Effectiveness of probiotics in the treatment of children with chronic abdominal pain and small intestinal bacterial overgrowth. A randomized placebo-controlled trial.

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Ethical review	Approved WMO
Status	Completed
Health condition type	Gastrointestinal signs and symptoms
Study type	Interventional

Summary

ID

NL-OMON39168

Source
ToetsingOnline

Brief title
SIBO study

Condition

- Gastrointestinal signs and symptoms

Synonym
chronic abdominal pain, small intestinal bacterial overgrowth

Research involving
Human

Sponsors and support

Primary sponsor: Jeroen Bosch Ziekenhuis
Source(s) of monetary or material Support: Gastrostart (NVGE) (aangevraagd);maagleverdarmstichting (wordt aangevraagd),Orthica,Winclove, Amsterdam

Intervention

Keyword: children, chronic abdominal pain, small intestinal bacterial overgrowth

Outcome measures

Primary outcome

Primary outcome measures are the percentages of patients with complete remission of chronic abdominal pain after the treatment phase (t = 1), at six months follow up (t = 2) and 12 month after starting the therapy (t=3). Clinical remission is defined as a decrease of the pain intensity score and pain frequency score of > 80%; significant improvement is defined as a decrease of pain intensity score and pain frequency score between 30% and 80% and treatment is considered unsuccessful if the scores improved < 30% or got worse.

Secondary outcome

Secondary outcome measures is the presence of small intestinal bacterial overgrowth.

Study description

Background summary

Chronic abdominal pain is present in 0.3-19% of school-going children in the US and Europe and is one of the most frequent reasons to visit a pediatrician1. In 29.1% of patients with chronic abdominal pain, pain persists for more than 5 years, despite frequent medical attention.

The pathogenesis of chronic abdominal pain remains unclear, although several mechanisms have been proposed to explain the symptoms of this condition. Recent studies have also pointed to an underlying gut microbial mechanism for chronic abdominal pain. When the microbial population native to the large intestine migrates proximally into the small intestine, a shift in the host-gut microbial relationship occurs, known as small intestinal bacterial overgrowth (SIBO). Similar to children with chronic abdominal pain, children with SIBO complain of nausea, abdominal pain, flatulence, diarrhoea and constipation.
In a recent study, small intestinal bacterial overgrowth has been reported in 91% of children with chronic abdominal pain compared to 35% in healthy children. They also found an association between small intestine bacterial overgrowth and irritable bowel syndrome in children.
There are no published data on the effect of probiotic treatment in children with chronic abdominal pain, but recent unpublished study results showed that 70% of children with chronic abdominal pain and small intestinal bacterial overgrowth have an improvement of symptoms after treatment with probiotics.

Study objective

The aim of this study is to find a succesful treatment for chronic abdominal pain and small intestinal bacterial overgrowth in children and at the same time improve the quality of life of these children. A second aim is to reduce the hospital visits and with that the costs.

Study design

70 children age 8-18 years will be randomized and receive probiotics or placebo.
Children in the probiotics group will be given daily probiotics for 8 weeks (8 grams of powder 4 x 10E9 cfu / g Bifidobacterium and Lactobacillus (Ecologic junior)). Children in the placebo group will be given daily placebo for 8 weeks.

Outcomes are assessed at several time points: a t=0 (at baseline; before randomisation), at t=1 (directly after finishing the treatment period), at t=2 (four months after finishing the treatment period) and at t=3 (ten months after finishing the treatment period).

We will use the following instruments:

•Abdominal pain diary (APD): Patients will be instructed to score pain intensity and pain frequency in an abdominal pain diary during the baseline period (a month prior to t=0), for a month prior to t = 1 and for a month prior to t = 2. Pain intensity will be scored using the validated six-face Faces Pain Scale-Revised 12: ranging from 1 (=no pain) to 6 (very much pain) (Fig. 1). Pain frequency will be scored as 0 = no pain, 1 = 0*20 min of pain, 2 = 20 40 min of pain, 3 = 40*90 min of pain and 4 = more than 90 min of daily pain.

The daily scores will be added up to obtain a pain intensity score (minimum score of 31 and a maximum score of 186) and a pain frequency score (with a minimal score of 0 and a maximum score of 124) for these different time points.

•Hydrogen breath test: Patients will take this hydrogen breath test three times, at t=0, t=1 and t=2. In this test, hydrogen exhaled in the breath is estimated using a gas chromatograph. Bacteria, especially anaerobic, colonizing the large bowel in health and small bowel in diseased conditions produce hydrogen by fermentation of unabsorbed carbohydrates. Though small amount of hydrogen is produced from limited amounts of unabsorbed carbohydrate reaching the colon, large amounts of hydrogen may be produced if there is malabsorption of carbohydrate in the small intestine allowing larger amount to reach the colon or if there is excess of bacteria in the small bowel. The hydrogen produced by the bacteria is absorbed through the wall of the small or large intestine or both. The hydrogen-containing blood travels to the lungs where the hydrogen is released and exhaled in the breath where it can be measured. Breath test will be performed after overnight fast. Before the test, subjects will be asked to brush their teeth and rinse mouth with antiseptic mouth wash and tap water, to eliminate an early hydrogen peak due to action of oral bacteria on test sugars. End-expiratory breath samples will be collected either in bag or syringes. At the start of the test, fasting breath hydrogen will be measured. A fasting breath hydrogen concentration above 20 ppm will be interpreted as small intestinal bacterial overgrowth.

•Microbiota analyze: faeces samples are collected at t=0 and t=1, before and after the intervention. In case of a positive effect of the probiotics we would like to gain insight in the possible mechanisms of probiotic intake on abdominal pain in children. Therefore, we would like to study the composition and functionality of the microbiota. DNA based techniques will be used for microbiota analyses.

Intervention

The probiotics consist of a mixture of Bifidobacterium and Lactobacillus (8 grams of powder 4 x 10E9 cfu Bifidobacterium and Lactobacillus (Ecologic junior)). This has te be used once a day for 8 weeks.

Study burden and risks

The dosage of Winclove 349 (4x10^9 daily dosage) is in accordance with most probiotic dosages used in studies and many commercially available products, ranging from 10^9-10^10 cfu/daily dose. It is not possible to state a general dose for probiotics; some have shown to be efficacious at lower levels, while other require substantially more. The dosage of Winclove 349 is based on prior human studies with similar probiotic products showing a health benefit and no adverse reactions. In addition, the strains in the product are commercially

available in other similar probiotic powder product sold thought out Europe in daily dosages varying from 1x109 - 1x1010.

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

Children aged 8-18 years are included if they meet the criteria for functional dyspepsia, IBS, functional abdominal pain (FAP) or abdominal migraine, based on the Rome III Criteria for Functional Bowel Disorders Associated with Abdominal Pain or Discomfort in Children and have small intestinal bacterial overgrowth, diagnosed on hydrogen breath test as a fasting breath hydrogen concentration > 20 ppm or an increase of H2 levels of > 12 p.p.m. over the baseline value after ingestion of glucose.

Exclusion criteria

Children with abdominal pain as result of inflammatory, anatomic, metabolic or neoplastic disease. Children who were prescribed antibiotics or probiotics in the last month. Children who are critically ill or admitted at the ICU. Children who receive feeding via a tube.

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:	Completed
Start date (anticipated):	02-03-2012
Enrollment:	70
Type:	Actual

Ethics review

Approved WMO Date:	20-02-2012
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	02-07-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO	

Date:	13-05-2013
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 20319
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL39061.028.11
OMON	NL-OMON20319