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Oral contrast agents for small bowel distension in MRI: influence of the osmolarity for small bowel distention

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Abstract To assess the effect of the osmolarity for small bowel distension in MRI, ten volunteers ingested at two separate occasions negative oral contrast agents with different quantity and osmolarity: (1) a water solution combined with 2.0% sorbitol and 0.2% locus bean gum (LBG) with a quantity of 1500 ml and an osmolarity of 148 mOsmol/l, (2) a water solution combined with 2.0% sorbitol and 2.0% barium sulphate with a quantity of 1000 ml and an osmolarity of 194 mOsmol/l. Small bowel distension was quantified on coronal 2D-TrueFISP images by measuring the small bowel diameters. There were no statistically significant differences in mean small bowel diameter between both contrast agents. The mean small bowel distension was 19.2 mm after ingestion of 1500 ml of sorbitol-LBG solution and 19.0 mm after ingestion of 1000-ml sorbitol–barium sulphate solution. Furthermore, all volunteers found the ingestion of 1000-ml solution more pleasant than the 1500-ml solution. The ingestion of 1000 ml of sorbitol–barium sulphate solution led to a sufficient small bowel distension compared to 1500 ml of sorbitol–LBG solution. The side effect rate of both solutions was low. Based on these data, we recommend a quantity of 1000 ml of sorbitol–barium sulphate solution as an alternative for 1500-ml sorbitol–LBG solution for optimal bowel distension.

Keywords Negative oral contrast agent · Osmolarity · Small bowel distension · MR imaging

Introduction

Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD) accounting for the main pathologies of the small bowel as malignant processes of the small bowel are rather rare [1].

Hydromagnetic resonance imaging (hydro-MRI) has replaced conventional enteroclysis (CE) in many centers worldwide and has been the imaging method of choice for the assessment of inflammatory disease of the small bowel [2]. In contrast to conventional enteroclysis hydro-MRI is a method for the distension of the small bowel based on oral administration of hyperosmolar solution and the following reduced resorption without nasoduodenal tube which leads to a strong bowel distension [3]. In addition, hydro-MRI offers the advantage of direct assessment of small bowel wall and the extramural complications of inflammatory diseases without radiation exposure [4, 5]. All these advantages lead to a high patient acceptance for the hydro-MRI examination.

It is well known that patients suffering from Crohn's disease are likely to be rather young, sick and already often have a history of bowel surgery [6–8]. Therefore, a maximum amount of 1500 ml of negative oral contrast agent which is normally given for small bowel distension in MRI [3], is too much in this patient group. However, diagnostic computed tomography scanning requires the oral ingestion of lower quantity of positive oral contrast agent with a maximum amount of 1000 ml contained iodine or barium sulphate [9].

The purpose of our study was to assess the effect of the osmolarity for small bowel distension in MR imaging in volunteers. Furthermore, the volunteer acceptance regarding side effects, quantity and taste was documented and compared.

Materials and methods

Ten healthy volunteers (four men and six women; age range 24–46 years, mean age 33) without a history of previous abdominal surgery, gastrointestinal disease or gastrointestinal symptoms such as post-prandial belching or nausea were included in this study. In accordance with the approving local institutional review board written informed consent was obtained from all subjects prior to being examined on four different occasions.

Bowel distending agent

The volunteers were examined on two separate occasions after ingestion of two different solutions of negative oral contrast agents. The interval between each examination was at least 48 h. First, the volunteers ingested a water solution as a baseline substance containing locust bean gum (LBG) with a concentration of 0.2% (Roeper, Hamburg, Germany) and 2.0% sorbitol (Merck, Darmstadt, Germany) in a quantity of 1500 ml and an osmolarity of 148 mOsmol/l. The choice of quantity and concentration of sorbitol–LBG solution was based on results of a previous study comparing additional additives of the small bowel distension in MRI [10]. In a second experiment, all volunteers ingested a water solution containing 2.0% sorbitol and 2.0% barium sulphate mixed with banana flavor and natural gum (Banana-Smoothie-Readie Cat, E-Z-Em, Westbury, NY, USA) with an osmolarity of 194 mOsmol/l at a quantity of 1000 ml. The choice of sorbitol–barium sulphate solution is based on the basis of typical amounts of barium as a positive contrast agent for computed tomography studies and the high osmolarity of this solution.

Examination protocol

To assure homogenization of bowel activity across subjects and examinations, all MR exams were performed following a fasting period: 6 h for sorbitol–LBG solution and 4 h for sorbitol–barium sulphate solution. The solutions were provided at room temperature for volunteer comfort. Prior to each examination, the respective contrast solution was orally ingested continuously at an evenly distributed rate. To ensure a consistent ingestion, volunteers were asked to drink 100–150 ml every 4 min. To enhance gastric emptying, 100 mg of erythromycin (Abbott Pharmaceutics, Wiesbaden, Germany) was administered intravenously directly following the ingestion of the first 100–150 ml of the contrast solution. Erythromycin in low doses can be used for faster emptying of the stomach [11, 12].

MR examinations were performed on a 1.5-T MR system (Magnetom Sonata, Siemens Medical Systems, Erlangen, Germany) equipped with a high-performance gradient system characterized by a maximum gradient amplitude of 40 mT/m and a slew rate of 200 mT/m/ms. For signal reception a set of two large 'flex surface coils' was used. Neither spasmolytic agents nor paramagnetic contrast compounds were applied intravenously. Coronal 2D images were collected using a fast T2-weighted steady state precession sequence (TrueFISP, TR/TE/flip 3.9/1.9/70°) each 5 min until to 30 min after contrast ingestion (0, 5, 10, 15, 20, 25 and 30). Patients were examined in the prone position, as this reduces bowel and respiratory movement, leading to higher image quality. Imaging parameters included: 35 cm field of view, 7-mm slice thickness with an intersection gap of 1 mm (25 slices), a matrix size of 144×256, and an acquisition time of 22 s. Imaging was performed under breath-hold conditions.

Data analysis

Images were quantitatively analysed independently by two radiologists, who were blinded to the quantity of oral contrast employed. The data sets were viewed and evaluated on a post-processing workstation (Virtuoso, Siemens Medical Systems, Erlangen, Germany). In a first step, the single coronal image depicting most small bowel loops was identified in consensus by both interpreters. Subsequently, each reader measured the diameters of eight small bowel loops spaced throughout the jejunum and the ileum. For the respective measurements bowel loops with maximal diameter were chosen. Thus, 16 bowel diameter measurements were obtained for each MR examination. Subsequently, a mean value for bowel distension was calculated for each individual on the basis of the 16 measurements.

For a qualitative assessment, MR images of all three examinations obtained from each volunteer were presented as hardcopies in a randomised and blinded fashion to two radiologists. These two readers had not been involved in the quantitative analysis. They were asked to rate the images regarding bowel distension in an ascending order for each volunteer. The distension was classified as follows: 0=very poor, 1=poor, 2=fair, 3=good, 4=excellent.

Side effects

Twenty-four hours after each MR exam, volunteers were questioned regarding the occurrence of side effects such as diarrhea, flatulence, vomiting or abdominal spasms. For this purpose, a standardized questionnaire was used, which was based on a four-point scale (0=no side effects, 1=mild side effects, 2=moderate side effects, 3=severe side effects). In addition, volunteers were asked about taste (0=excellent, 1=well, 2=tolerated, 3=poor) and about quantity (0=well tolerated, 1=tolerated, 2=much, 3=too much).

Statistical analysis

Mean small bowel distension values obtained for each exam were compared with respect to the given quantity using a paired *t*-test. Qualitative results concerning the grade of distension as well as the grades of discomforts were compared using the Wilcoxon rank test for each pair separately. For the adaptation to multiple samples, a Bonferroni correction was employed. For all statistical analyses, a p value< 0.05 was considered to indicate a statistically significant difference.

Results

Each contrast was ingested within the target time of 45 min for sorbitol–LBG solution and of 30 min for sorbitol–barium sulphate solution by all volunteers at all occasions. The high contrast between the bright, liquid containing small bowel lumen and the dark surrounding tissues on the TrueFISP images (Fig. 1) permitted a distinct delineation between bowel wall and bowel lumen. Quantitative comparison of the two solutions has shown no statistically differences between the two solutions (Fig. 2). The mean value of the distension for the 1500-ml sorbitol–LBG solution amounted to 19.2 mm (range of the mean values at all scanning time 20.3–16.1 mm) and 18.8 mm (range of the mean values at all scanning time 19.5–15.8 mm) for the 1000-ml sorbitol–barium sulphate solution (Fig. 3a, b). The highest small bowel distension of the 1500-ml sorbitol–LBG solution was arrived at scanning points 0 and 5 min after oral ingestion and amounted to 19.8 mm in both scanning time, however decreased to 18.7 mm at scanning point 30 min. No statistically significant difference in loop diameter was found between ileum and jejunum about the all scanning time (Fig. 4a, b). The mean loop diameter after ingestion of 1000 ml of the sorbitol–barium sulphate solution amounted to 18.5 mm at scanning point 0 min and increased of 19.3 mm at scanning point 30 min. The qualitative assessment of small bowel distension underscored the results of the quantitative evaluation. The average grade in qualitative bowel distension rating (average value across all subjects and the two readers) was 3.1 for sorbitol–LBG solution and 2.9 for sorbitol–barium sulphate solution.

All volunteers have found the ingestion of 1000-ml sorbitol–barium sulphate solution to be more pleasant than 1500-ml sorbitol–LBG solution. The side effect rate of both solutions was low. Regarding diarrhea, flatulence, vomit-

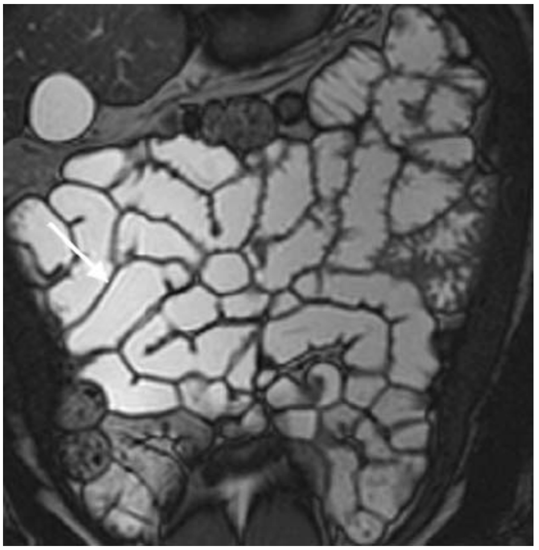

Fig. 1 2D True-FISP image after small bowel distension with 1000 ml of sorbitol–barium sulphate containing 2.0% of sorbitol as an osmotic sugar alcohol and 2.0% barium sulphate as a positive contrast agent. The bowel wall is characterized by a hypointense signal, whereas the bowel lumen (*arrow*), distended by the watery solution, exhibits a very hyperintense signal

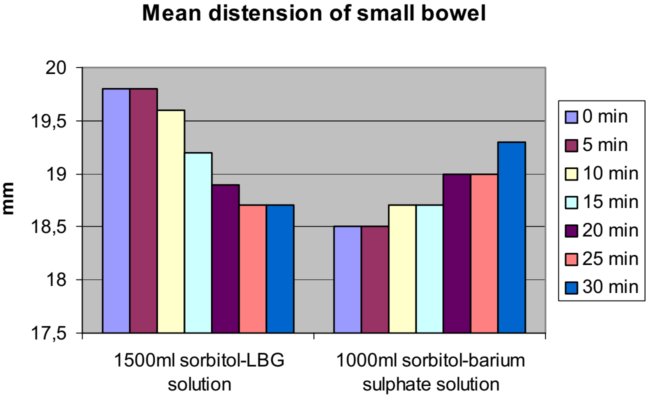

Fig. 2 Quantitative assessment of bowel distension. No statistically significant differences were found in bowel loop diameters between the two quantities (1500-ml sorbitol–LBG solution and 1000-ml sorbitol–barium sulphate)

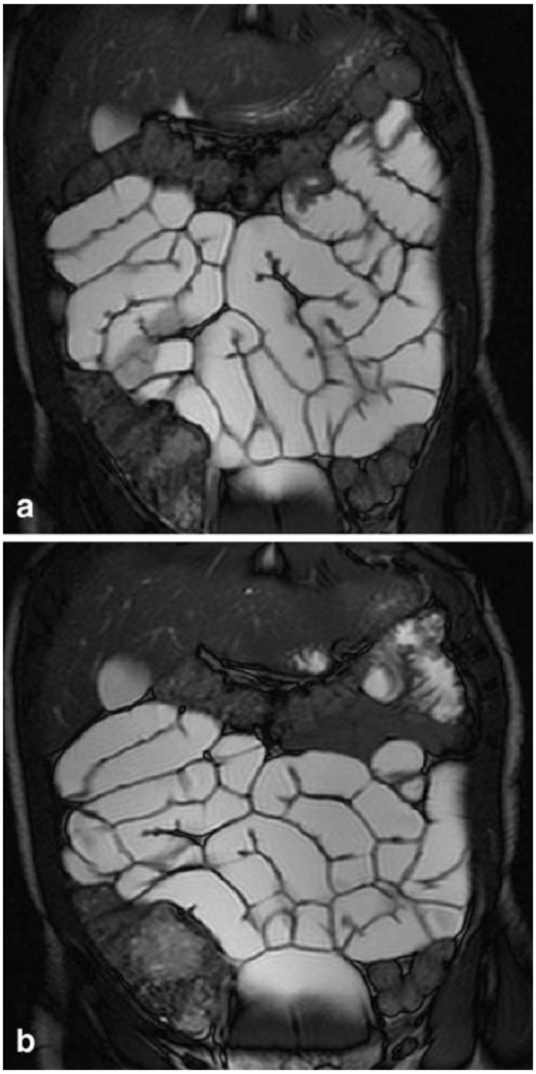

Fig. 3 a, **b** TrueFISP images of a 31-year-old female volunteer in coronal plane. The figures show a distended small bowel in the time 0 min (**a**) and 30 min (**b**) after finishing ingestion of 1500-ml sorbitol–LBG solution

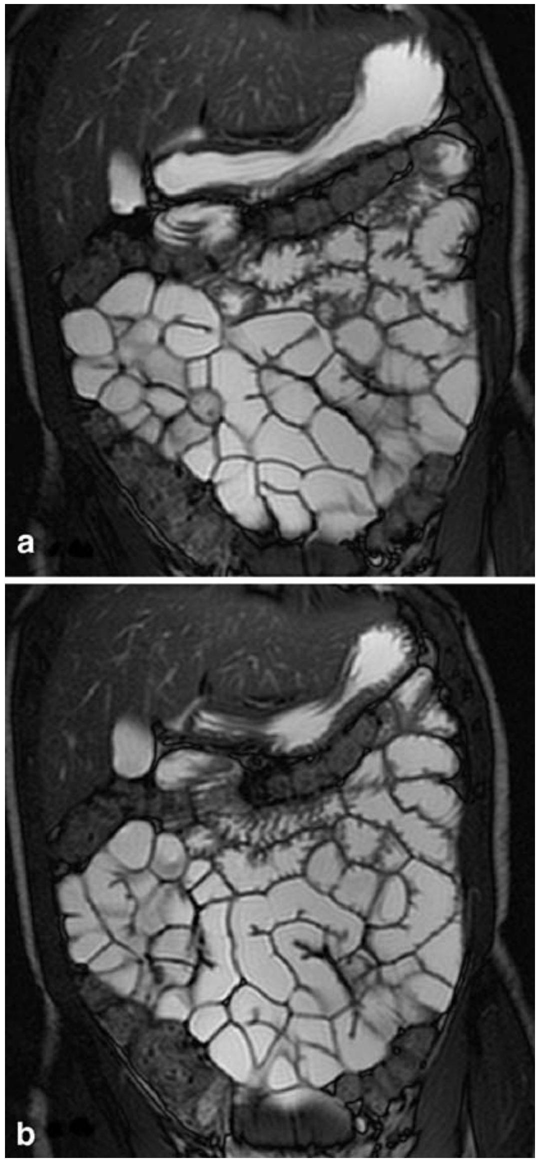

Fig. 4 a, **b** TrueFISP images of the same 31-year-old female volunteer in coronal plane. The figures show a distended small bowel in the time 0 min (**a**) and 30 min (**b**) after finishing ingestion of 1000-ml sorbitol–barium sulphate solution

ing, abdominal spasms and taste there were no statistically significant differences for both solutions (Fig. 5).

Discussion

The presented data carry three messages we believe to be important. (1) The reduce of the solution quantity of oral contrast agents is possible to achieve a sufficient small bowel distension. (2) There were no statistically significant differences in small bowel distension after an oral ingestion of 1500 ml of sorbitol–LBG solution and 1000 ml of sorbitol–barium sulphate solution. (3) The solution osmolarity plays the decisive role for small bowel distension.

A sufficient small bowel distension is essential for detection of small bowel pathologies because collapsed bowel loops can hide even large lesions or may falsely suggest the presence of pathology such as wall thickening [13–15]. The small bowel distension is based on two components: the oral ingestion of hyperosmolar solution with following reduced water absorption and the additional bowel wall secretion of water into the bowel lumen (Fig. 6a–c). Thus, the combination of hyperosmolar additives lead to high distension because of reduced absorption and high water secretion. Conventional enteroclysis (CE), the infusion of contrast medium via a nasoduodenal tube directly into the

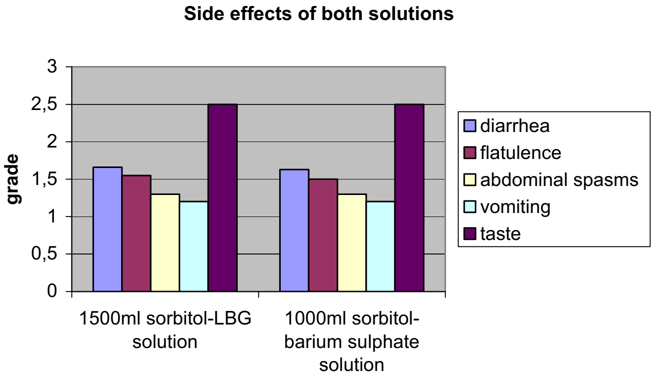

Fig. 5 Side effects of the two quantities. Primarily side effects like diarrhea, flatulence, vomiting, abdominal spasms and taste no statistically significant differences were found between the two solutions

small bowel, is a precise, rapid method for small bowel examination. CE has been effective in the detection or exclusion of small bowel disease. The main advantage of CE relates to the fact that jejunum and ileum can be readily distended. However, CE is invasive and painful, and it exposes the patient to a relatively high dose of ionizing radiation. Furthermore, it provides only indirect information on the state of the bowel wall [2, 6, 7].

The idea of using water with or without hyperosmolar additives as an oral contrast media for small bowel distension in MR imaging is not new and goes back to the end of the 1990s. Therefore, several different attempts were undertaken but after all they ended up with rather disappointing results [9, 16]. Water appears to be ideal as an MR contrast agent for the delineation of the small bowel [9, 16]. The main reason for leaking intestinal distension is rapid absorption of the ingested water due to the low osmolarity and amounts to 2 mOsmol/l (own measurement). In whole body PET/CT Antoch et al. [9] compared three patients groups each containing 20 patients after an oral ingestion of 1500-ml mannitol–LBG solution, 800-ml barium sulphate and 2000-ml tap water for the small bowel distension. In their study tap water has shown the lowest distension because of the rapid absorption. Therefore, the water absorption can be prevented by thickening the water phase with suitable agents. Thus, suitable additives preventing or at least delaying the absorption of water are desirable.

Locust bean gum (LBG) is a simple galactomannan polysaccharide derived from the endosperm of the *Ceratonia siliqua*, the European carob tree. LBG has a large hydrophilic molecule and very high water-binding capacity by means of a ‘gelling’ mechanism. Thus, a water solution containing LBG in a concentration of 0.2% has an osmolarity of 30 mOsmol/l (own measurement). It is known for its thickening properties and used in ice creams, dairy gels and canned products. In addition, LBG builds a physical barrier on the bowel mucosa and reduces stomach and small bowel peristaltic and by these means reduces the water absorption. Furthermore, LBG decreases serum lipid level. LBG dos not have any pharmacological action on its own and it reaches the colon in intact form and is eliminated with the feces [17]. LBG–water solutions are nonnutrient, colorless and tasteless. In an initial study to assess osmotic and non-osmotic additives for small distension Lauenstein et al. [3] have found that 1500 ml of 0.2% LBG–water solution led to lower small bowel distension compared to 1500 ml of 2.5% and 0.2% mannitol–LBG solution.

Sorbitol is obtained by reducing glucose, a hexose sugar. Due to their hyperosmolarity sorbitol solutions have been used for a long time for the production of sublingual pills and for osmotic therapy by head insults [17, 18]. The maximum daily dose of sorbitol is 30 g/day. A fraction of sorbitol is absorbed by the small bowel and is metabolized to fructose, lactate and pyruvate [17]. However, the main part reaches the colon where it is metabolized by the bowel flora to lactulose and consecutively to acetic acid and lactate. The latter explains the laxative effect of high doses of

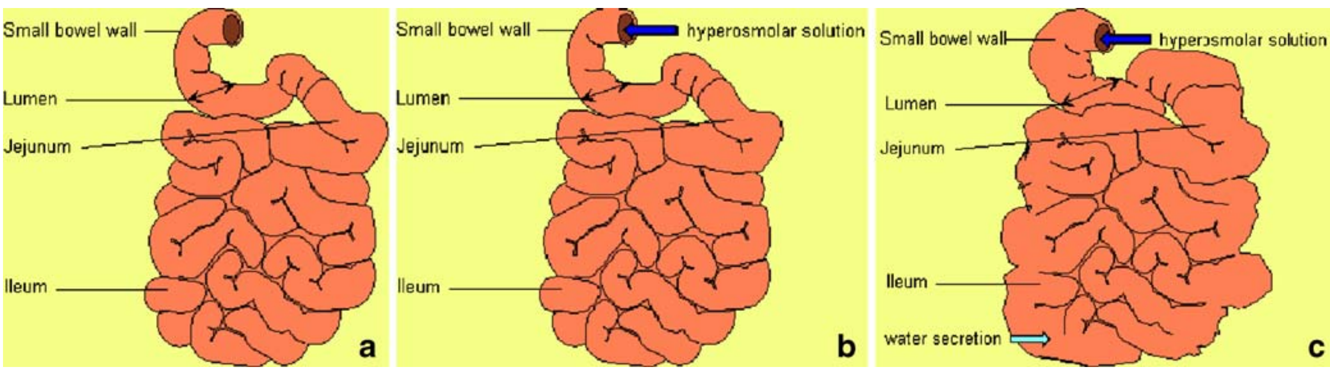

Fig. 6 a–**c** The principles of small bowel distension after ingestion of hyperosmolar solution. **a** The not distended small bowel loops prior to ingestion of an oral solution. The loop lumen distends after ingestion of hyperosmolar solution and the following reduced water absorption (**b**). The hyperosmolar solution in the bowel loops causes a water secretion in the bowel lumen. This leads to a high distension of the bowel loops (**c**) sorbitol. A rise of explosive colonic gases (hydrogen and methane) like by mannitol is not observed [17]. Throw additive of sorbitol to the LBG–water solution in a concentration of 2.0% the osmolarity increases from 30 to 148 mOsmol/l (own measurement). Ajaj et al. [10] have found in an initial study to compare different additives for the small bowel distension in MRI that there are no statistically significant differences in small bowel distension after an oral ingestion of 1500 ml of 2.5% mannitol–LBG or 2.0% sorbitol–LBG solution. However, sorbitol–LBG solutions led to lower side effects rate than mannitol–LBG solution regarding diarrhea and flatulence.

Barium sulphate is one of the most widely investigated intraluminal contrast agents and can provide good contrast of the gastrointestinal tract. Diagnostic computed tomography examinations of the intestine requires usually the oral ingestion of 1000 ml of positive contrast agent containing iodine or barium for mandatory distension of the small bowel and its delineation from surrounding tissues as well as the administration of an intravenous contrast agent for delineation of vascular structures and characterization of parenchymal alteration [9]. Barium and iodine are known to have similar atomic numbers (barium 56, iodine 53), which causes very similar linear attenuation for each substance density [19]. In addition, barium and iodine solutions as an oral contrast agent expected to have a sufficient small bowel distension by a high osmolarity. The additive of 2.0% sorbitol to barium sulphate solution leads to increase of the solution osmolarity. Thus, the water absorption will be prevented and the water secretion of the small bowel into the bowel lumen will be increased. All these leads to a high distension of the small bowel by lower solution quantity. It is known that Crohn's disease mostly affects the terminal ileum and/or the ileocecal region. Therefore, a good distension also of the terminal ileum and ileocecal region is necessary to detect inflammations in these regions [20–22]. Borthne et al. [23] examined 23 healthy volunteers using 50% gastrografin solution as an oral contrast agent with an iodine concentration of 185 mgI/ml. In this study volunteers ingested in two randomized groups 300 or 400 ml of gastrografin solution after a fasting period of 2 respectively 3 h. The small bowel distension including terminal ileum was excellent in 87–96% of cases. In addition, well distension of ascending and transverse colon was observed in 83–86% of all volunteers [23]. However, the hypertonic gastrografin led to high side effects like diarrhoea followed by nausea. A good distension of the ileocecal region leads to better visualisation of the terminal ileum [24] and its assessment regarding inflammation and the possibility to quantify the inflammation activity [25]. To improve the ileocecal region Narin et al. used an additional rectal water enema to the oral hydro-MRT containing 0.2% locus bean gum and 2.5% mannitol in patients with Crohn's disease. The oral ingestion of an oral contrast agent and the application of rectal enema did not only allow the assessment of small bowel including the ileocecal region but too the colonic segments [24].

In conclusion, the presented data indicate that no statistically significant differences in small bowel distension after an oral ingestion of 1500 ml of sorbitol–LBG solution by an osmolarity of 148 mOsmol/l and 1000 ml of sorbitol–barium sulphate solution by an osmolarity of 194 mOsmol/l. Both solutions led to a sufficient small bowel distension and the side effects rate was low. In addition, there were no statistically significant differences regarding side effects and taste. Clearly, there are limitations of the present study. First and foremost, it needs to be proven if data and results from a healthy volunteer group can be transferred to the clinical routine where patients with abdominal pathologies are examined. Thus, further studies including patients with small bowel diseases have to be performed. Based on these data, since barium sulphate is inexpensive, harmless and available in all radiologic departments, we recommend a quantity of 1000 ml of sorbitol–barium sulphate solution as an alternative for 1500-ml sorbitol–LBG solution for optimal bowel distension.

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