OUTLINE OF THESIS

The majority of children with constipation respond well to conservative treatment, such as laxatives and behavioral therapy. But it is those children who are refractory to conventional therapy that present as a difficult group for the health care professional. In these children with refractory constipation additional diagnostic testing is validated. Colonic manometry is a method to investigate colonic motility in these children and gives diagnostic information as well as an chance to learn about the pathophysiology of constipation. New catheters give the opportunity for longer measurements that might offer additional information. This thesis focuses on the use of motility testing in this group of children, discusses potential novel therapeutic options and the cost of childhood constipation.

Due to its wide prevalence and chronic nature, it has become clear that constipation is a significant source of health care expenses and a potential target for reducing health care cost. Chapter 1 discusses healthcare utilization and healthcare cost of children with constipation in the United States using a national survey that collects data on the specific health services that people use, how frequently they use them and the cost of these services.

Colonic manometry has increased our knowledge of the pathophysiology of gastrointestinal disorders and has impacted diagnosis and treatment of chronic constipation in children. The presence of HAPCs is the key feature to differentiate normal from abnormal colonic motility. Little is known about the factors that initiate these HAPCs and how to influence them. Chapter 2 describes a study that aims to examine the role of colonic distention as a physiologic mechanism of HAPCs initiation.

There are two main methods to perform manometry studies in children with severe defecation disorders. One requires the use of water perfusion and the other uses strain-gauge pressure transducers mounted within the catheter (solid state catheter). Colonic manometry is usually performed using water perfusion but solid-state catheters have potential advantages such as the possibility for ambulatory and prolonged studies. In Chapter 3 a head-to-head comparison is made between water-perfused catheters and solid-state catheters in the detection of HAPCs. Standard testing motility testing in children with severe defecation disorders comprises of approximately 3-4 hours. Colonic motility however, shown a diurnal pattern and some motor events are infrequent and/or occur mostly at night. In Chapter 4 we performed 24 hours colonic manometry studies in children who were referred for colonic motility testing.
The prevalence of constipation seems to be higher in children who suffer from obesity compared to the general population.\textsuperscript{16, 17} These studies, however, have not used the Rome III criteria and no underlying mechanism has been established yet. The study in \textbf{Chapter 5} was designed to determine the prevalence of functional constipation in morbidly obese children according to the Rome III criteria and to evaluate whether a possible higher prevalence was due to delayed colonic motility.

As mentioned before, not all children with constipation do well with conventional treatment. \textbf{Chapter 6} discusses the currently available novel and alternative therapies that can be considered in those children. One of the potential new drug for constipation was tegaserod, a selective serotonin agonist. In \textbf{Chapter 7} a single center experience with this medicine is described. Tegaserod was pulled of the market in 2007 after retrospective analysis of data from clinical studies showed a statistically significant difference in cardiovascular ischemic events in adult patients taking the medicine compared to those on placebo. It can only now be prescribed for compassionate use.
REFERENCE LIST


7. Peppas G, Alexiou VG, Mourtzoukou E, Falagas ME. Epidemiology of constipation in Europe and Oceania: a systematic review. BMC Gastroenterol 2008;8:5.


