Non-pharmacological management of abdominal pain-related functional gastrointestinal disorders in children

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Background: **Abdominal pain-related functional gastrointestinal disorder (AP-FGID) comprises of 4 main conditions: functional dyspepsia, irritable bowel syndrome, abdominal migraine and functional abdominal pain. AP-FGIDs are diagnosed clinically based on the Rome IV criteria for FGIDs of childhood. There is limited evidence for pharmacological therapies.**

Data sources: **This review article discusses non-pharmacological management of AP-FGID based on the current literature including systematic reviews, randomized controlled trials, cohort and case control studies. We aim to provide a comprehensive overview on the available evidence for the pediatricians and pediatric gastroenterologists involved in managing children with AP-FGID.**

Results: **Managing AP-FGIDs can be challenging. This should follow a stepwise approach with focused history, identification of "red flag" signs and symptoms, physical examination and investigations done following initial consultation. Family needs explaining that there is nothing seriously wrong with the child's abdomen. This explanation and reassurance can achieve symptom control in large number of cases. Non-pharmacological interventions are delivered through lifestyle and dietary changes and bio-psychosocial therapies. Dietary interventions vary depending on the type of AP-FGID. Bio-psychosocial therapies such as hypnotherapy, cognitive behavioral therapy and yoga aim at stress reduction.**

Conclusion: **There is increasing evidence for use of non-pharmacological interventions in children with AP-FGID.**

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Key words: **abdominal pain;
behavioral intervention;
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Introduction

Abdominal pain is a common symptom among children and adolescents.[1] It is also common for parents to consult health professionals as they can find it challenging to identify the cause of the pain.[1] Apley and Naish first described the term "recurrent abdominal pain (RAP) of childhood" following their community based study of 1000 school children in Bristol, United Kingdom.[2] They defined RAP as three or more episodes of abdominal pain occurring over a period of at least three months, with pain sufficient to cause some impairment of function.[1] Even after more than five decades, this definition of RAP holds good and is used internationally.[3]

RAP in children is not associated with a serious organic pathology in most cases. The Rome IV criteria for childhood functional gastrointestinal disorders (FGID) has described a number of conditions which can present with RAP in children.[4,5] For the purpose of concordance, we use the term abdominal pain-related FGIDs (AP-FGID) throughout this review article which includes functional dyspepsia (FD), irritable bowel syndrome (IBS), abdominal migraine (AM) and functional abdominal pain (FAP).[4] Table 1 describes the diagnostic criteria for the conditions presenting as AP-FGID. The pharmacological interventions are often of limited benefit in children presenting with AP-FGID.[6] This article describes the non-pharmacological management of the children presenting with AP-FGID.

Epidemiology of AP-FGIDs

The exact prevalence of AP-FGID is not known. However, population based epidemiological studies from Europe and America show prevalence rates ranging from 0.5%

Table 1. Diagnostic criteria for different groups of AP-FGID[4]

Functional dyspepsia
Functional dyspepsia has been defined by the Rome IV criteria and must include 1 or more of the following bothersome symptoms at least 4 days per month for at least 2 months before the diagnosis is made:
1) Postprandial fullness;
2) Early satiation;
3) Epigastric pain or burning not associated with defecation;
4) After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.

Irritable bowel syndrome
IBS has been defined by the Rome IV criteria and all these must be fulfilled for at least 2 months before a diagnosis of IBS can be made:
1) Abdominal pain at least 4 days per month associated with one or more of the following:
   a) Related to defecation;
   b) A change in frequency of stool;
   c) A change in form (appearance) of stool;
2) In children with constipation, the pain does not resolve with resolution of the constipation (children in whom the pain resolves have functional constipation, not irritable bowel syndrome);
3) After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.

Abdominal migraine
Rome IV criteria have specified certain characteristics for diagnosis of abdominal migraine and all these criteria should be fulfilled at least twice in the preceding 6 months:
1) Paroxysmal episodes of intense, acute periumbilical, midline or diffuse abdominal pain lasting 1 hour or more (should be the most severe and distressing symptom)
2) Episodes are separated by weeks to months.
3) The pain is incapacitating and interferes with normal activities
4) Stereotypical pattern and symptoms in the individual patient
5) The pain is associated with 2 or more of the following:
   a) Anorexia;
   b) Nausea;
   c) Vomiting;
   d) Headache;
   e) Photophobia;
   f) Pallor.
6) After appropriate evaluation, the symptoms cannot be cannot be fully explained by another medical condition.

Functional abdominal pain – Not otherwise specified epidemiology
This has been described in the Rome IV criteria for FGIDs and is characterised by a set of criteria all of which should be fulfilled at least 4 times per month for at least 2 months before diagnosis is made:
1) Episodic or continuous abdominal pain that does not occur solely during physiologic events (e.g., eating, menses);
2) Insufficient criteria for irritable bowel syndrome, functional dyspepsia, or abdominal migraine;
3) After appropriate evaluation, the abdominal pain cannot be fully explained by another medical condition.

AP-FGID: abdominal pain-related functional gastrointestinal disorders; IBS: irritable bowel syndrome; RAP: recurrent abdominal pain.

to 25%.[2,7-9] A community-based study of 507 children in the USA noted that 13% of middle school students and 17% of high school students experienced weekly abdominal pain.[10] The same study also found that 8% of all students had consulted a physician for abdominal pain in the previous year.[10] Study undertaken in a rural community in Malaysia, 161 of 1462 sampled school children fitted the Apley's criteria for RAP describing a prevalence of 11%,[11] It was also found that children who had consulted their doctors for RAP were also more likely to have higher school absence due to their abdominal pain.[11] A study in China involving 5403 school children aged 6 to 18 years showed the prevalence of IBS to be 13.25%; the prevalence was much higher among girls (male:female, 1:1.8).[12] Studies from diverse geographical settings have indicated a similar prevalence of AP-FGID in children.[2,7-13]

Etiology of AP-FGID

The exact etiology of AP-FGID in children remains yet to be fully understood.[9] The most plausible explanation is that it is likely to be a complex interplay of hereditary and environmental factors.[13] It is likely that gastrointestinal infections, inflammation, visceral hypersensitivity, psychological stress, allergy and disordered gut motility may all play a part in the development of AP-FGID in children.[3,5]

Study of 103 children referred with RAP to the pediatric gastroenterology services in Bristol, UK found no identifiable pathology in 72 children and of these IBS was identified as the commonest diagnosis (37 out of 72).[14] A study conducted in a tertiary center in the USA presenting with RAP, no organic pathology was identified in 107 of 114 patients.[15] A pre-evaluation questionnaire completed by parents revealed symptom profiles consistent with the Pediatric Rome II Criteria for one of the AP-FGID in 73% of 107 cases.[15] A Sri Lankan study involving 55 children (aged 5-15 years) with RAP, no organic cause was identified in >75% of cases.[16] These studies indicate that children referred with RAP to the specialist centers for an expert opinion often do not have an identifiable organic pathology and is largely due to AP-FGID.

Some studies from Asian countries suggest that gastrointestinal infections such as giardiasis in children manifested as RAP only and following its treatment, the pain resolved.[9,17] A prospective cohort multicenter study from the Italy and Columbia involving 64 patients aged 4-14 years, children exposed (n=32) to an acute diarrhea of infectious etiology (rotavirus, salmonella, adenovirus, norovirus and *Giardia lamblia*), significant increase in AP-FGID were reported in the exposed group as compared to controls (n=32) within 1 month and 3 and 6 months later.[18]

Psychological stress has been postulated to cause AP-FGID; probably due to changes in the 'brain-gut axis', altering the perception of visceral sensation.[5] This may lead to a phenomenon known as 'visceral hyperalgesia'. Di Lorenzo et al have demonstrated 'visceral hyperalgesia' in small groups of children with RAP wherein heightened anxiety states were also noted.[19] A biophysical model has also been proposed as a cause for AP-FGID. This is possibly controlled by the child's response to biological factors, governed by an interaction between the child's temperament, his family and school environments.[5] It has been postulated by Crushell et al that symptoms of AP-FGID in children may also be influenced by the parental conceptual model of illness.[20] In a study of 319 young adults with history of FAP in their childhood, participants reported parental history of chronic pain in their childhood and increased utilization of health service for their FAP.[21]

Abnormal gastric motility as a result of a constipation-induced cologastric brake has been suggested as a possible pathophysiological mechanism especially for symptoms in functional dyspepsia.[22] In a case-control study of 41 children (aged 4-14 years) in Sri Lanka, liquid gastric emptying and antral motility parameters were found to be significantly impaired in children with functional dyspepsia as compared with healthy controls.[22] Another study from Italy with 42 children affected by FD (Rome II criteria) showed that 28 children had functional constipation and normalization of bowel habit improved gastric emptying as well as dyspeptic symptoms.[23]

Due to strong familial trends noted in children with RAP and IBS, there has been an ongoing interest in finding a genetic association. A positive association has been noted in patients reporting gastrointestinal symptoms, especially abdominal pain with a mutation in a sodium channel gene (SCN5A).[24] In a questionnaire study with 10 699 respondents in the US which represented 6060 twin pairs, the concordance for IBS was significantly higher in monozygotic (17.2%) as compared to dizygotic (8.4%) twins; this supports a genetic contribution to IBS.[13] Studies have also shown that children with AM go on to develop cranial migraine in later life and genetic associations are increasingly being recognized especially with the hemiplegic variant.[25]

History taking and examination

AP-FGID is a group of conditions with diagnostic criteria described by the Rome IV criteria for FGIDs (Table 1). The most important step is to elicit a detailed history about the abdominal pain and any other associated symptoms including onset, duration, frequency, site, character, triggering or relieving factors. For example, the abdominal pain may be relieved following defecation in IBS. A change in stool frequency and/or consistency may be associated with the abdominal pain and use of a stool form chart such as Bristol stool form chart is useful in objectively assessing this. A study of 200 children with RAP from the Netherlands reported occult constipation in 92/200 children.[26] A sense of incomplete evacuation may be reported by children and adolescents with IBS; however this by itself is not diagnostic of IBS.[3] Associated symptoms of bloating, an urgency to go to the toilet, loss of appetite, nausea and vomiting also provide important information.[3,4]

The diagnosis of AM is strengthened by presence of associated headache, photophobia, and history of cranial migraine in the child or family.[4] Although not included in the Rome IV criteria as a FGID, chronic abdominal wall pain (CAWP) is a possible variant of FAP and is manifested by a chronic and unremitting abdominal pain, with minimal or no relationship to food intake or defecation.[27] Relationship to posture, such as lying down, sitting, standing or during exercise has been described with CAWP.[28]

Anxiety states have been known to exacerbate the ongoing symptoms in AP-FGID such as IBS and FAP.[29] It is common for parents to describe their child as a "little worrier" (especially in IBS).[3] It is therefore important to explore emotional and psychological issues at school such as bullying, anxiety about performance in exams, friendship difficulties or issues at home such as financial difficulties, recent parental separation, divorce or ill-health. It is also important to enquire about a recent history of gastrointestinal infections as this may be a trigger for onset of symptoms in AP-FGID.[3]

An enquiry about the family history of FGIDs symptoms (such as IBS, FAP, migraine) among parents or siblings should be made. History of chronic pain in parents has been reported to be co-existent especially in children with FAP.[22]

During the consultation, it is essential to specifically enquire about "red flag" symptoms as these may indicate a serious underlying organic pathology.[3] The

Table 2. Red flag symptoms[3,30]

Abdominal pain or diarrhea that wakes the child from sleep
Delay in onset or progression of puberty
Faltering growth
Family history of inflammatory bowel disease, celiac disease
History of significant weight loss
Multiple episodes of bleeding per rectum
Pain abdomen in right upper/lower quadrant
Persistence of severe vomiting or diarrhea
Persistent joint pains
Recurrent unexplained fever
Stools that may be difficult to flush away
Unexplained pallor

"red flag" symptoms are listed in Table 2. However, a Dutch study of 200 children (aged 4-16 years) referred to secondary care with RAP (Apley criteria for RAP) showed that the Rome III criteria for abdominal pain were not found to be specific enough to rule out organic causes and alarm symptoms did not differentiate between organic and functional abdominal pain.[30] As AP-FGID is relatively common, occasionally an organic pathology may co-exist e.g. IBS symptoms are not uncommon in children with inflammatory bowel disease (IBD).[3,30] Although presence of "red flag" symptoms does not exclusively indicate an organic pathology for RAP, absence of the alarm symptoms increases the likelihood of AP-FGID.[30] It is therefore important that if any or a combination of the "red flag" symptoms are reported in child who fits criteria for AP-FGID, appropriate investigations are necessary to exclude an underlying organic condition such as IBD.

A focused but detailed history may indicate a particular diagnosis and this should be followed by a detailed physical examination. It is important to review the previous growth trajectory and plot the height and weight on an age and sex appropriate growth chart as significant faltering in growth may be considered as a red flag sign. Physical signs such as anemia, jaundice, mouth ulcers, skin rash or arthritis may suggest an organic pathology (e.g. IBD, celiac disease).[3] When a child is asked to point with one finger to the area of the abdominal pain it is often centered around the umbilical region in IBS and epigastric region in FD. Scars in the abdominal wall may indicate previous diagnostic laparoscopies or surgeries already done for the symptoms. Examination of the perianal region may show prominent skin tags, fissures or fistulae (indicative of Crohn's disease), soiling or hard feces at the anal opening (indicative of functional constipation).[3]

The child is likely to to be too tense to allow a useful abdominal palpation and distraction techniques may be needed in such cases which can often be achieved by discussing about other aspects of their life such as school, friends or even a planned holiday.[3] If CAWP is suspected, Carnett's sign which is considered to be positive if the abdominal pain increases when the abdominal muscles are contracted, by straight leg raising or lifting head and shoulders while lying supine may be helpful.[27,28] It is important to take utmost care not to miss any organomegaly, tenderness and/or abdominal mass in the right iliac fossa.

Diagnosing children with AP-FGID

There is no definitive laboratory or radiological investigations available to make a positive diagnosis of AP-FGID and an attempt should be made to rule out the organic pathologies at the initial consultation. Staggered investigations are likely to raise anxiety among children and parents; hence a set of investigations after a thorough history and physical examination is likely to be most effective at reassuring the family in excluding organic causes.

Presence of red flag signs or symptoms (Table 2) should prompt specific investigations to exclude conditions like celiac disease and IBD. A recent pediatric study (n=782) from Italy demonstrated an increased prevalence of celiac disease in children presenting with AP-FGID symptoms (15/782) and was largely amongst those with IBS symptoms (12/270 i.e. 4.4%).[31,32]

Following investigations are suggested as a baseline: serological screening for celiac disease, inflammatory markers (erythrocyte sedimentation rate, C-reactive protein, plasma viscosity or orosomucoid), liver function tests, serum amylase, full blood count, stool sample for microscopy and culture with specific request to look for ova, cyst and parasites (including *Giardia* and other protozoa especially by triple feces test or PCR for *Dientamoeba fragilis*) and abdominal ultrasonography.[3,17] Total IgE with specific radioallergosorbent tests (RASTs) to food allergens or skin prick tests may also be considered if history is suggestive of diet related symptoms.[3] It may however be noted that most food allergies are not IgE-mediated and a negative RAST or skin prick test does not rule out food allergies.

Therapeutic trial may be considered to treat occult constipation (even when there isn't an abnormal defecation pattern) adequately with laxatives and establish regular defecation pattern before AP-FGID is diagnosed.[26] Stress can trigger constipation and the abdominal pain can improve following treatment of constipation although the underlying cause needs to be addressed for complete resolution of the problem.[4]

Unnecessary investigations should to be avoided and symptoms concordant with the Rome IV criteria should help clinicians to make a positive diagnosis

of AP-FGID.[4] However, in difficult cases where the diagnosis may not be clear from the history, and/or physical examination, and especially those with concerns regarding IBD should be referred to pediatric gastroenterologists for reassessment and specialist investigations which may include gastrointestinal endoscopy and MRI of the small bowel.[3]

Evidence base for non-pharmacological management of AP-FGID

AP-FGID in children is known to cause significant limitation to life activities and the aim for any therapeutic intervention should be to improve their quality of life. The child's abdominal pain should be minimized, stool consistency and frequency normalized, episodes of exacerbation minimized in the cases where complete remission may not be achieved. It is important to reassure the parents (and the child if age appropriate) that there is no serious underlying disease and explain the diagnosis of AP-FGID. Having established the diagnosis, often a bigger challenge for the clinician is to find effective treatment strategies. There is limited evidence for use of pharmacological agents in treating AP-FGID in children and very often children (and parents) dislike taking medicines daily. This may leave the clinician to look for alternative non-pharmacological therapies. These may include the following: 1) dietary interventions; 2) probiotics, and, 3) Bio-psychosocial modifying therapies mainly hypnotherapy, cognitive behavioural therapy, yoga, acupuncture and physiotherapy.

Dietary interventions

Dietary interventions are generally more willingly accepted by parents (and children) and it should form an important strategy in managing children with AP-FGID.[33] We reviewed the evidence base for the following commonly used interventions:

High fiber diet

A cross-sectional study of 41 children with RAP compared with 41 children in control group in Brazil[34] found that children with RAP had lower intake of total fiber than the control group (13.4 g/day) (P=0.008). A Cochrane review compared fiber supplements with placebo in two studies and had 83 participants. Significant beneficial effect of fiber supplementation was not found, the pooled odds ratio for improvement with treatment was 1.26 with wide confidence intervals.[35] A recent meta-analysis with 3 randomized controlled trials (RCTs) comparing use of dietary fiber supplements with placebo for AP-FGID in children (aged 5-17 years) found lack of evidence for high fiber supplementation as a dietary manipulation.[36]

Partially hydrolyzed guar gum (PHGG)

PHGG is a soluble fiber, dissolves in water, and acts like a prebiotic modulating intestinal microbiota. A recent RCT from Italy with 60 children (aged 8-16 years) compared children with FAP treated either with PHGG or fruit juice (control group). Improvement was seen in 43% children (n=30) given PHGG as compared to 5% noted in control group (n=30).[37] Benefit from PHGG with normalization of bowel movements was largely seen in the IBS sub-group with alternating diarrhea and constipation and this was statistically significant. Similar beneficial findings were also reported in an earlier observational study from the UK.[38]

Elimination diet

This is often tried in clinical practice and may be beneficial in some children. An exclusion diet may be trialed in cases where the history is convincing for food allergies. This should be done under the guidance of a specialist pediatric dietician to ensure that the overall nutritional content of the food remains balanced. A Cochrane review (included two studies) compared lactose-containing diet with lactose-free diet in 90 participants, but no definite conclusion regarding its benefit could be drawn from the way the data were presented.[35]

Fermentable oligo-, di-, mono-saccharides and polyols (FODMAPs) have been considered to play a role in triggering gastrointestinal symptoms in children with RAP and IBS.[33] Food that may need to be avoided are plums, prunes, beans, lentils, milk (if lactose intolerant) or wheat. The low FODMAP diet consists of a 6-week intensive elimination phase followed by a structured reintroduction phase if symptoms have decreased substantially. The effect of low FODMAP diet amongst 90 children with IBS was evaluated prospectively using a symptom questionnaire with a mean follow up of 15.7 months; significant improvement in abdominal pain, bloating, flatulence and diarrhea were reported by participants while on low FODMAP diet (P<0.001 for all).[39]

Avoidance of non-steroidal anti-inflammatory drugs and foods that may aggravate symptoms (e.g., caffeine, spicy and fatty foods) is suggested in children with FD.[4] AM may respond to avoidance of potential triggers such as caffeine, nitrite and amine-containing foods.[4,40] Beneficial effect of low-amine diet was noted in children with cyclical vomiting syndrome (also considered to be a migraine variant) in an observational study from the UK.[41]

Probiotics

Probiotics are live microorganisms which are known to have beneficial effect on the host, when consumed in adequate amounts.[42] There is an increasing interest in clinical practice about use of probiotics in the treatment or prevention of different gastrointestinal disorders. It is postulated that the beneficial effects of probiotics are due to enhancement of gut barrier function, inhibition of pathogen binding and modulating gut inflammatory response.[42,43] Probiotics may also reduce visceral hypersensitivity associated with both inflammation and psychological stress.[43] Probiotics can also alter colonic fermentation and stabilize colonic microbiota.

Possible mechanisms that are suggested through which probiotics exert their action are:[42] (1) binding to small- and large-bowel epithelium and production of substances that may inhibit pathogenic organisms (2) modulating the gastrointestinal lumen toward an anti-inflammatory state and (3) converting undigested carbohydrates into short-chain fatty acids and improving gut function. Probiotics exhibit direct effect on intestinal tight junction integrity (disruption seen in IBD), prevent *Escherichia coli*-induced derangement of tight junctions, secrete proteins that stabilize intestinal tight junctions, reverse increased intestinal permeability and reduce severity of alcohol-induced gut hyper-permeability (the latter two effects were described in rat model).[42]

A randomized double-blind, placebo controlled trial from Italy[42] involving 141 children (83 had IBS and 58 had FAP) aged 5-14 years were treated with *Lactobacillus rhamnosus* GG (LGG) (n=71) or placebo (n=70) for 8 weeks. All children underwent a double-sugar intestinal permeability test at the entry and at the end of the trial; reduction in abnormal permeability results was noted after treatment with LGG. Significant reduction in both frequency and severity of abdominal pain was reported in children who were treated with LGG (48/71) as compared to the placebo group (n=37/70) (P<0.03) and this benefit persisted at the end of a follow-up period at 8 weeks.[42] Similar beneficial effect was noted in an earlier RCT with use of LGG in FAP disorders and the success was most notable in the IBS subgroup.[44]

A double-blind, placebo-controlled, crossover trial with 59 children[45] (aged 4-18 years) from 5 tertiary pediatric centers (4 in Italy and 1 in India) were randomized to receive either VSL#3 (contains 8 beneficial species of bacteria) or a placebo for 6 weeks. VSL#3 was reported to be superior to placebo both in primary (subjective assessment of relief of symptoms) and secondary endpoints (abdominal pain/discomfort, abdominal bloating/gassiness and family assessment of life disruption.[45]

A meta-analysis to investigate the quality of the current evidence regarding the effect of LGG in the treatment of AP-FGID in children and adolescents found probiotics to be more effective than placebo; this is especially noted in children with IBS. No difference in response was found between children with FAP or FD who received placebo or LGG.[46]

Another randomized double-blind placebo controlled trial[47] recruited 60 children (aged 6-16 years) who were either treated with *Lactobacillus reuteri* DSM 17938 or an identical placebo for 4 weeks. Significant lowering in pain intensity was reported by children treated with *Lactobacillus reuteri* as compared to the placebo control group.[47]

Bio-psychosocial modifying therapies

Hypnotherapy

AP-FGID have been found to have similar psychosocial profiles and responds similarly to psychological therapies.[48] Various studies have demonstrated the beneficial effect of hypnotherapy in children with AP-FGID and this persisted for up to five years after completion of therapy.[3,49] A hypnotic state is induced by trained therapists in gut-directed hypnotherapy, and the child is guided to respond to suggestions towards control and normalization of gut functioning, stress reduction and ego-strengthening. Hypnotherapy acts by normalizing altered visceral sensation, reducing colonic phasic contractions and reversing patients' negative thoughts about their condition.

A RCT comparing hypnotherapy (n=27) with standard medical treatment (n=23) showed that 68% of children in the study group remained in remission after a mean follow-up duration of 4.8 years as compared to only 20% in the control group.[49] Another RCT from Germany involving 38 children aged 6 to 12 years, brief hypnotherapeutic-behavioral intervention program in 20 children (recruited for therapy) reported significant reduction of pain scores and pain-related disability (55%) when compared to those in waiting list (n=18, served as control) who reported only 5.6% reduction.[50] A recent systemic review[51] which included three RCTs comparing hypnotherapy to control, statistically significant improvement in quality of life was reported in one trial while two trials reported improvement in school attendance and the benefit was persistent even after 1 year of completion of therapy. The authors recommended that hypnotherapy should be considered as the first line therapy in the management of children with AP-FGIDs.[51]

A study of 34 children[52] with FAP aged 6-15 years who were randomly assigned to receive standard medical care with or without self directed home-based audio-recorded guided imagery hypnotherapy treatment demonstrated superior success in the former group

(63.1% *vs.* 26.7%) and treatment effects were sustained 6 months after completion of therapy.[52] In a RCT of 260 children[53] with FAP randomized either to receive 6 face-to-face sessions of individual hypnotherapy by a qualified therapist over a 3-month period or hypnotherapy delivered through self-exercises at home with CD, success rates were comparable and almost equally effective.

Cognitive behavioral therapy (CBT)

Several RCTs have demonstrated the effectiveness of psychological therapies for pediatric FAP. CBT demonstrates its psychotherapeutic effect by addressing dysfunctional emotions, maladaptive behaviors and cognitive processes and contents through a number of goal-oriented, explicit systematic procedures. Behavioral procedures include identification of verbal and non-verbal pain behavior and how family members, teachers and caregivers react to it and are addressed by interventions such as physical exercise to promote relaxation, breathing exercises and muscle relaxation techniques taught by trained therapists.[54] Cognitive procedures may include stopping thoughts related to pain and replacing negative thoughts by positive ones, distraction when pain arises (e.g. watching television or playing games, doing mental arithmetic) and imagination to encourage the child to think about pleasant things when confronted with pain.[54]

In a RCT from the US involving 200 children with persistent FAP, subjects were randomized either to receive a three-session intervention of CBT targeting parents' responses to their children's pain complaints and children's coping responses, or a three-session educational intervention that controlled for time and attention. The group treated with CBT aimed at reducing protective parental responses and increasing child coping skills was demonstrated to be significantly effective ($P<0.01$) in reducing children's pain and symptom levels compared to the latter.[55]

Another RCT[56] demonstrated the positive effect of distraction in which symptom complaints of pain by children (aged 8-16 years) with FAP ($n=104$) and well children ($n=119$) nearly doubled in the group where parents were trained to give attention and were reduced by half in the distraction group. RCT involving 48 patients[57] (11-17 years) presenting with chronic headache, abdominal or musculoskeletal pain and associated functional disability were randomized either to receive CBT through the internet ($n=26$) and patients on the waiting list who were continued on medical therapy served as the control ($n=22$).The internet treatment group demonstrated significantly greater reduction in activity limitations and pain intensity and internet treatment was rated as acceptable by all children and parents.[57]

A Cochrane review identified CBT as a promising psychological therapy in treatment of children with AP-FGID although these RCTs have considerable methodological drawbacks such as small sample sizes and high dropout rates. A recent RCT[51] with 104 children aged 7-18 years randomized either to receive CBT or intensive medical care found that six sessions of CBT was equally effective as medical treatment 1 year after treatment.

Yoga

This consists of general relaxation exercises, breathing exercises, focused training for abdominal muscle relaxation and positive reinforcement and may be considered as a form of behavioral therapy. It can be considered as a sport-like activity and may be attractive option for older children to stay fit. In a Dutch study[59] of 20 children aged 8-18 years who received supervised training (10 sessions) on Hatha yoga from a children's yoga teacher and also practiced at home. Yoga exercises resulted in significant reduction of pain intensity and frequency in children with FAP and IBS.[59] Similar beneficial effects of yoga were also noted in other case studies and reviews.[52,60]

Acupuncture

This exerts beneficial effects by release of endogenous opiates and triggering of serotoninergic inhibitory pathways. An adult study which compared beneficial effects of acupuncture ($n=20$) [Tianshu acupuncture (ST 25) and Dachangshu acupuncture (BL 25)] in IBS with western medication (Trimebutine maleate, $n=20$) found that acupuncture was superior in relieving symptoms.[62] In a Korean study of 40 children who received acupuncture therapy ($n=20$) for RAP; pain intensity and medication requirement were significantly reduced in comparison to the control group ($n=20$).[63] A recent Cochrane review (17 RCTs with 1806 adult participants) showed greater benefits amongst participants treated with acupuncture as compared to two antispasmodic drugs (pinaverium bromide and trimebutine maleate).[64]

Physiotherapy

CAWP in children may benefit from physiotherapy as described in an observational study from the UK where 42 out of 49 children (85%) aged 6-16 years showed

improvement following physiotherapy.[28] The beneficial effect is likely to be due to correction of the eccentric use of abdominal muscles and retraining the abdominal muscles (work concentrically providing better support with less effort). In another study,[65] 25 children with RAP treated with a combination of physiotherapy and psychological treatment was found to be effective in reducing pain and tender points score in comparison to those who were treated with physiotherapy alone (n=23).

Authors' personal opinion

The management of children with AP-FGID can pose a challenge to clinicians worldwide as there is a lack of clear consensus on how to effectively manage these conditions. There is no universally proven therapy which will work in all children and pharmacological interventions may prove unsuccessful in a significant number of cases. Families often may not want to give their children long-term pharmacological therapies but are more likely to accept non-pharmacological therapies. The effective management of children with AP-FGID will largely be dependent on the physician developing a trusting relationship with the child and the family.

Majority of children with AP-FGID will improve with a positive diagnosis followed by counseling, reassurance that there isn't anything seriously wrong, education about their condition and a personalized plan for coping with the symptoms. Stressful triggers such as bullying at school, difficulties in relationship with parents or peers, unrealistic academic expectations, etc. should be identified and addressed early. It is important to emphasize the need for positive reinforcement.

Modification to the child's diet should be initiated and monitored by a specialist pediatric dietician. Dieticians should ensure a nutritionally balanced diet is given to the child while starting any dietary intervention. Children with AP-FGID are often on self-initiated food exclusion regimen which may not be nutritionally adequate. A detailed dietary history including type and amount of food and drinks consumed by the child should be recorded. High fiber diet may have a beneficial role in constipation predominant IBS (IBSC) while low fiber diet may be beneficial in diarrhea predominant IBS (IBSD). High fiber diet may not be tolerated by children as it is often associated with intestinal gas production, increased cramps and flatulence.[38] A trial of PHGG may be beneficial in children with IBS with alternating diarrhea and constipation. Low amine diet may be useful in children with abdominal migraine while elimination diet is likely to be useful in functional dyspepsia. Probiotics have been demonstrated to be safe and should be considered in children when symptoms of AP-FGID have been triggered off by an episode of gastroenteritis. Table 3 highlights dietary interventions (including probiotics) that are considered to be useful in specific types of AP-FGID. A recently published systemic review looking at non-pharmacologic therapies for children with AP-FGID and included 24 RCTs with 1390 children (aged 3-18 years) supported the use of probiotics, hypnotherapy and CBT although evidence for dietary fiber supplements were inconclusive.[6]

Table 3. Dietary interventions that may be useful in specific types of AP-FGID

Dietary interventions	AP-FGID types
High fiber diet	Constipation predominant IBS
Low fiber diet	Diarrhea predominant IBS
Partially hydrolyzed guar gum	IBS with alternating diarrhea and constipation
Low amine diet	Abdominal migraine
FODMAP diet	IBS with alternating diarrhea and constipation, diarrhea predominant IBS
Elimination diet, avoidance of NSAIDs	Functional dyspepsia
Probiotics	IBS, functional abdominal pain

AP-FGID: abdominal pain-related functional gastrointestinal disorders; IBS: irritable bowel syndrome; NSAIDs: nonsteroidal anti-inflammatory drugs; FODMAP: fermentable oligo-, di-, mono-saccharides and plolyols.

Bio-psychosocial therapies such as hypnotherapy, CBT, yoga, acupuncture may be beneficial in selective cases of AP-FGID. However, these therapies are to be only delivered by trained specialist pediatric therapists and hence are often beset by their unavailability in most centers. There is also need for multiple numbers of sessions which further creates difficulty in implementing such therapies in routine clinical practice. To a certain extent, this may be overcome by use of pre-recorded therapies in audio CDs, DVDs which can be used at home after an initial session with the therapist or from the beginning after proper explanation. Internet delivered therapies may also be used and may have better acceptance among older children and adolescents.

In a small subset of patients with severe disabling AP-FGID symptoms, it can be a challenge to find an effective treatment and a number of strategies may need to be tried before symptom control is achieved. We feel the chances of achieving success are better in these difficult cases when managed by a multi-disciplinary team comprising of consultant with expertise in pain management, pediatric gastroenterologist, psychologist, psychotherapist, access to trained pediatric alternative therapists (such as hypnotherapy, acupuncture etc), close liaison with school and social care.

Conclusions

AP-FGID remains a diagnosis of exclusion and is made clinically from a detailed focused history and exclusion of somatic disease. Use of the Rome IV criteria will clarify lot of uncertainties about the symptoms and investigations should be kept to the minimum and aimed at ruling out other serious pathologies. Most cases of AP-FGID in children can be successfully managed by an appropriate explanation regarding the diagnosis and time initially spent at explaining and reassuring the child and their families is worth investing for long term success. It is important to explain to the family the expected benefits and possible side effects before commencing any therapy. Although pharmacological therapies have traditionally been more commonly used in clinical practice; non-pharmacological therapies are likely to be better accepted and tolerated by children. Multi-disciplinary team approach is likely to be more successful in difficult cases.

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