Complementary therapies in paediatric gastroenterology: prevalence, safety and efficacy studies

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General introduction and Outline of the thesis

Part of the following article is used for this chapter: Vlieger AM, Benninga MA. Complementary therapies for pediatric functional gastrointestinal disorders. J Pediatr Gastroenterol Nutr 2008;47(5);707-709.
Introduction

The term *alternative medicine* encompasses a broad range of treatment modalities that fall outside the domain of western medicine. It incorporates many different approaches and methodologies, ranging from ancient techniques like acupuncture and ayurvedic medicine to chiropractics, homeopathy, spiritual healing and body-mind medicine. It is frequently grouped with the term *complementary medicine*, which generally refers to the same interventions when used in conjunction with conventional medical treatments, under the umbrella term *complementary and alternative medicine*, or CAM. Most of these CAM disciplines not only aim to relieve symptoms and restore wellness, like in conventional medicine, but also to help the individual in a process of self-healing within a holistic view of health, in which body, mind and spirit are addressed. The use of CAM therapies is prominent these days: a study in 2002 among 30.000 U.S. adults showed that 36% had used some form of CAM in the past year. Among children CAM use is also high, ranging from 11% to 23% of the patients visiting a general paediatrician and higher prevalences up to 68% in children with chronic or life-threatening diseases. With this widespread use, it is rare for a paediatrician these days not to be asked by parents about CAM treatments for the medical condition of their child.

Definitions

What is considered a complementary or alternative therapy in one country may be considered conventional medicine in another. Therefore, the definition of CAM is usually broad and general: “Complementary and Alternative Medicine is a broad domain of resources that encompasses health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the dominant health system of a particular society or culture in a given historical period. CAM includes such resources perceived by their users as associated with positive health outcomes. Boundaries within CAM and between the CAM domain and the domain of the dominant system are not always sharp or fixed”. Others have offered various definitions and distinguishing characteristics. The National Centre for Complementary and Alternative Medicine (NCCAM), part of the National Institute of Health, defines CAM as “a group of diverse medical and health care systems, practices, and products, that are not currently part of conventional medicine. The Cochrane Collaboration has adopted the following definition: CAM refers to a spectrum of diagnostic and therapeutic modalities that complement mainstream medicine by contributing to a common whole, by satisfying a demand not met by orthodoxy or by diversifying the conceptual frameworks of medicine.
The terms *integrative medicine* (IM) or *integrated medicine* are also often used in the field of CAM and indicate the combination of conventional medicine and those complementary treatments which have some scientific proof of efficacy. However, IM is not synonymous with using the best of complementary and alternative medicine. It has a far larger meaning and mission in that it calls for restoration of the focus of medicine on health and healing and that it emphasizes the centrality of the patient-physician relationship. 17

**History of CAM**

In the middle ages, two types of healers were practicing medicine in Western Europe. The first group were the physicians or “doctores medicinae”, who studied the works of the Greek masters at universities and often belonged to the upper classes. The other group consisted of folk healers, specialized in treating fractures and wounds, using herbs, oils and creams and living among the peasant population. This period can be seen as the start of the distinction between conventional and alternative medicine, although physicians in those days did not have much reliable knowledge yet and folk healers often applied useful treatments. 18

This changed in the nineteenth century when conventional medicine started to develop a more scientific basis for its treatments, and knowledge of anatomy and physiology was rapidly increasing. In 1865, when Thorbecke introduced the Law on Practicing Medicine, an official separation was made in the Netherlands between academically trained physicians on one hand and alternative healers on the other. 19 Alternative treatments in those days consisted mainly of herbalism and homeopathy, but in the beginning of the twentieth century an enormous array of other unconventional therapies started to gain popularity like magnetism, paranormal healing, and iridology. Osteopathy and chiropractic, both derived from the tradition of “bone-setting”, were developed and Asian immigrants introduced Eastern medical systems like acupuncture and the Indian Ayurvedic medicine.

At the end of the twentieth century, there was an explosion in the use of these alternative therapies and CAM began to develop as an entirely separate discipline. Complex societal factors have influenced the use of CAM such as a declining faith in the ability of science and technology to solve the problems of health and disease, and societal trends toward individualism, with individuals being less prepared to accept traditional authority, and seeking greater levels of control and empowerment over their lives. 20 With the rise in information on CAM through all kinds of media, people became more aware of the possibilities outside of conventional medicine. Furthermore, there was a great desire for “holistic” medicine. People increasingly didn’t want to be treated anymore as a body with, for example, a kidney problem, but they needed the accompanying social and
psychological aspects of their diseases addressed as well. Another common reason for turning to CAM was an increasing concern about the adverse effects of conventional medicine. Many of the CAM therapies are considered “natural” by the general public and thus safer and gentler in some way than the armamentarium of modern medicine. For long, the medical division between CAM and conventional medicine has been characterized by conflict, intolerance and prejudice on both sides. The increased interest in CAM however, together with the patients’ wishes for a more holistic treatment and an active participation in their disease management, has resulted in an attitude change of many physicians. Recent surveys show that most physicians are aware of their patients’ interest in using CAM, believe that CAM may have beneficial effects and are eager to seek reliable evidence-based information about CAM. This change in attitude has also resulted in the development of a new field in medicine: the so-called integrative medicine. As stated above, integrative medicine reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic approaches, including the best from alternative and complementary therapies to achieve optimal health and healing. More than 40 academic medical institutions in Northern America have already incorporated integrative medicine in their medical curriculum and offer an integrated approach to their patients. The popularity of this integrative approach can be considerable with, for example, more than 1000 of patient visits each month to the integrative medicine department of the Memorial Sloan Kettering Cancer Centre in New York. Also in European countries popularity of IM is increasing, suggesting that the future might involve some integration of the best of CAM in conventional medicine.

**Classification of CAM**

Alternative and complementary medicine practices are as diverse in their foundations as in their methodologies. Practices may incorporate or base themselves on traditional medicine, folk knowledge, spiritual beliefs, or newly conceived approaches to healing. The National Centre for Complementary and Alternative Medicine has classified complementary and alternative therapies into five major groups. For detailed information on these therapies, the reader is referred to websites and recent books on CAM and integrative medicine.

1. Whole medical systems

Whole medical systems are built upon complete systems of theory and practice. Often, these systems have evolved apart from and sometimes earlier than conventional medicine. Well-known examples of whole medical systems that have developed in
Western cultures are homeopathy and naturopathic medicine. Examples of systems that have developed in non-Western cultures include traditional Chinese medicine (TCM) and ayurvedic medicine.

**Homeopathy** has been developed by Samuel Hahneman in the 18th century and became popular in Europe and later in the US during the second half of the 19th century. Homeopaths seek to stimulate the body’s ability to heal itself by giving very small doses of highly diluted substances that in larger doses would produce illness or symptoms (an approach called “like cures like”).

**Naturopathic Medicine** is based on the belief that health is influenced by nature’s own healing power, which gained interest during the 18th and 19th century in Germany. Naturopaths aim to support the body’s ability to heal itself through the use of dietary and lifestyle changes together with CAM therapies such as herbs, massage, and joint manipulation.

**Traditional Chinese Medicine** is one of the oldest medical systems, probably dating back to the first century BC. TCM is based on the concept that diseases result from disruption in the flow of qi (energy) and imbalance in the forces of yin and yang. Practices such as herbs, meditation, massage, and acupuncture seek to aid healing by restoring the yin-yang balance and the flow of qi.

**Ayurvedic Medicine** is a system of traditional medicine native to India. It aims to integrate the body, mind, and spirit to prevent and treat disease. Therapies used include herbs, massage, and yoga.

2. Mind-body medicine

Mind-body practices take a holistic approach to health and explore the interconnection between the mind, body, and spirit. Therapists work under the premise that the mind can affect bodily functions and symptoms. Some techniques that were considered CAM in the past have become part of conventional medicine such as patient support groups and cognitive-behavioural therapy. Other mind-body techniques are still considered CAM, including meditation, yoga, (self-)hypnosis, prayer and therapies that use creative outlets such as art, music, or dance.

3. Biologically based practices

Biologically based practices only use natural remedies including herbs, animal-derived extracts, vitamins, minerals, fatty acids, amino acids, proteins, prebiotics and probiotics, and whole diets. Phytotherapy is the practice of healing with the use of herbs. Often it is part of whole medical systems like TCM or naturopathic medicine.
4. Manipulative and body-based practices
These practices feature manipulation or movement of body parts, such as is done in chiropractic care, massage, manual therapy and osteopathic manipulation. Often these body-based practices are part of whole medical systems, like Naturopathic Medicine and Ayurvedic Medicine.

5. Energy medicine
Energy medicine is a domain that deals with putative and verifiable energy fields. There are two types of energy medicine:

**Biofield therapies** are based on the concept that human beings are infused with a subtle form of energy. Some forms of energy therapy manipulate these biofields of subtle energy by applying pressure and/or manipulating the body by placing the hands in these fields. Examples include qi gong, Reiki and Therapeutic Touch. Some proponents of energy field therapies claim that it can also act across long distances. Examples of this form of distant healing are prayer and paranormal healing.

**Bioelectromagnetic-based therapies** involve the unconventional use of electromagnetic fields, such as pulsed fields, magnetic fields, or alternating-current or direct-current fields.

Classifying CAM therapies can be problematic. What was once identified as “alternative medicine” may have already become part of conventional medicine, either due to compelling evidence for its efficacy or a strong demand of the public. Probiotics is an example of a CAM therapy that nowadays is becoming integrated in conventional medicine. Probiotics, defined as health promoting bacteria, were already prescribed in the eighties by homeopaths, naturopaths and orthomolecular medicine therapists. This was long before conventional medicine became interested in their effects on health and disease. Therefore, questionnaires, surveying the prevalence of CAM use often have probiotics mentioned in their list of possible CAM treatments. Furthermore, publications on probiotics are indexed in Medline under the subset of complementary medicine. With the vast increase in research in probiotics in the last decade, however, one can hardly consider it a CAM treatment anymore. It is likely that the ongoing research on the efficacy and safety of other CAM therapies will result in a continuing shift of the demarcation between CAM treatments and mainstream medicine.

**Evidence-based use of CAM**
Throughout health care, there has been an increasing emphasis on the practice of evidence-based medicine. This means that clinical decision taking is nowadays based
on the integration of individual clinical expertise with the best available external clinical evidence from systematic research, hereby taking into account patients’ predicaments and preferences. More than a decade ago the phrase “evidence-based use of complementary and alternative medicine” was a bit of an oxymoron. The general perception of the medical community was that all CAM was quackery and simply did not and could not work. Any experienced effect by an individual patient could not be anything but a placebo-effect. Furthermore, scientific research in the CAM field was scarce and often of poor quality with many methodological limitations. Over the last 10-15 years, however, CAM research capacity has developed considerably. This has mainly been the result of the establishment of nationwide CAM research institutes, that have supported and coordinated CAM research. Examples of such institutes are the National Centre for Complementary and Alternative Medicine, which is an independent component of the National Institute of Health in the US, and the Research Council for Complementary Medicine in the UK. The number of randomized controlled trials (RCT) of CAM indexed in MEDLINE increased from fewer than 200 in 1982 to 1200 in 2002. In 2008, in total more than 7500 CAM trials were reported. In children there were virtually no good trials until 1975. From 1975, there was a significant steady growth for over twenty years, with around 90 articles per year published at the end of the nineties. It is now estimated that more than 1600 CAM trials involving children aged 18 years or younger are indexed in MEDLINE. Moreover, not only the amount of CAM research has grown; the overall quality has also improved. Reports on randomized controlled trials of CAM interventions have been shown to be as good as that for conventional medicine interventions. In the field of paediatric CAM, however, the quality of reports of randomized controlled trials was considered considerably lower than that found for conventional medicine. The authors of this survey suggested that this was caused by the fact that the paediatric CAM community conducted fewer RCT’s and was therefore less experienced. This increase in CAM research has resulted in compelling evidence for some of the CAM treatments. There is, for example, now good evidence for the effectiveness of some herbal remedies, such as St John’s Wort in treating depression, and devil’s claw for low back pain. Furthermore, acupuncture has been shown to work for chemotherapy induced vomiting and nausea as well as post-operative nausea. On the other hand, some other therapies are now proven ineffective for certain indications. Cochrane reviews failed to show, for example, that therapeutic touch promotes wound healing, or that spinal manipulation alleviates primary and secondary dysmenorrhea. For most CAM modalities, however, reliable RCT’s, investigating their effectiveness for individual indications are lacking.
CAM studies in paediatric gastroenterology

In the field of paediatric gastroenterology, many disorders exist for which conventional treatment options are limited, often only resulting in some symptomatic relief. This is especially true for functional gastrointestinal disorders like gastro-oesophageal reflux, irritable bowel syndrome, functional abdominal pain and defecation disorders. These conditions can be bothersome, often affect daily activities and are associated with a high medical consumption. A large proportion of children with functional GI disorders remains symptomatic for years despite conventional treatment. Also the treatment of children with organic gastrointestinal disorders, like inflammatory bowel disease, can be challenging, with frequent and severe side-effects of medication and disease relapse despite optimal maintenance therapy. It is reasonable to assume that parents of both group of patients may become dissatisfied with conventional medicine and consult practitioners of alternative medicine.

In the field of paediatric gastroenterology there is preliminary evidence for efficacy of some CAM therapies. An overview will be given here of the most commonly used complementary modalities. Some emphasis is on the use of probiotics and hypnotherapy, since these CAM treatments are studied in more detail in this thesis.

1. Probiotics

It is not surprising that most of the CAM intervention studies in paediatric gastroenterology have been focusing on the therapeutic effects of probiotics. They have, among others, been studied in constipation, Crohn’s disease, infantile colic’s, functional abdominal pain and/ or irritable bowel syndrome, infectious and antibiotic-associated diarrhoea. All these disorders will be briefly discussed here.

Constipation

Several trials have investigated the effect of probiotics in children with constipation. In a group of 84 children with constipation, the probiotic Lactobacillus GG was not an effective adjunct to lactulose therapy. In another study in 45 children, Lactobacillus casei rhamnosus was as effective as magnesium oxide in increasing the number of bowel movements with less side effects. Finally, a pilot-study in 20 children showed promising effects of a mixture of probiotics containing bifidobacteria and lactobacilli. These results suggest that probiotics can have a role in the treatment of childhood constipation, but differences exist between the different probiotic strains.
Crohn’s disease

Probiotics are widely used by paediatric patients with Crohn’s disease (CD) in an attempt to improve their health, but so far only one controlled study has been performed to evaluate the efficacy. The addition of the Lactobacillus GG to standard therapy did not prolong remission in children with CD.\(^{51}\) This is in agreement with similar studies in adults.\(^{52}\)

Infant colic

One study examined prospectively the effect of the probiotic Lactobacillus Reuteri in ninety breastfed colicky infants in comparison with simethicone. On day 28, 39 patients (95%) were responders in the probiotic group and 3 patients (7%) were responders in the simethicone group, suggesting that probiotics may have a role in the treatment of infantile colic.\(^{53}\)

Functional abdominal pain disorders

The efficacy of probiotics in the treatment of functional abdominal pain disorders was examined in two studies with in total 154 children. The first study showed that consumption of Lactobacillus GG resulted in some decrease of abdominal bloating in children with IBS, but no effect was seen on abdominal pain.\(^{54}\) In the other study, no effect was seen in children with functional abdominal pain and functional dyspepsia, but the probiotic moderately decreased abdominal pain in IBS children.\(^{55}\)

Antibiotic-associated diarrhoea

Ten trials have evaluated the effectiveness of probiotics in preventing antibiotic-associated diarrhoea in children. A Cochrane analysis, performed in 2007 showed that reduction of the risk of developing diarrhoea was associated with the use of Lactobacillus GG, Saccharomyces boulardii or Bifidobacterium lactis & Streptococcus thermophilus, but intention to treat analysis showed non-significant results overall. It was concluded that the current data are promising, but it is premature to routinely recommend probiotics for the prevention of paediatric antibiotic-associated diarrhoea.\(^{56}\)

Infectious diarrhoea

Lactobacillus GG and Saccharomyces boulardii have also been shown to be moderately effective in the treatment of acute, infectious diarrhoea. Both probiotics were associated with a decrease in the number of days with diarrhoea and significantly reduced the risk of diarrhoea > 7 days.\(^{57,58}\)
2. Hypnotherapy

Hypnosis first emerged as a treatment for medical conditions in the late 1700s, but it was not until more than 150 years later that the first clinical studies on hypnosis were performed. It was recognized as a legitimate medical tool by the British Medical Society in 1955 and by the American Medical Association in 1958. Since then, many clinical studies have been performed demonstrating the effectiveness of hypnotherapy. Nonetheless, its use is not widespread within conventional medicine, mainly because hypnosis has a negative perception among many medical practitioners. Perpetuating misconceptions about hypnosis, due to popular stage hypnotherapists, may play a major role in this negative perception.59

When using hypnosis, a patient is introduced into a hypnotic state and guided by a therapist to respond to suggestions for changes in subjective experience, alterations in perception, emotion, thought or behaviour.60 The hypnotic state has several elements such as a feeling of ease or relaxation, an absorbed attention, an absence of judging, and disorientation towards time and location.

Most research on the utility of hypnosis has been performed in the adult population. Children are, in general, more hypnotizable than adults, suggesting that hypnosis may be more effective with them. However, only a limited number of paediatric RCT’s has been performed. Publications on the use of hypnosis in children with gastrointestinal problems are scarce and comprise several case histories and small controlled studies. First, two studies in paediatric oncology patients showed that hypnotherapy can reduce nausea and anticipatory vomiting.61,62 Furthermore, hypnosis has been used as an adjunct in the treatment of children with severe constipation, but no controlled studies have been performed to date.63 The successful use of hypnosis has also been described, in combination with behavioural treatment, in children with functional dysphagia and food aversion.64 Finally, three uncontrolled studies have shown the feasibility of the use of (self-)hypnosis and guided imagery in children with recurrent abdominal pain. 33 children, all refractory to conventional therapy received 3 to 9 sessions of hypnotherapy, resulting in a significant improvement in 29 children.65-67

3. Herbals and botanicals

Herbs have been used for hundreds of years for GI complaints in both adults and children, but good scientific evidence of their effectiveness is scarce. Peppermint, which is commonly found in over-the-counter preparations for IBS, has been found effective in the treatment of IBS in children: in a small randomized, double-blind controlled 2-week trial 76% of the patients receiving enteric-coated peppermint oil capsules reported a decrease in symptom severity versus only 19% in the placebo group.68 The mechanism of action is thought to be from the menthol component of peppermint that relaxes gastrointestinal smooth muscle by blocking calcium channels.69 The effect of mint was also tested in a
RCT in children with infantile colic: a herbal tea, containing chamomile, vervain, fennel and mint, resulted in elimination of colic’s in 57% of the study group compared to 26% in the placebo group. Chinese herbal medicine may offer improvement in some adults with irritable bowel syndrome (IBS), and a superior post-treatment effect was found with individualized formulations in comparison to standardized preparations, but no studies have been performed in children with IBS. Despite the fact that herbs are popular in the self management of childhood constipation, no good RCT’s exist on its use. A recent observational study investigated the use of a Japanese herbal medicine in 15 severely constipated children. It had a favourable clinical effect on constipation and anorectal manometry showed an improvement in rectal reservoir functions.

4. Homeopathy

In children, many clinical trials have been conducted to investigate the effectiveness of homeopathy, but most of these trials have looked at prevention or treatment of respiratory tract infections. Only a few studies have been performed in paediatric gastroenterology. Jacobs et al performed three double blind clinical trials, all demonstrating a positive treatment effect of individualized homeopathic treatment for acute childhood diarrhoea. Combined analysis of these studies showed a duration of diarrhoea of 3.3 days in the homeopathy group compared with 4.1 in the placebo group. One observational cohort study in 204 children < 12 years compared the effect of a standard homeopathic preparation with a conventional drug (scopolamine) in the treatment of abdominal cramps. The analysis showed comparative improvements with both treatments spasms, pain, sleeping disturbances and crying. However, no double-blind RCT has been performed with this homeopathic preparation to confirm these findings.

5. Massage therapy

Massage is a commonly used CAM modality in patients with chronic disorders. Its use is based amongst others on the assumption that massage may reduce excitation of visceral afferent fibres and possibly affect central pain perception and processing. Recently it was shown that massage can also increase vagal tone and gastric motility. It is therefore reasonable to assume that (abdominal) massage can play a role in gastrointestinal disorders. A review on 4 controlled trials of abdominal massage for chronic constipation in adults concluded that massage therapy could be a promising treatment for chronic constipation, but more rigorous trials should evaluate its true value. Awaiting these trials, many paediatricians advocate its use in children with constipation for promoting bowel activity and relaxation the abdominal wall. Bishop et al. carried out an observational study in 50 children, age 3 to 14 years, who had chronic constipation and/or encopresis. Six sessions of 30 minutes of reflexology treatment (a special form of massage in which manual pressure is applied to specific zones of the
feet that are believed to correspond to different areas of the body, thereby effecting therapeutic change) resulted in an increase in bowel movements and a decrease in faecal incontinence episodes.\textsuperscript{80}

6. Acupuncture

Acupuncture is part of the traditional Chinese medicine and has become very popular in western countries in the last decades. Animal studies have shown an effect of acupuncture on acid secretion, gastrointestinal motility and visceral pain.\textsuperscript{81} Furthermore, it is known that acupuncture and acupressure ameliorate postoperative nausea.\textsuperscript{82} These findings suggest that acupuncture also might be effective for other gastrointestinal problems, but results of randomized controlled trials have been disappointing so far. Mixed results were found on the effect of acupuncture on rectal sensations in IBS patients and no effect was seen on their quality of life and symptom scores.\textsuperscript{83-85} To date, no good studies have been performed examining the benefits of acupuncture in children with gastrointestinal disorders. Only one small non-controlled study examined the effect of acupuncture in 17 children with constipation. An increase in bowel movements was found from 1.4 to 5 per week.\textsuperscript{86}

In conclusion, several complementary therapies seem to show some promise in the treatment of children with gastrointestinal symptoms. With the above mentioned limited treatment options in mind, this information may be relevant for paediatricians and paediatric gastroenterologists. In the continuing search for optimal therapeutic regimens, it is interesting to investigate the efficacy and safety of some of these CAM modalities. Needless to say that this should only be done in well designed, randomized-controlled trials.
Outline of the thesis

The studies in this thesis discuss the use of CAM modalities in paediatric patients in the Netherlands and more in detail two forms of complementary medicine: hypnotherapy and probiotics. The main focus is on the use of CAM in paediatric gastroenterology. This thesis can therefore be divided in three parts. Part I- The Use of Complementary and Alternative medicine in Paediatrics – investigates the use of CAM modalities by paediatric patients in the Netherlands. Part II - Hypnotherapy for children with Functional Abdominal Pain or Irritable Bowel Syndrome – describes two highly prevalent disorders in paediatrics (functional abdominal pain and irritable bowel syndrome) and the efficacy of gut-directed hypnotherapy in the treatment of these disorders. Part III - Probiotics in Infant Formula – discusses the safety and tolerance of a combination of two probiotics: L. paracasei ssp. paracasei and B. animalis ssp. lactis in healthy infants.

Part I - The Use of Complementary and Alternative medicine in Paediatrics

International studies have shown that CAM use in children is high with prevalences up to 68% in children with chronic or life-threatening diseases.\(^8^7\) When the research for this thesis was started, not much was known about CAM use in Dutch children. According to the Dutch Centre for Statistics, in year 2004 around 5% of the children under the age of 18 had paid one or more visits to an alternative therapist.\(^8^8\) A study in 1998 showed that the prevalence of CAM use in a group of Dutch paediatric oncology patients was 31%.\(^8^9\) Facts and figures on CAM use in Dutch children in general paediatric clinics, however, were lacking. We therefore determined the prevalence of and reasons for the use of complementary and alternative medicine (CAM) by paediatric patients. We also investigated whether parents had discussed their child’s CAM use with their paediatrician and their need for appropriate information on CAM. (Chapter 1).

Research on the use of CAM in paediatric patients with gastrointestinal diseases has also been limited so far and was focused mainly on children with inflammatory bowel disease.\(^9^0-9^2\) Chapter 2 describes a study in which we assessed CAM use in 749 children with different GI diseases, both organic and functional gastrointestinal disorders. We determined which patient and disease characteristics, such as health status or duration of symptoms, were associated with CAM use in this patient group and we assessed parent’s attitude towards paediatric CAM research and their willingness to participate in future safety and efficacy studies.
Part II - Hypnotherapy for children with Functional Abdominal Pain or Irritable Bowel Syndrome

Functional abdominal pain (FAP) and irritable bowel syndrome (IBS) are functional gastrointestinal disorders, both characterized by chronic abdominal pain. In Chapter 3 an overview is given of the available literature on chronic abdominal pain and more specifically on functional abdominal pain and irritable bowel syndrome. Epidemiology, pathophysiology, diagnostic work-up, therapeutic options and prognosis are being discussed.

Most patients with either functional abdominal pain or irritable bowel syndrome have spontaneous remission of their disease within one or two years, but a substantial proportion of patients continue to experience long lasting symptoms, even into adulthood. Since 1984 it is known that gut-directed hypnotherapy (HT) is highly effective in the treatment of adult IBS-patients. We undertook a randomized controlled trial and compared clinical effectiveness of HT with standard medical therapy in children with FAP or IBS. (Chapter 4)

The mechanisms by which hypnotherapy produces therapeutic effects in adults with IBS are not completely elucidated. Evidence of efficacy in the absence of a plausible explanatory scientific model however can be insufficient to change the opinions of the greater part of the medical community on the use of hypnotherapy. As such, hypnotherapy also needs to be studied mechanically. Studies in adults have suggested that gut-directed hypnotherapy impacts IBS by improvement of visceral hypersensitivity, which is thought to play a central role in IBS. We conducted a study to investigate if gut-directed hypnotherapy could influence rectal sensitivity in children with FAP or IBS. This was done by performing a rectal barostat before and after three months of therapy. (Chapter 5)

Evidence from adult literature exists that an improvement in IBS symptoms after hypnotherapy parallels improvement in psychological symptoms. We measured psychological profiles of children with FAP or IBS, by using questionnaires, filled out by parents and children. This was done before and after standard medical care and hypnotherapy. Chapter 6 describes the effect of gut-directed hypnotherapy on these psychological profiles.

Part III - Probiotics in Infant Formula

Several studies have shown that the addition of probiotics to infant formula is a way to increase the number of beneficial bacteria in the intestine in order to promote a gut flora resembling that of breastfed infants. However, it has been recommended that each infant formula with added bacteria should be marketed only if a full evaluation of benefits and safety has been performed. We undertook a randomized controlled trial, called the PINGO study (Probiotica In Neonatale Groei en Ontlasting), to evaluate the safety and
tolerance of a prebiotic-containing infant formula, supplemented with *L. paracasei* ssp. *paracasei* in combination with *B. animalis* ssp. *lactis* (also called *Bifidobacterium* Bb-12) in early infancy. The results are presented in Chapter 7. *Bifidobacterium* Bb-12 has already been studied extensively in infants. Addition of these species to regular infant feeding has been found to result in normal infant growth with an increase of the number of faecal bifidobacteria.97-100 *L. casei* CRL-431 has shown positive effects in the treatment of diarrhoea in children,101 but so far, no safety studies in infants has been performed with *L. casei* CRL-431.

The addition of probiotics to an infant formula can result in a change of the gut flora. In chapter 8 we describe the results of microbiological analysis of the stools of the infants from the PINGO study to see if significant differences could be found between the group of infants receiving probiotics and the placebo group.

This thesis ends with a summary and discussion of the results of the preceding chapters. Suggestions for future research on complementary therapies in paediatric gastroenterology are being given.
Reference List


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