A randomized controlled trial on the effect of laxative therapy in children with functional abdominal pain

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Primary objective: to establish the effectiveness of laxative therapy in children with functional abdominal pain.Secondary objective: to establish if laxative therapy is effective in all functional abdominal pain syndromes, including functional...

Ethical review	Not approved
Status	Will not start
Health condition type	Gastrointestinal disorders
Study type	Interventional

Summary

ID

NL-OMON43096

Source
ToetsingOnline

Brief title
Laxative therapy in children with functional abdominal pain

Condition

- Gastrointestinal disorders

Synonym
functional abdominal pain, irritable bowel syndrome

Research involving
Human

Sponsors and support

Primary sponsor: HagaZiekenhuis
Source(s) of monetary or material Support: Financiële ondersteuning is gezocht bij het CZ-Fonds

Intervention

Keyword: Children, Constipation, Functional abdominal pain, Rome criteria

Outcome measures

Primary outcome

Percentage of patients being pain free (complete remission).

Secondary outcome

1. Percentage decrease of the pain.

Clinical remission is defined as a decrease of 80%, moderate success as a decrease of 50-80% and lack of success as <50% decrease of the Wong-Baker Faces Pain Score, as noted in the diary in the last week of the run in period and the last week of the intervention period.

2. Based on descriptive statistics an estimation will be made if the success of laxative therapy is specific for one or more functional abdominal pain syndromes (according to the Rome criteria for functional abdominal pain syndromes).

Study description

Background summary

Introduction
Chronic abdominal pain is a frequent complaint in children in the age of 4-16 years, with a prevalence of 10-15%. It has considerable impact on the life of the patients and their families; quality of life (QoL) has been described to be

the same as QoL of children with inflammatory bowel disease. It is often cause of school absenteeism (in an earlier study in The Hague 15% of the patients with abdominal pain was absent at least once a week). Adolescents with chronic abdominal pain tend to be more depressed and socially isolated.
Only in a minority of the patients an organic cause is found. By definition, patients without an organic cause have the diagnosis *functional abdominal pain*.

In some studies in adults with functional abdominal pain (particularly irritable bowel syndrome, IBS) in several countries, the economic burden on the society has been calculated. This appeared to be high concerning the direct costs (doctors visits and diagnostics) as well as the indirect costs (work absenteeism). In a recent study in The Netherlands, the costs of IBS in children have been calculated to be ¤2500 per patient per year.

The standard therapy of functional abdominal pain (explanation, reassurance and life style advice after exclusion of organic disease) leads to recovery in 35-50% of the patients. With hypnotherapy, the results are better: in a recent study, 71% had at least 50% reduction of their pain score. At long term follow up after 5 to >10 years, up to 40% of the patients still has abdominal pain.
Recently, we performed an observational study in 200 children, referred to secondary care in the Juliana Children*s Hospital/Haga Teaching Hospital in The Hague because of chronic abdominal pain. After exclusion of an organic cause, all patients with functional abdominal pain had laxative therapy. Herewith 99% of these 200 patients became pain free; they remained pain free during the follow up period of at least 6 months (mean 18 months).
This result needs to be confirmed in a randomized placebo-controlled trial.

According to the *Rome criteria* of functional gastrointestinal disorders, symptom clusters of functional abdominal pain are recognized: irritable bowel syndrome (IBS), functional dyspepsia, functional abdominal pain, functional abdominal pain syndrome and, more rarely, abdominal migraine.
Investigations into the pathophysiology are almost exclusively directed to IBS and - less often - to functional dyspepsia. The pathophysiology of IBS is multifactorial; stress is considered an important factor. Functional dyspepsia, defined by upper abdominal complaints, is considered a problem of the proximal part of the gastrointestinal tract and is treated with inhibitors of acid secretion and prokinetics with only moderate success; in 2 publications, indications have been found for a causal relation with constipation.
In the above mentioned study in The Hague, all children with functional abdominal pain had laxative therapy, regardless of their presenting symptom cluster. In that observational study, laxative therapy appeared to be successful in nearly all patients with functional abdominal pain, regardless of their presentation, including patients with functional dyspepsia. Remarkably, in patients with IBS we found the same results with laxative therapy in patients with the diarrhea type of IBS (IBS-D) as in the patients with the constipation type of IBS (IBS-C).

If these results would be confirmed, this should have important consequences for the therapy of functional dyspepsia (laxative therapy in stead of inhibitors of acid secretion and prokinetics) and the therapy of IBS-D (treatment with laxatives as in paradox diarrhea in stead of treatment with anti-diarrhea drugs).

Rationale
1. Because of the impact of chronic abdominal pain in children and the long term prognosis with impressive consequences for the life of the patients and for the society, it is important to aim at optimal therapy. Literature on laxative therapy in children with abdominal pain is extremely sparse; controlled trials are not available. A single controlled trial in adults has major methodological imperfections.
Therefore, the good result of the earlier observational study needs to be confirmed in a randomized placebo-controlled trial.

2. Confirmation of the effectiveness of laxative therapy in patients with functional dyspepsia and IBS-D would shed new light on the pathophysiology of these disorders, and give way to a quite new therapeutic strategy for the patients.

Study objective

Primary objective: to establish the effectiveness of laxative therapy in children with functional abdominal pain.
Secondary objective: to establish if laxative therapy is effective in all functional abdominal pain syndromes, including functional dyspepsia and IBS-D.

Study design

A randomized placebo controlled multicenter study.

Population:
Children (age 4,0 -16,0 years of age) with the diagnosis functional abdominal pain.

Inclusion criteria
In order to be eligible to participate in this study, a subject must meet all of the following criteria:
1. age 4-16 years;
2. chronic abdominal pain since at least 2 months;
3. organic causes excluded according usual criteria.

Exclusion criteria
A potential subject who meets any of the following criteria will be excluded from participation in this study:

1. insufficient knowledge of the Dutch language;
2. earlier therapy with generic macrogol;
3. participation of a sibling in the study;
4. abdominal pain less than 2x per week in the diagnostic phase according to diary.

Intervention

Macrogol 4000, generic form with addition of a flavouring, is used as laxative. Starting dosage is 20 g/day in 200 ml fluid per 10 g macrogol. In case of insufficient result, the dosage is to be increased with 10 g/day (in extra 200 ml) every 2 days until a maximal dosage of 50 g/day (in 1000 ml fluid). This dosage should be continued till the end of the 4 weeks intervention unless the consistency of the stool is too loose. The dosage should be adjusted according to the stool consistency, with help of the stool chart (adapted Bristol Stool Form Scale). The dosage will be not be described in terms of grams, but as the number of spoons (one spoon = 10 g macrogol).
Maltodextrin, with addition of the same flavouring, is used as placebo. This is a fully resorbable carbohydrate, that is not to be expected to have any effect on the motility of the bowel. Because of the caloric load, it is not ethical to give the same dosage (in grams) as in case of macrogol, for which reason the dosage will be described in terms of spoons instead of grams: the spoons in the boxes of the placebo contain only 3 grams of maltodextrin. When patients need the maximal dosage because the placebo has no laxative effect, they get 5 spoons/day = 15 g (60 kcal)/day. One spoon of maltodextrin should be solved in 50 ml water.
There is no evidence that extra water has a laxative effect, unless the child is used to drink less fluid than recommended: in that case, the normalization of the fluid intake by means of an extra litre of water (in case of 200 ml per spoon of maltodextrin) could have a laxative effect. Therefore, the amount of water is restricted to 50 ml per spoon of maltodextrin, resulting in a maximum of 250 ml extra water/day.
The spoons and cups are packed within the boxes and are not visible from outside. Several spoons and cups are packed within each box, to prevent that * in case of loss of a spoon or cup * the patient has to ask for a new one and therewith has to explain to the hospital personnel what kind of spoon or cup he uses.

Study burden and risks

The burden associated with participation consists of some extra time needed to explain the study after the diagnosis functional abdominal pain is made and an extra visit for the patient to hand in the informed consent form and to give the medication. During intervention and follow up several telephone calls will take place.

Macrogol 4000 has a high molecular weight which makes it unabsorbable. It is a long linear polymeric molecule to which water molecules adhere. After oral ingestion it leads to increase of the amount of fluid in the bowel. The intestinal fluid that is not absorbed is cause of the laxative effect.
Some complaints can result as long as defecation is still unsufficient. However this is part of the patient's problem. The risk is negligible. Allergic reactions are very rare.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. age 4-16 years;
2. chronic abdominal pain since at least 2 months;

3. organic causes excluded according to usual criteria

Exclusion criteria

1. insufficient knowledge of the Dutch language;
2. earlier therapy with generic macrogol;
3. participation of a sibling in the study;
4. abdominal pain less than 2x per week in the diagnostic phase according to diary.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	120
Type:	Anticipated

Ethics review

Not approved

Date:	27-05-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL57752.098.16