.4	47.3	46.8	1.016	0.43
Psychological wellbeing	44.1	45.6	47.9	47.2	48.3	47.3	49.5	46.8	2.569	0.06
Autonomy and parent relation	53.7	52.4	54.8	55.3	55.9	56.0	53.7	53.3	−0.726	0.62
Peers and social support	53.8	52.0	52.9	51.4	54.7	51.1	54.5	52.6	1.235	0.46
School environment	50.0	49.6	54.0	52.1	54.3	53.1	53.1	53.8	0.844	0.58
KIDSCREEN parents										
Physical wellbeing	41.3	42.3	42.1	44.4	45.5	43.5	47.5	46.3	0.605	0.72
Psychological wellbeing	40.6	41.6	44.7	43.7	47.4	47.0	49.5	45.3	1.854	0.25
Autonomy and parent relation	54.2	53.7	54.0	55.8	54.8	57.8	53.7	56.3	−2.590	0.12
Peers and social support	54.0	53.0	55.1	53.2	55.0	54.5	55.7	54.2	0.647	0.68
School environment	50.1	51.8	52.7	52.9	54.7	52.5	54.3	52.6	1.851	0.17

Groups did not differ on any of the outcome measures before treatment. For the QoL scales, higher scores reflect better wellbeing. European normdata: mean 50.0. β = coefficient; GEE = generalized estimating equations; PFS = pain frequency score; PIS = pain intensity score; QoL = quality of life; SMC = standard medical care; YT = yoga therapy.

caused by the suggestion that benefits of the treatment would persist and become even more effective over time or by the ongoing use of home exercises by the participants or that sustained YT is necessary for a significant effect. Most of our participants applied YT at home when suffering from abdominal pain. Sustained yoga practice and discipline seems to be the most important factor to reach long-term effectiveness.

Mechanisms by which yoga can reduce pain are not well understood. Increased knowledge of the pathophysiology of AP-FGIDs has led to a biopsychosocial model, in which physiological, psychological, and emotional factors interplay (31). YT is likely to exert its effect on the psychosocial factor of this model. Stress and anxiety are known triggers for symptoms of AP-FGIDs (32). Studies have shown that the practice of yoga reduces perceived stress and negative feelings, and that it improves psychological symptoms by lowering the levels of anxiety and anger, in both adults and children (33–35). Studies focusing on meditation have proved that stress reduction is accompanied by altered brain activation. After a mindfulness-based stress reduction program, changes in gray matter concentration were demonstrated in brain regions involved in emotional regulation and arousal, measured by MRI (36). This is interesting because increased gray matter density in IBS patients was observed in brain regions involved in the stress and arousal circuit (37–39). Furthermore, meditation can produce increases in relative left-sided anterior activation that is associated with reductions in anxiety and negative affect and increases in positive affect (40). Future studies are needed to clarify whether YT also results in changes in brain structures and activity in children with AP-FDIGs.

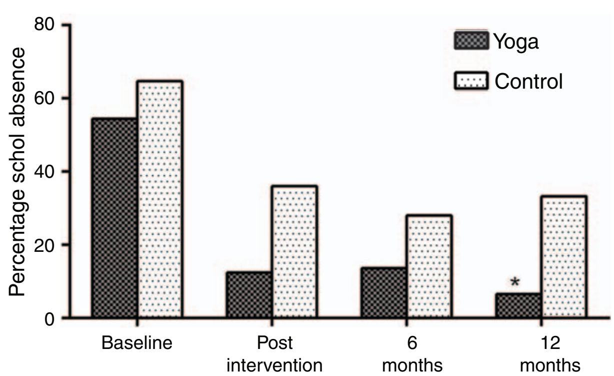

FIGURE 3. Percentage of school absence at least once a month at different time points. $^{*}P < 0.05$ between groups.

The present study demonstrated that YT was superior to SMC in reducing school absence. This is an important finding because abdominal pain ranks second in the causes of absence from school (4). Children with low school attendance or drop outs are at increased risk for displaying social emotional problems, risky behavior, and having limited economic opportunities (41). Improvement of functional disability after YT was previously reported in adolescents (11) and young adults with IBS (28). Yoga may appear as an important intervention to increase general functioning and social participation.

Both groups received treatment by the same physician; therefore, results were not distorted by expertise bias. Lack of significant effects in the control group, however, is a remarkable observation because an improvement is often reported in intervention trials in children with AP-FGIDs (29,30). Contrary to our study, these studies incorporated a more active nature of control conditions, such as extra appointments with the physician. It is well known that the patient–practitioner relationship and an active listening approach may account for a considerable part of treatment effectiveness (42–44). This underlines the importance of attention and a supportive relationship between a patient and a physician in treating children with AP-FGIDs.

Limitations of our study are common to many nonpharmacological trials for chronic pain, include the inability to blind participants to their treatment assignment, and differential attrition between groups. Because participants are not blinded, response expectancy may spuriously amplify differences in treatment effect between groups because people assigned to SMC may expect to not get better without YT. Four times as many participants from the SMC group did not finish the complete study period compared with the YT group. This attrition was partly because of disappointment of allocation to SMC; after randomization, 4 children immediately withdrew from the study. Data, however, were analyzed by GEE, which can handle missing data in longitudinal studies under the assumption that such data are missing completely at random (45). To further explore the influences of this attrition bias, per protocol analyses were performed for the primary outcome. No significant difference between YT and SMC was shown for the overall treatment response ($ß = -0.194$, $P = 0.739$). Nevertheless, at 12-months follow-up, still 57% of the children reached treatment response after YT versus 29% after SMC ($P = 0.173$). Unfortunately, data were not sufficient to explore the efficacy for different AP-FGID subgroups.

Based on earlier observed data, we verified that the subject attrition in this study was not associated with one of the covariates or the dependent variable. Results at 12-months follow-up may be considered as a reliable representation.

Behavioral therapies based on relaxation, such as HT and CBT, have shown to be effective therapies with long-lasting effects for children with IBS and FAP. Success rates up to 85% were reported after HT (29). A disadvantage of CBT, however, is that parents can be reluctant in accepting the existence of psychosocial influences on their child's symptoms and often refuse to engage with psychological services (46). Also, HT suffers from definite misgivings and beliefs in negative myths surrounding hypnosis. This may be different with YT, which is becoming very popular and more common in Western countries. Furthermore, YT is simple, can be easily applied at home, and therefore may have lower costs than HT and CBT.

Future research should compare yoga to other relaxation-based therapies to determine which treatment has the most potent and sustained effect and whether there is an individual likelihood that increases the responsiveness to a particular therapy. More research is needed regarding whether different intensity and duration of YT may increase effectiveness directly after therapy. Also the efficacy for different AP-FGID subgroups should be explored. To further distinguish the effects of YT from the natural course of AP-FGIDs, effects of follow-up should be compared with waitlist controls. Persisting symptoms however, were reported in 30% to 40% of children with FAP, up to 15-years follow-up (7,47). Furthermore, most children included in this study are complaining of abdominal pain for >2 to 5 years. A spontaneous remission within 12 months is therefore less likely.

In conclusion, yoga may be an effective intervention for AP-FGIDs in childhood. For the first time, we demonstrated that 10 weeks of yoga intervention resulted in a significant reduction of school absence and improved abdominal pain at 12-months follow-up.

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