Pediatric Functional Abdominal Pain Disorders



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CAMPAIGN ON F.A.P.

Comic leaflet for children

🚎 ESPGHAN



CAMPAIGN ON F.A.P.

Support leaflet





UK trainee reported percentage comfort levels with the diagnosis and management of DGB



Sasegbon A, et al. Neurogastroenterol Motil 2023

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Sasegbon A, et al. Neurogastroenterol Motil 2023

Important problem?



- 1. High prevalence
- 2. High cost
- 3. School absence
- 4. Low QoL
- 5. Depression and anxiety

History

- 14 y.o. girl, developmentally normal
- Periumbilical abdominal pain every day with radiation to the epigastric region for the past 6 months
- Pain wax and weans, most of the time crampy, sometimes wakes her up at night
- Defecation pattern is completely normal
- Not related to meals
- Tried "everything"
- Missing school

Are Rome criteria useful-helpful?



History of Rome Criteria



Children

Functional Disorders: children and adolescents Disorders of Gut-Brain Interaction (Rome V)

H1. Functional nausea and vomiting disorders

- H1a. Cyclic vomiting syndrome
- H1b. Functional nausea and functional vomiting
- H1c. Rumination syndrome
- H1d. Aerofagia

H2. Functional abdominal pain disorders

- H2a. Functional dyspepsia
- H2b. Irritable bowel syndrome
- H₂c. Abdominal migraine

H2d. Functional abdominal pain, not otherwise specified

H3. Functional defecation disorders

- H3.1 Functional constipation
- H3.2 Nonretentive fecal incontinence

Hyams JS, Di Lorenzo C, et al. Gastroenterology 2016

Prevalence of functional abdominal pain



Korterink J. et al PlosOne 2015

Multisite pain characteristics in a cohort of children with FAPDs (n = 406)

11 (70)
295 (73%)
200 (49%)
2 [1-3]*
172 (42%)
143 (35%)
134 (33%)
110 (27%)
94 (23%)
87 (21%)
30 (7%)

Comparisons between children with FAPDs with vs without multisite pain on abdominal pain, psychosocial distress, functional disability, and HRQoL

Variables	With multisite pain (n = 295)	Without multisite pain (n = 111)	<i>P</i> value
Abdominal pain episodes/2 wk.	12 [6-20]*	7 [3-14]	<.001
Abdominal pain intensity (0-10)	3.2 [2.3-4.2]	2.8 [2.2-3.9]	.03
Anxiety (t score)	54 [45-62]	45 [39-54]	<.001
Depression (t score)	46 [42-53]	43 [41-47]	<.001
Functional disability	10 [5-19]	5 [1-9]	<.001
PedsQL total score	77.2 [65.2-87]	88 [81.5-93.4]	<.001
PedsQL physical function	78.1 [62.5-90.6]	90.6 [81.3-96.9]	<.001
PedsQL emotional function	70 [50-85]	90 [80-95]	<.001
PedsQL social function	95 [80-100]	95 [85-100]	.27
PedsQL school function	75 [60-85]	85 [75-95]	<.001
PedsQL psychosocial function	76.7 [63.3-86.7]	88.3 [80-93.3]	<.001

Chumpitazi B, et al. J Pediatr 2021

Children with functional gastrointestinal disorders with and without co-existing nausea

- Nausea is a prevalent comorbid symptom in patients with functional abdominal pain disorders: 53% have been proven to experience nausea at least two times a week.
- Children with nausea report more feelings of anxiety and depression and lower overall health-related quality of life than children with a functional abdominal pain disorder without nausea.
- Addressing the presence of nausea in children with functional gastrointestinal disorders seems essential to customize their treatment and improve overall quality of life.

Bruijn CMA, et al. Neurogastro & Motil 2023

Risk & Protective factors for AP-DGBI in children



Zia JK, et al. Gastroenterology 2022

Organic or functional?

Diagnostic workup?





Doctor's Incorrect Agenda



Doctor's Correct Agenda



Medical history and Physical examination alarm symptoms

- Weight loss
- Failure to thrive
- Severe vomiting/ diarrhea
- GI-bloodloss
- Fever
- IBD in family

- Oral ulcers
- Perianal fissures
- Arthritis
- Hepatosplenomegaly
- Icterus



No alarm symptoms: 94% functional

El Chammas et al. J Ped 2013; Zeevenhooven J Ped 2020

Increased prevalence celiac disease in pediatric patients with IBS A 6-Year Prospective Cohort Study

Functional Gastrointestinal Disorder	Patients, No.	Patients With Celiac Disease, No.	Prevalence of Celiac Disease, % (95% CI)
Irritable bowel syndrome	270	12	4.4 (2.5-7.6)
Functional dyspepsia	201	2	1.0 (0.2-3.5)
Functional abdominal pain	311	1	0.3 (0.1-1.7)
Abdominal migraine	0	0	0.0 (0.0-0.0)

Christofori C, et al. Jama Pediatr 2014

Clinical Evaluation of Inflammatory and Blood Parameters in the Workup of Pediatric Chronic Abdominal Pain

- Fecal calprotectin, anti-tTG, G lamblia, CRP, ESR, Hb:
 - sensitivity 90%
- Fecal calprotectin, anti-tTG, G lamblia:
 - sensitivity 88%
- - In the presence of **>** 1 alarm symptoms
 - sensitivity 92%

Zeevenhooven J, et al. J Pediatr 2020

The Use of Fecal Calprotectin Testing in Paediatric Disorders: A Position Paper of the European Society for Paediatric Gastroenterology and Nutrition Gastroenterology Committee

Statement 13

15 (a) FC levels in children with FAPDs are similar to healthy controls.15 (b) FC levels in children with IBS symptoms are slightly higher than in healthy controls but lower compared with children with IBD.

Ribes Koninckx C, et al. JPGN 2021

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Recommendation 13

The ESPGHAN expert group recommends to use FC as a tool to differentiate functional abdominal pain disorders from organic diseases. (GoR; Strong) Agreement 92.9% Mean 8.3 Abstentions: 1

Ribes Koninckx C, et al. JPGN 2021

The value of abdominal ultrasound in functional abdominal pain



Value of Abdominal Sonography in the Assessment of Children with Abdominal Pain

- 676 children with abdominal pain underwent US
 - 644 children with RAP
 - 32 children with acute or subacute abdominal pain
- Abdominal abnormalities were sonographically detected in 10 children with RAP (2%)
- Acute pain (56%)

Yip WC, et al. J Clin Ultrasound 1998

Algorithm for Evaluation of Chronic Abdominal Pain and Stratification of Suspicion for Significant Endoscopic Findings



High Risk Features

- (+) Hemoccult
- Fecal Calprotectin > 200 µg/g
- Report of Unexplained bloody stools
- (+) TTG
- Albumin < 3 g/dL

- Iron deficiency anemia
- Extra-intestinal IBD findings
- Nocturnal stooling
- 1st degree relative with IBD or EoE
- History of food impaction

- Significant diarrhea
- Esophageal Stricture
- Significant weight loss/growth failure
- Elevated ESR

Mark JA, et al. Clin Pediatr 2019

Diagnoses after EGD with or without Colonoscopy for Abdominal Pain



Mark JA, et al. Clin Pediatr 2019



Rexwinkel R, Eur J Pediatr 2022

Therapeutic algorithm for IBS in children



Thapar N, et al. Nat Rev Primers 2020

The Golden Half Hour in Chronic Pediatric Pain Feedback as the First Intervention

- Elicit parent and child expectations at the outset (diagnostic tests)
- Validate Symptoms, families feel dismissed/stigmatized when mental health referral is made for what they perceive is a physical problem
- Offer a positive diagnosis
- Provide education
- Emphasize a multidisciplinary intervention plan (medical intervention, with psychological intervention, increased physical activity)
- Stay Connected follow-up visits every 4-6 wks
- Offer an Optimistic Appraisal

1e phase of treatment of FAP or IBS

- Reassurance & diagnosis
- Explain concept of hypersensitivity
- Explain causes
- Back to school!





Mechanisms Underlying the Irritable Bowel Syndrome (IBS)

Korterink JJ, et al. Nat Rev Gastroenterol Hepatol 2015

Parent Attention vs. Distraction



- Pain induced by water load test
- Parents randomized to using distraction or attention in their interaction with children in pain
- All mothers felt distraction was inappropriate response to pain

Walker LS, et al. Pain 2006



Di Giorgo R, et al. Gut 2015

Specific dietary interventions for pediatric disorders of gut-brain interaction

INFANT REGURGITATION

Breast feeding: Elimination of cow's milk in mother's diet Non-breastfed:

Thickening (additive or formula) Cow's milk elimination

Colic Prevention diets

INFANT COLIC

Breastfeeding: Elimination of cow's milk in mother's diet

Other elimination diets

Non-breastfeeding: Cow's milk

elimination



PAIN PREDOMINANT DGBI (mostly IBS) Soluble Fiber

Low FODMAP diet Single carbohydrate elimination Enzyme supplementation

Other diets (e.g., gluten restriction)



Nurko S, et al. Am J Gastroenterol 2022
Reported symptoms by ingestion of suspected food



Légeret C, et al. Eur J Pediatr 2023

Food intolerances in 2036 children and adolescents in Switzerland



Légeret C, et al. Eur J Pediatr 2023

Tests performed for diagnosis of food intolerance



Légeret C, et al. Eur J Pediatr 2023

Food intolerances in children and adolescents in Switzerland

- Eating behavior in children influenced by consumption of social media
- 16% of children and adolescents avoid foods, half of them without any medical advice
- 50% affected patients avoid foods without guidance by professional dieticians, risking possible negative impacts on their physical and mental health

Dietary interventions for Functional Abdominal Pain Disorders in children: a Systematic Review

- Articles 4806 Selected 12
- 819 children, aged 4-18 years
- Trials investigating fibers, FODMAP diet, fructans, fructose restricted diet, prebiotic (inulin), serumderived bovine immunoglobulin and vitamin D supplementation were included
- No studies were found on treatment with additional fluid intake or histamine-free diet

CM de Bruijn, et al. Expert Rev Gastroenterol Hepatol. 2022

FODMAP

- Fermentable
- Oligosaccharides (fructans, (FOS and GOS))
- Disaccharides (lactose)
- Monosaccharides (fructose)
- And
- Polyols (sugar alcohols)
 - artificial sweeteners sorbitol, mannitol, maltitol, and xylitol



FODMAP



Simren M, Tack J. Nat Rev Gastroenterol Hepatol 2018

Breath hydrogen test Typical Australian diet versus Low FODMAP diet



Halmos AP, et al. Gastroenterology 2014

Gastrointestinal symptoms during different diets





Halmos AP, et al. Gastroenterology 2014

RCT: gut microbiome biomarkers are associated with clinical response to a low FODMAP diet in children with IBS



- Less abdominal pain occurred during the low FODMAP diet vs. TACD [1.1 episodes/day vs. 1.7 P < 0.05]
- Compared to baseline (1.4 0.2), children had fewer daily abdominal pain episodes during the low FODMAP diet (P < 0.01) more episodes during the TACD (P < 0.01)

Dietary interventions for Functional Abdominal Pain Disorders in children: a Systematic Review

 Based on the current evidence, the use of fibers can be discussed in daily practice due to their favorable treatment outcomes and lack of side effects

Local immune response to dietary antigens triggered by bacterial infection leads to food-induced abdominal pain



Aguilera-Lizarraga J, et al. Nature 2022

Ebastine

- Ebastine is a second-generation HRH1 antagonist that currently is indicated for allergic rhinitis and chronic idiopathic urticarial
- Ebastine does not penetrate the blood-brain barrier, it does not produce cognitive/psychomotor impairment or seda-tion, compared with placebo
- Side effects are rare and include headache, excitement, diarrhea, constipation, asthenia, and gastric intolerance

Wouters MM, et al. Gastroenterology 2016

Effect of ebastine on global symptom relief and abdominal pain



Wouters MM, et al. Gastroenterology 2016

Treatment of non-constipated IBS with the histamine 1 receptor antagonist ebastine 20mg: a randomized, double-blind, placebo controlled trial



Decraecker L, et al. Gut 2024

Psychosocial interventions for the treatment of Functional Abdominal Pain Disorders in Children: A systematic review and meta-analysis



- 2657 children, aged 4-18 years
- 12 compared CBT to no intervention
- 5 CBT to educational support
- 3 yoga to no intervention
- 2 HT to no intervention
- 2 gut-directed HT to HT
- 2 guided imagery to relaxation
- 7 looked at other unique comparisons

M. Gordon, et al. Jama Pediatr 2022

Social learning CBT vs Education support: parents-children

- 200 children (7-17) with Apley critera for abdominal pain for at least 3 months
- 3-session intervention of cognitive-behavioral treatment targeting parents' responses to their children's pain complaints and children's coping responses
 - Relaxation training
 - Working with parent and child to modify family responses
 - Cognitive restructuring

Social learning CBT vs Education support: parents-children



Levy RL, et al. Am J Gastroenterol 2010

Hypnotherapy

• Hypnotherapy (HT):

Six sessions according to Manchester protocol

- general relaxation (e.g. breathing exercises)
- control of abdominal pain and gut functioning
- ego strengthening suggestions

Child is in control!



Gonsalkorale WM, et al. Int J Exp Hypn 2006

Effect of therapy on pain intensity scores



Vlieger A, et al. Gastroenterology 2006

Results – Clinical remission



Vlieger A, et al. Am J Gastroenterol 2012





Van Tilburg M, et al. Pediatrics 2009

Baseline characteristics

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)

Rutten J, et al. Jama Pediatr 2017

Success defined as at least 50% reduction in the pain frequency and pain intensity score



Rutten J, et al. Jama Pediatr 2017

Parents reported adequate relief



Rutten J, et al. Jama Pediatr 2017

Results

• Significant improvement in:

- Anxiety
- Depression
- QoL
- Pain beliefs
- Treatment effect not related to:
 - Prepuberty and older children
 - IBS or FAPS
 - Anxiety or depression
 - Therapist

Rutten JMTM, et al. JAMA Pediatr 2017

Long-term follow up

p=.9999 p=.607 p=.555 p=.607 p=.505 p=.607 p=.607 p=.505 p=.607 p

Adequate relief: iHT: 83.8% vs CD: 80%

Treatment success*:

	CD group	iHT group	p-value
After therapy	21 <mark>(</mark> 34.4%)	37 (52.1%)	.041*
1 year follow-up	38 <mark>(</mark> 62.3%)	48 (69.6%)	.382
5.8 years follow-up	39 <mark>(</mark> 67.2%)	42 (66.7%)	.946

Rexwinkel R, et al. JPGN 2022

Hypnosis4abdominalpain.com

Hipnosisdolorabdominal.com

Hypnosebijbuikpijn.be / hypnosebuikpijn.nl Hypnosebeibauchschmerzen.de

Hypnosis For AbdominalPain

Home For whom? At

In development: Swiss-German, French, Swedish, Hungarian, Italian and Portugese

Welcome

10-15% of the world's children suffer from abdominal pain – too many! **Our research reveals** that listening to self-hypnosis recordings helps more than 70% of children. Using selfhypnosis also reduces medical and psychological visits, improves quality of life, increases school attendance, self-confidence – and even sleep improves!

Abdominal pain is troublesome and annoying

By missing school, not playing sports or being with friends, abdominal pain impacts many parts of children's lives. **This ongoing pain is caused by irritable bowels**. Genetic predisposition, personality traits and home or school stress can play a role in irritable bowel syndrome. Listening to hypnosis recordings can help these children.

Hypnosis at home is a great solution



Smartphone app- delivered gut- directed hypnotherapy improves symptoms of self- reported irritable bowel syndrome: A retrospective evaluation

- 2843 patients with self-reported IBS commenced the free sessions
- 1428 (50%) purchased the app
- 253 (9%) completed all 42 sessions!



Peters SL, et al. Neurogastroenterol Motil 2023

Pharmacologic treatment of functional abdominal pain disorders: a systematic review



- 17 RCTs
- 1197 children, aged 4-18 years
- Antispasmodics, antidepressants, antibiotics, antihistaminic, antiemetic, histamine-2-receptor antagonist, 5-HT4-receptor agonist, melatonin, and buspirone
- No studies included on laxatives, antidiarrheals, analgesics, antimigraines, and serotonergics

Rexwinkel R, et al. Pediatrics 2021

Antispasmodics

Kline	N=50, 8-17y	2 weeks pepermint	GRADE:
2001	IBS	oil vs. placebo	very low

- Improvement in severity of symptoms: 71% vs. 19% (p<0.001)
- No adverse effects reported
- Quality:
 - No concealment of allocation
 - Attrition bias
 - Small sample size



Amitriptyline vs placebo

90 children,5 centers,4 wks rx,5 years tocomplete it



Saps et al. Gastroenterology 2009

Neurostimulation for abdominal pain-related FGIDs in adolescents: a randomised, double-blind, sham-controlled trial

- Percutaneous electrical nerve field stimulation (PENFS) external ear to modulate central pain pathway
- 115 Adolescents, 11–18 years, AP-FGID
- PENFS (n=60) with an active device or sham (n=55)



Kovacic K, et al. Lancet Gastroenterol Hepatol 2017

Percutaneous Electrical Nerve Field Stimulation





Kovacic K, et al. Lancet Gastroenterol Hepatol 2017

The Placebo Response in Pediatric Abdominal Pain-Related Functional Gastrointestinal Disorders: A Systematic Review and Meta-Analysis

Daniël R. Hoekman, MD^{1,*}, Judith Zeevenhooven, BSc^{1,*}, Faridi S. van Etten-Jamaludin, BSc², luke Douwes Dekker, MD³, Marc A. Benninga, MD, PhD¹, Merit M. Tabbers, MD, PhD¹, and Arine M. Vlieger, MD, PhD⁴

Objective To investigate the magnitude and determinants of the placebo response in studies with pediatric abdominal pain-related functional gastrointestinal disorders.

Study design The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and CINAHL were searched for systematic reviews and randomized placebo-controlled trials concerning children 4-18 years of age with an abdominal pain-related functional gastrointestinal disorder. The primary outcome was the pooled proportion of subjects assigned to placebo with improvement as defined by the authors. The effect of trial characteristics on the magnitude of the placebo response was investigated using univariate meta-regression analysis. **Results** Twenty-one trials were identified. The pooled proportion of subjects with improvement was 41% (95% CI, 34%-49%; 17 studies) and with no pain was 17% (95% CI, 8%-32%; 7 studies). The pooled standardized mean difference on the Faces Pain Scales compared with baseline was -0.73 (95% CI, -1.04 to -0.42; 8 studies). There was significant heterogeneity across studies with respect to both outcomes. Lower dosing frequency (P = .04), positive study (P = .03), longer duration of treatment (P < .001), and higher placebo dropout (P < .001) were associated with higher repert of the placebo on Faces Pain Scales conducted in the Middle

East (P = .002)percentage of f Conclusions 419/0 the randomization schedule (P = .02), and in studies with a higher

vith abdominal pain-related functional gastrointestinal disorders improve

Hoekman DR, et al. J Pediatr 2017

Do children just grow out of IBS?



- Spontaneous resolution over 2 years FU
- Treatment with..... not associated with treatment success

Giannetti E, et al. J Pediatr 2017
Conclusions

- Successful management of patients with functional pain disorders with a trusting, positive, patient-physician relationship
- Fibers and probiotics only play a minor role
- The role of FODMAP diet should be established in future larger trials
- CBT, hypnotherapy and neurostimulation are effective treatments
- Evidence for the use of pharmacological treatment is lacking
- Labeling??? Placebo??

Questions?

