Evaluation of potential practical oral contrast agents for pediatric magnetic resonance imaging

Preliminary observations*

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Abstract. Development of a practical oral contrast agent for magnetic resonance imaging is necessary to improve differentiation of bowel from adjacent structures. In order to find a readily available, inexpensive, non-toxic, palatable solution for use in the pediatric population, several formulas, milk products and a common oral sedative were evaluated in vitro. T1, T2 and signal intensity measurements were performed on a 1.5 T system. Similac with standard iron proved to be a useful high signal intensity agent on multiple pulse sequences. Early in vivo experience in four normal volunteers indicates that this agent provides excellent delineation of the stomach and duodenum from contiguous viscera. Distal small bowel visualization is less predictable. Further clinical trials should confirm the utility of this solution, which contains a combination of iron salts and paramagnetic metallic ions.

With the evolution of abdominal magnetic resonance imaging (MRI), it has become increasingly obvious that an effective bowel contrast agent is needed. The limited tissue contrast between bowel loops and contiguous structures in the upper abdomen may pose diagnostic difficulties. Any means of differentiating the gastrointestinal tract from adjacent viscera and soft tissue masses will be clinically useful.

Early experience with MRI contrast solutions has focused on high signal intensity agents [1–3], although some recent attention has been directed toward development of low signal intensity materials [4, 5]. Many of these are not ideal because of high cost, toxicity, and adverse side effects. The purpose of this study was to perform in vitro and limited in vivo investigation of several practical, low cost, high signal intensity contrast agents. These materials were selected because of ready commercial availability and because no preparation was required.

Materials and methods

All in vitro and in vivo images were performed on a General Electric 1.5 T Signa MRI system. Images were obtained using spin-echo and gradient recalled acquisition techniques.

Sixty cc's of each of the following materials were suspended in plastic syringes: 1) Chloral hydrate suspension (commonly used sedative) in a concentration of 100 mg/cc 2) Similac with low iron (1.5 mg elemental iron/liter) (Ross Laboratories, Columbus, Ohio) 3) Similac with standard iron (12 mg elemental iron/liter) (Ross Laboratories, Columbus, Ohio) 4) Isomil with standard iron (12 mg elemental iron/liter) (Ross Laboratories, Columbus, Ohio) 5) Whole milk 6) Skim milk 7) Breast milk 8) Ice cream sediment (inert plastic used as hardening agent layered on top) 9) Tap water. The syringes were spaced 2 cm apart. A 256 x 128 pixel matrix size was utilized with 2 signal averages to obtain three 5 mm axial sections through the samples. The interslice gaps were 5 mm. Pulsing sequences included spin-echo imaging with a SE 500/20, SE 1000/20, SE 1500/20, SE 2000/20, SE 2000/40, SE 2000/60 and SE 2000/80. Within each solution central operator-selected regions of interest were then chosen, from which T1 and T2 relaxation times, and a direct measurement of signal intensity were obtained. Additionally, a gradient refocusing technique (GRASS) was utilized to obtain additional signal intensity measurements. In this particular pulse sequence, because of known clinical applicability, pa-
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Results

In vitro evaluation

The T1 and T2 relaxation times of each of the solutions are plotted in Figs. 1 and 2.

In each of the signal intensity figures the contrast materials are positioned according to Fig. 3. Direct signal intensity measurements of each of the agents are illustrated in Fig. 4–7.

In vivo evaluation

Similac with iron was selected for clinical evaluation in 4 normal volunteers, because of its high signal characteristics on multiple pulse sequences. Whole milk was evaluated as a comparison. Scans through the upper abdomen in all patients revealed excellent separation of contrast-filled stomach and duodenum from adjacent viscera following administration of oral Similac with iron. The delineation was apparent on T1, proton density, T2 and GRASS sequences (Fig. 8). No adverse effects were noted and each volunteer stated that the chocolate-flavored Similac with iron was very palatable. In contrast to the Similac with iron, whole milk did not provide high signal intensity contrast in the upper abdomen on T1 or proton density weighted images.

In the distal small bowel contrast enhancement with Similac with iron was less predictable. In the 2 patients studied, there was some differentiation of enhanced bowel from unenhanced colon on proton density and T2 weighted pulse sequences. However, the contrast was not homogenously distributed throughout the bowel and therefore, on some of the T1 weighted axial scans the enhanced small bowel could not be clearly distinguished from unenhanced colon.

Discussion

In the past, one of the limitations of abdominal MR imaging has been a lack of suitable gastrointestinal contrast material. Although investigations into some contrast agents have been performed, an ideal material has not been identified [6]. The characteristics of such an “ideal” agent should include absence of toxicity or side effects, palatability, low cost, ease of preparation and reliable bowel marking. It is uncertain as to whether the ideal contrast will provide high or low signal intensity within the bowel [4]. One of the disadvantages of the high signal intensity agents is possible obscuration of high

Fig. 1. T1 relaxation times of solutions

Fig. 2. T2 relaxation times of solutions

Fig. 3. Positions of solutions on Figures 4B to 7B

Parameters included a TE of 12 msecs, a TR of 22 msecs, and a flip angle of 15°.

Following the in vitro testing, Similac with standard iron and whole milk were given to 4 normal fasted volunteers ranging in age from 10–28 years. Spin-echo images (SE 600/20, SE 1800/20, SE 1800/80) and breath-holding gradient refocused images (22/12, -15°) were then obtained in an axial plane through the upper abdomen. The scans were obtained 5 minutes following ingestion of 500 ml of the solutions. In 2 of these patients additional scanning, through the mid-abdomen, was performed 40 minutes after ingestion. Each scan was evaluated for the quality of visualization of the upper gastrointestinal tract.