Evidence-based guideline development in paediatric gastroenterology

Tabbers, M.M.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: https://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE (Digital Academic Repository)

UvA-DARE is a service provided by the library of the University of Amsterdam (http://dare.uva.nl)

Download date: 14 Jun 2020
Outline of the thesis
Outline of the thesis

Clinical practice guidelines can facilitate translation of new research findings into clinical practice and are seen as powerful tools to achieve effective care, reduce variability in daily practice, and may reduce costs. In 2000, the Dutch Paediatric Association (NVK) started with the development of paediatric guidelines. In 2007 the department of paediatric gastroenterology and nutrition of the Emma’s Children’s Hospital / AMC together with the department of general practice, Erasmus MC University Medical Centre were asked to develop a national guideline concerning constipation in children, which was at that time still lacking.

Chronic constipation in childhood has an estimated prevalence of 3% in the Western world. This debilitating condition is characterized by infrequent painful defecation, faecal incontinence, and abdominal pain. It causes distress to the child and family and can result in severe emotional disturbances, and family discord. In general, a thorough medical history and complete physical examination including a rectal digital examination, are usually sufficient to confirm the diagnosis of functional constipation. Treatment of functional constipation is mainly based on clinical experience and consists of a combination of education, toilet training and oral laxatives. However, many differences exist between all involved health care professionals with respect to diagnostic and therapeutic options.

As part of this thesis, between 2008 and 2009 a national guideline has been developed concerning paediatric constipation. During this process, we performed a study in an attempt to get more insight into the pathophysiology of constipation. Approximately 95% of children with constipation are suffering from functional constipation. In a minority of patients an organic cause can be found of which Hirschsprung’s disease (HD) is the most common gastrointestinal disorder. To discriminate between functional (constipation) and organic disease (HD) histological aspects of colonic mucosa and submucosa are often examined. Hirschsprung’s disease (HD) is a congenital disorder characterized by the absence of ganglion cells in the large bowel, leading to functional obstruction and colonic dilatation proximal to the affected segment. It is unknown if also other histological differences exist, besides the lack of ganglion cells, of the different rectal mucosal layers between children with therapy-resistant functional constipation and children with HD. In chapter 1 we report a study in which we evaluate the thickness and organization of the rectal mucosal muscle in patients with functional constipation and Hirschsprung’s disease (HD). In order to develop an evidence-based guideline, we have performed different systematic reviews concerning diagnostics and treatment which will be discussed in chapter 2,3,4,5 and 6. In chapter 2 we systematically evaluated the value of an abdominal X-ray, of the colonic transit time, using radio-opaque markers and also the value of a rectal ultrasound.
The cornerstone of the treatment of childhood constipation consists mainly of education, demystification and toilet training in combination with oral and sometimes rectal laxatives. However, these treatment strategies are rather experience based than evidence-based. In chapter 3, we evaluate and rate the available evidence with respect to the effect of dietary measures and laxatives in childhood constipation. Despite the use of intensive behaviour and laxative treatment approximately 50% of patients are difficult to treat. Consequently, non-pharmacological treatments, such as fibre, fluid, physical movement, pre-and probiotics, behavioural therapy, multidisciplinary treatment and alternative medicines (including acupuncture, homeopathy, mind-body therapy, musculoskeletal manipulations like osteopathic and chiropractic manipulations and spiritual therapies like yoga) are widely used. To evaluate the scientific strengths of these often unknown treatments we report in chapter 4 the quantity and quality of all current evidence for the effect of the non-pharmacological treatments used for childhood constipation. Chapter 5 describes a fourth systematic review, in which we also include data regarding the effectiveness and safety of anal dilatation, behavioural treatments (such as biofeedback) and surgical disimpaction. Patients in placebo arms of randomised controlled trials in a variety of disorders often experience considerable clinical improvement. In up to 30-60% of paediatric and adult patients with IBS subjective and objective improvement has been reported. Surprisingly, there is a paucity of large patient samples, placebo-controlled studies of high quality reporting the efficacy of laxative agents in paediatric and adult patients with constipation. In Chapter 6 we present a fifth systematic review concerning the effect of placebo in children with functional gastrointestinal disease including functional constipation and irritable bowel syndrome.

Probiotics are currently gaining worldwide popularity for their presumed health-promoting effects. Probiotics are defined as live micro-organisms which when administered in adequate amounts confer a health benefit on the host. However, there is a lack of trials investigating the efficacy and safety of different probiotic strains in paediatric constipated patients. To date, two randomised, placebo-controlled trials with the fermented dairy product containing *Bifidobacterium lactis* DN-173 010 have been performed in adults: one in patients with IBS and constipation, and one in constipated women with a defecation frequency <3 times/week. Both trials showed a significant increase in stool frequency in the probiotic group compared to the control group in subjects presenting less than 3 stools per week. No adverse events were reported. Based on these results in adults, we performed a randomised, double-blind, controlled multicentre trial. Chapter 7 reports the effect of this specific probiotic strain “*Bifidobacterium lactis* strain DN-173 010” in constipated children. Furthermore, a significant increase in defecation frequency was reported in constipated adults after the ingestion of a yoghurt containing *Bifidobacterium breve*, *Bifidobacterium bifidum* and *Lactobacillus acidophilus*). In chapter 8 we describe the results of a small pilot study using the *Bifidobacterium breve* in children with constipation.
The systematic reviews described in this thesis were performed during the process of the Dutch guideline development of the guideline “Constipation in children from 0-18 years”. Unfortunately, it is well known that many guidelines are not used in daily practice unless they are actively implemented. Implementation of guidelines is a great challenge because evidence about the most effective and efficient guideline implementation strategies in various different circumstances is still lacking. Furthermore, valid measurement of changes in practice due to successful implementation of clinical practice guidelines is complicated by the action of different implementation strategies at the same time. Chapter 9 describes the methodology used for implementation of another previous developed paediatric national evidence-based guideline and the success factors according to specific indicators. More importantly, general recommendations for future guideline implementation projects are given in this chapter.