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Original Article

Evaluation of different small bowel contrast agents by multi - detector row CT

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Abstract: Objective: This study aims to evaluate the effects of different oral small bowel contrast agents towards the intestinal dilatation and intestinal wall structure exhibition by the abdominal multi - detector row CT (MDCT) examination. Methods: 80 patients were performed the whole abdominal CT examination, then randomly divided into four groups, with 20 patients in each group. 45 minutes before the CT examination, the patients were served with a total of 1800 ml pure water, pure milk, dilute lactulose solution and isotonic mannitol solution, respectively. Results: The images were blinded read by two experienced abdominal radiologists in the workstation, the cross-sectional diameters of duodenum, jejunum, proximal and terminal ends of ileum of each patient were measured, then the analysis of variance was performed to analyze the differences in the intestinal dilatation among the experimental groups. The scoring method was used to score the intestinal dilatation and intestinal structure exhibition. The diluted lactulose solution and 2.5% mannitol exhibited the best intestinal dilation degrees. Similarly, the diluted lactulose solution and 2.5% mannitol exhibited the highest scores in the entire small bowel dilatation degree and intestinal structure exhibition. Conclusions: 2.5% osmotic mannitol and the diluted lactulose solution enabled the full dilatation of small bowel, and could clearly exhibit the wall structure.

Keywords: Multi-slice spiral CT, small bowel, oral contrast agent, CT-enterography

Introduction

Because the small bowel was long and winding, the clinical diagnosis towards the small bowel diseases always had the great challenges. Small bowel capsule endoscopy is a fantastic way to check the small intestine recently, but the lack of imagine of outside wall, as well as capsule endoscopy detention in luminal stenosis and diverticula, the application was restricted. Propelled double-balloon endoscopy of small intestine was more complex, in which the success rate depends only on the surgeon. In the past two decades, the imaging diagnostic technology of intestinal diseases had been rapidly developed, especially with the improvements of multi - detector row CT (MDCT) technology, the CT intestinal imaging had become the front-line inspection technology towards the inflammatory bowel diseases, especially towards the clinical examination and follow-up of intestinal Crohn's disease [1-12], and it had also been widely used in the inspection of such intestinal diseases as intestinal ischemia, unexplained gastrointestinal bleeding and intestinal tumors, etc [13-20]. Intubation bolus injection of contrast CT (CT-enteroclysis), which would expand the whole small intestine uniformed, caused poor tolerance because of complex operation and time-consuming, as well as additional radiation since the catheter must be inserted under fluoroscopic from nasal to intestine. The CT enterography, which used the oral administration of neutral contrast agent combined with the intravenous iodine contrast agent, could clearly show the details of intestinal walls, because it was convenient and non - invasive, thus it was easy to be accepted by the patients and the clinicians. However, the prerequisite of a successful CT enterography was the contrast agent that could make the entire intestinal cavity exhibits the uniform dilatation consistency, as well as the good contrast between the intestinal cavity and walls, through

the oral administration. A variety of oral contrast agents had been used in the CT enterography [21-26], but the small bowel dilatation degrees and the intestinal cavity and walls contrast degrees were not entirely consistent, water should be the best oral contrast agent in gastrointestinal CT, but the absorption lasted too short to expand jejunum and ileum, only bolus injection made a good expansion in small intestine. This study aimed to evaluate the abilities of different oral contrast agents in the intestinal dilatation and intestinal wall details exhibition, thus finding a good contrast agent, with good taste, easy acceptance by the patients and easy modulation, while inexpensive and no side effects, for the CT enterography.

Materials and methods

Patients and grouping

80 patients, who were performed the whole abdominal CT examination in the Yiwu Chinese Medicine Hospital from June to Oct 2010, were collected, the patients with intestinal obstruction were excluded, including 42 males and 38 females, with the mean age as 52.65±15.56 years old. The patients were randomly divided into four groups, the purified water group, the 2.5% isotonic mannitol group (Double-Crane Pharmaceutical Co., Ltd., Anhui, 250 ml: 50 g/bottle), the pure milk group (3.5% fat content, Shanghai Bright Dairy & Food Co., Ltd.), and the lactulose group (1:30-fold dilution, Dandong Kangfu pharmaceutical Co., 10 ml/ampule), with 20 patients in each group, all the patients were administrated 250 ml 25% mannitol and 1000 ml pure water to clean the intestinal tract the night before the examination. And before the examination, the patients of each group took a total of 1800 ml pure water, pure milk, 2.5% mannitol and diluent lactulose solution, which was divided into 4 times and 450 ml/each time, the administration time was 3 minutes, with the interval as 15 minutes, and the last 450 ml was administrated 5 minutes before the CT scan, which could fill the stomach. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Zhejiang University. Written informed consent was obtained from all participants.

Scanning program

20 mg 654-2 (Koncz Pharmaceutical Co., Ltd. Wuhu 1 ml: 10 mg/ampule) was intramuscularly injected 5 minutes before the examination, followed by the abdominal plain CT scan, then 90-100 ml ioversol (350 mg/ml, 100 ml, Can) was intravenously injected for the following 25 s, 45 s, 65 s enhanced scanning. The CT machine was the SIEMENS Definition AS 20 (Germany), with the CARE DOSE 4D intelligent dose software for the scanning to reduce the radiation dose towards the patients. The scanning range was from the diaphragm top to the pubic symphysis, the scan parameters were as the follows: tube voltage 120 kV, tube current 150 mAs, tube rotation time 0.5 S, pitch 1.0, 12 mm/rotation when entering the bed, the Kernel coefficient B31 f smooth, FOV 220-300 mm, the high-pressure syringe was the LF binocular syringe (Tyco, Canada), the contrast agent was ioversol (350 gI/L), with the injection flow rate as 2.5-3.5 ml/s. the detection acquisition thickness was 0.6 mm, the reconstruction thickness was 1.5-5 mm, with the reconstruction interval as 1.5-3 mm. the enhanced scanning was divided into three phases, and the data were acquired 25 s, 45 s, 65 s after the intravenous injection of contrast image, among wherein the original images at the 45 s were sent to Siemens MMWP (multi modality workplace) for the MPR, VR and MIP reconstruction.

Measurement evaluation index

The quantitative evaluation indexes, the entire small bowel were divided into four groups, namely the duodenum, jejunum, ileum and iliac terminus, because the intestinal walls were thin, there existed some difficulties in measuring the wall thickness, so the cross-sectional diameters (wall-wall) of the 4 groups' small bowel, which had the best dilatation degree in each group, were measure in this study, and the results were recorded for the statistical analysis.

Counting evaluation indexes: two radiologists with the abdominal CT experience and more than the degree of attending physician, read the images in E-world PACS (Ningbo tomorrow technology Co. Ltd.) and obtained the consensus, it was regulated that the 0, 1, 2 and 3 points were corresponded to the entire small

Table 1. Statistical analysis of average widths of entire small bowel cavity among the 4 groups

Contrast agent	Pure water group	Pure milk group	Diluted lactulose group	2.5% mannitol group	*P*
Small bowel grouping	Bowel cavity width	Bowel cavity width	Bowel cavity width	Bowel cavity width	
Group 1	2.15±0.13	2.28±0.19	2.37±0.25	2.15±01.3	
Group 2	1.52±0.28	1.94±0.09	1.96±0.27	2.15±01.3	
Group 3	1.01±0.05	1.71±0.12	1.77±0.14	2.15±01.3	
Group 4	0.99±0.06	1.50±0.11	1.57±0.14	2.15±01.3	
Entire small bowel	1.44±0.49	1.86±0.32	1.98±0.35	1.99±0.27	
Group 1 VS group 2, 3, 4					<0.05
Group 3, 4 VS group 2					<0.05
Group 3 VS group 4					>0.05

Note: The group 1, 2, 3 and 4 were the pure water group, the pure milk group, the diluted lactulose group and the 2.5% mannitol group.

Table 2. Scoring results of entire small bowel dilation, wall structure exhibition degree and bowel wall-cavity contrast of the 4 groups

Contrast agent	Entire small bowel dilatation scoring	Wall structure exhibition degree scoring
Water	7	0
Pure milk	45	13
Lactulose	55	15
Mannitol	56	16

bowel dilatation degrees as 0 to 30%, 30-50%, 50-80% and greater than 80%. The unclear wall structure exhibition was recorded as 0 point, while 1 point for the clear exhibition. The above scoring data were performed the tabulation for the record.

Statistical methods

The width measurement data of small bowel of each group were expressed as mean ± SD, the intergroup and intragroup analysis of variance (F test) were performed, respectively, with $P<0.05$ considered as the significant difference, and the statistical software was SPSSI6.0.

Results

Dilatation indexes

The average widths of small bowel cavity of the pure water group, the pure milk group, the diluted lactulose group and the 2.5% mannitol group were 1.44±0.49, 1.86±0.32, 1.98±0.35 and 1.99±0.27, respectively, and the other three groups exhibited the statistical difference when compared with the pure water group, $P<0.05$, which were better than the pure water. The comparisons among the 2.5% mannitol group, the diluted lactulose group and the pure milk group also exhibited the statistically significant difference, $P<0.05$, the results of the 2.5% mannitol group and the diluted lactulose group were superior to the pure milk group. The comparison between the mannitol group and the lactulose group showed no significant difference, $P>0.05$ (**Table 1**).

The dilatation scores of whole small bowel

It could be seen from the scores of entire small bowel dilatation and intestinal wall structure exhibition that the pure milk group, the 2.5% mannitol group and the diluted lactulose group were higher than the pure water group, the isotonic mannitol group and the diluted lactulose group were higher than the pure milk group, while the scores of the isotonic mannitol group and the diluted lactulose group were very similar (**Table 2**). In accordance with intestinal dilation score, pure water got low score, milk was moderate and 2.5% mannitol and lactulose diluted was high (**Figure 1**).

Discussion

With the development of MDCT technology, the multi-plane reconstruction (MPR) and maximum intensity projection (MIP), as well as the volume rendering (VR) technologies, the CT-enterography had been widely used in the clinical diagnosis of small bowel diseases, especially in the recent years, the oral adminis-

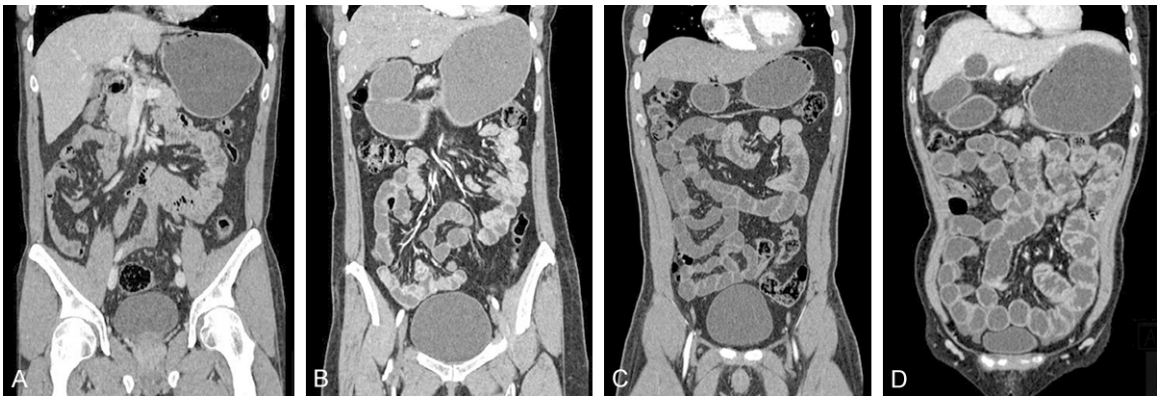

Figure 1. Pure water, pure milk, 2.5% mannitol, diluted lactulose as oral contrast agent in normal appearance of small bowel on coronal MPR CT enterography images. A. Abdominal enhanced CT coronal MPR image with pure water as the oral contrast agent, the entire small intestine was basically collapsed, difficult to distinguish the intestine-intestinal wall. B. Abdominal enhanced CT coronal MPR image with pure milk as the oral contrast agent, most small intestines expanded during the procedure, the intestine-intestinal wall could be clearly distinguished, but the dilatation degree and consistency were not enough. C. Abdominal enhanced CT coronal MPR image with 2.5% mannitol as the oral contrast agent, the entire small intestine was uniform, with good dilatation, and the intestine - intestinal wall structure was clearly shown. D. Abdominal enhanced CT coronal MPR image with the diluted lactulose as the oral contrast agent, the entire small intestine was uniform.

tration of neutral contrast agents, combined with the intravenous injection of iodinated contrast, made the CT-enterography much more wider application [22-24, 26].

In the early years, the positive contrast agent that was used to mark the small bowel for the abdominal CT examination had been less used in the clinical application for it would be easy to form the artifacts and conceal the tiny intestinal lesions, and only used to diagnose such intestinal Crohn's complications as abscess, intestinal fistula and intestinal obstruction, etc. [8, 27]. Because the positive contrast agent would not only produce the heap-like and radiation strip-like artifacts, but also be easy to miss the lesions with the enhancement of small bowel, which would reduce the density difference between the intestinal cavity and the intestinal wall.

The neutral oral contrast agents studied in this article had the CT values close to water, when filled the intestinal tract, the contrast between the intestinal cavity and the intestinal wall would be soft, without generating the volume effect-induced artifacts, thus it could not only effectively expand the intestine, clearly show the details of intestinal wall structure in the enhanced CT scanning, but also be suitable for the reconstruction of abdominal CTA and CTU, etc.

Because the pure water could be easily obtained and inexpensive, with good oral administration tolerance, thus it was used in the CT examination towards the upper gastrointestinal tract earlier than the neutral oral contrast agents, especially for the management of adhesive small bowel obstruction [28]. However, due to the rapid absorption of water by the small bowel, it would result in the reduction of intestinal contents, thus the filling degree of small bowel would be poor, so it limited the application of water as the oral contrast agent in the MDCT enteroclysis [5, 7, 26]. In order to overcome this shortage of water, the trans-nasal catheter was inserted to the duodenal-jejunal bending, and the water was rapidly bolus-injected into before the scanning, and finished the CT-enterography before the water was absorbed, so the consistent good dilatation of small bowel and clear exhibition of wall structure would be obtained. The intubation - CT-enterography needed to be performed under the fluoroscopy, with the mean time-consuming as 11.2 minutes and about 6.4 mGy fluoroscopic radiation during the small bowel catheterization procedure (range, 3.3-14.6 mGy), the abdominal MDCT examination was about 9.5 mGy, so during the catheterization process, the patients were subject to the additional radiation [23, 29]. Meanwhile, the intubation was complicated, time-consuming, and the

catheterization procedure was under the fluoroscopy, increasing the risk of ionizing radiation, and the patients' tolerability would be poor, which also limited the widespread use of this method. The results of this study showed that the oral administration of pure water as the oral contrast agent made the small bowel lack the consistency of filling dilatation, the collapsed bowel exhibited no clear structures of intestine-wall-extra-intestinal fat (**Figure 1A**), and thus it could not be used in the diagnosis of small bowel lesions.

Compared with the vegetable oil emulsions, the pure milk contained lowed fat contents, thus when it was used as the contrast agent for the CT-enterography, the patients' tolerance would be better, slowing down the small bowel movements, resulting in a better intestinal dilatation, and could clearly exhibit the intestine-wall-extra-intestinal fat. The researchers believed that using the milk as the contrast agent, the intestinal dilatation and intestinal exhibition would be less than VoLumen (a barium sulfate suspension not containing mannitol), but because it was cheap, easy to be accepted and less abdominal discomfort, it could still account for a place in the CT-enterography. In this study, 3.5%-fat milk (Shanghai Bright Dairy & Food Co., Ltd.) was selected as the oral contrast agent, the results showed that the consistency of entire small bowel dilatation was significantly better than the pure water (**Figure 1B**), and the duodenal and iliac structures could be much more clearly displayed, the intestinal dilatation degree of the pure milk group still had the significant difference with the 2.5% mannitol group and the diluted lactulose group, $P<0.05$, therefore it could be concluded that as the intestinal contrast agent, the pure milk was litter less than the 2.5% mannitol and the diluted lactulose solution in the capabilities of intestinal dilation and wall details exhibition. The study showed that milk could be used as an oral contrast agent in CT enterography, but the dilation in the proximal jejunum was showed poorly as well as the intestinal wall.

2.5% Mannitol was cheap, easily obtained and adjusted, thus it was suitable towards the CT-enterography, while the 20% mannitol solution was the hypertonic solution, after the oral administration, because of the intestinal hypertonic status, the fluids within the intestinal wall vessels was induced the extravasation, which increased the capacity of intestine, the bowel would then rapidly expand, further stimulated the intestinal wall, the nervous reflex would then accelerate the bowel movements, exhibiting the cathartic effect, so it could be used to clean the bowel before the test. However, when it was diluted to 2.5%, near the isotonic solution, it could avoid the rapid intestinal peristalsis, maintaining the liquid inside the intestine for a longer period, thus the intestinal consistent dilatation would be obtained. When intravenously injected the iodinated contrast for the MDCT scanning, the clear small bowel structure could be exhibited (**Figure 1C**). The qualitative scoring and quantitative assessment of 2.5% mannitol in the intestinal dilatation and intestinal details exhibition were significantly better than the pure water and the pure milk, and in fact was better than iodine-based contrast by producing significantly better bowel distension and visibility of mural features with improved image quality without additional adverse effects [30].

As the oral contrast agent of CT-enterography, the dilatation effect of lactulose was based on that it was the intestinal disaccharide synthesized by lactose and galactose, its inherent chemical structure enabled it not to be deteriorated and fermented in water, thus it could not be absorbed by the intestine, it could stably combine with the water molecules, thus impeding the absorption of water molecules, so that the intestine would dilate because of the agglomeration of its inside contents [23]. In this study, lactulose was diluted 1:29-fold to prepare the solution state for the MDCT angiography, the results showed that the degrees small bowel dilation and intestinal wall structure exhibition of the diluted lactulose group were better than the water group and the pure milk group, $P<0.05$, and had no significant statistical difference with the isotonic mannitol group, $P>0.05$, the qualitative score was also very close (**Figure 1D**).

As the oral contrast agent, 2.5% mannitol had no significant contraindications. In our hospital, 2.5% mannitol was used as the conventional oral contrast agent for the intestinal abdominal CT examination, and it could clearly exhibit the

wall structure. However, in the situations such as the abdominal and pelvic cystic mass and the expanded biliary tree, which were closely related with the small bowel, the distinction would be difficult, and it could not be used in the plain scanning. In the abdominal CT examination towards the appendicitis patients with aquatic body weight, it would be difficult to distinguish the expanded appendix, peri-abscess and small bowel filled with 2.5% mannitol. The improved positive contrast agent had been tried in the inspection of above lesions, though it could easily distinguish the small bowel from the other cystic lesions, it reduced the exhibition of enhanced small mucosal details. It was once reported that Volumen 26 contained a small amount of barium, the solution CT value was about 20-40HU, relatively higher water, this kind of CT value would not be too high to affect the detailed exhibition of enhanced wall structure, but it would be conducive towards the distinguish of abdominal, pelvic and retroperitoneal cystic masses from the small bowel.

The disadvantages of this research

Firstly, 2.5% mannitol and diluted lactulose solution had the good dilation and wall details display capabilities, but there was no patient with the abdominal fat, thus the abilities of small bowel dilation and details exhibition were still subject to the certain restrictions. The patients with more intra-abdominal fat could be much more clearer displayed the intestine-wall-peri-intestinal fat structures, but this study did not formally quantitatively evaluate the differences of CT-enterography in the intestine-wall-peri-intestinal fat structure exhibitions towards the patients with different body mass index.

Secondly, certain research used different intestinal motility inhibitors for the CT-Enterography and MR-Enterography examination to diagnose the small bowel Crohn's disease [31], with the equivalent diagnostic performance. In this study, 80 patients were all injected 20 mg 654-2 as the motility inhibitor, thus it was unable to evaluate its intestine dilatation degree and side effects.

Thirdly, there were more studies of low-dose CT-Enterography [32-35], this study failed to carry out the research towards the low-dose abdominal CT scan program in the conditions of reducing the radiation dose while did not affect the diagnostic imaging qualities.

Fourthly, the Crohn's disease was a chronic degenerative condition, and the patients were subject to a lifetime frequent follow-up, the MDC Enterography had the hazard of ionizing radiation, so the MR Enterography was the preferred screening method towards the follow-up of intestinal Crohn's disease, as well as the preferred method towards the examination of children's and adolescents' intestinal lesions [5, 36-38]. This article did not evaluate the values of 2.5% mannitol and diluted lactulose solution for the MR-Enterography inspection.

Conclusions

2.5% mannitol and diluted lactulose solution could make the entire small bowel exhibit the consistent dilatation, after the intravenous injection of iodine contrast, the enhanced CT scanning could clearly show the intestine-wall-extra-intestinal fat structures, the above two oral contrast agents were also suitable for the conventional s abdominal CT examination.

Disclosure of conflict of interest

None.

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