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Natural oral contrast agents for gastrointestinal magnetic resonance imaging

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ABSTRACT

Magnetic resonance imaging is an exclusive imaging method which can distinguish injured tissues from the healthy tissues or organs without using ionizing radiation. Magnetic resonance imaging is able to provide quantitative data regarding the anatomical and physiological features of each specific organ. Magnetic resonance imaging is a non-invasive method, but contrast agents are necessary to enhance the visualization of inaccessible organs in some organs such as gastrointestinal (GI) imaging. Various types of contrast agents have been used in studies including intravascular administration and oral materials. Oral contrast agents can be the artificial materials or natural factors. Natural contrast agents consist of fruit juice or pulps. Some advantages have been reported regarding the natural types of contrast agents over the artificial agents including better taste and tolerability. We briefly reviewed the different types of contrast agents and focused on the studies in which natural oral contrast agents used to investigate their efficacy in increasing the gastrointestinal magnetic resonance imaging clarity.

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Introduction

Magnetic resonance imaging (MRI) has a wide spectrum of clinical applications as an advanced imaging approach including diagnosis, staging and management of diseases because of its physical properties. In this exceptional non-invasive imaging technique, powerful magnetic fields and radio-waves are used to obtain quantitative anatomical, physiological and metabolic information of human body without applying any ionizing radiation. This is the advantage of MRI compared to other imaging modalities such as computed tomography methods. In this regard, MRI can be used in the treatment of chronic diseases and longitudinal studies. The ability of MRI in providing multiplanar 3D images with high resolution, which accurately discern soft tissues and demonstrate visually inaccessible organs, made it an exclusive imaging technique. In this study, we aim to briefly review the issue of contrast in MRI technique, especially natural oral contrast agents, which are used in gastrointestinal MRI imaging.

Literature review

Contrast agents

Density of proton spin (number of protons), longitudinal and transvers relaxation times (T1 and T2) and intensity of the magnetic field are the main variables, which regulate the contrast of the images obtained by MRI and determine the signal intensity (SI). Increased proton density and/or decreased T1 will increase the signal intensity. On the other hand, decreased proton density and/or decreased T2 will lead to decreased signal intensity (1).

MRI is an expensive technique, it is non-inva-

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sive, noticeably sensitive to tissue differences and it does not need any contrasting materials to demonstrate the vessels and flow. Sufficient contrast can be provided during imaging of healthy soft tissues due to significant difference of relaxation times. Although some unusual and inflamed tissues can be discerned from other healthy tissues due to their intrinsic differences, some pathological situations and injured tissues may not show enough changes in relaxation times (2). In these conditions, applying MRI contrast agents can locally increase the difference between relaxation times. Generally, clinical contrast agents act through shortening the tissue T1 and T2 relaxation times.

Available contrast agents are divided into different groups based on various properties including the administration methods, presence of metal center, chemical composition, magnetic features and different range of applications. MRI contrast agents can be applied intravenously or administered orally based on the targeted tissue. Intravenous administration of contrast agents is a routine method in majority of scans such as neurologic and musculoskeletal MRI imaging, extracellular mediators and blood pool agent imaging, while oral application of contrasting agents is mostly used for GI and hepatobiliary scans.

Oral contrast agents

The efficacy of abdominal MRI imaging is hindered due to various technical limitations such as artifacts caused by flow and motion including pulsatile blood flow, cerebrospinal fluid circulation, respiration, beating heart and peristalsis (3).

Difficulty of distinguishing soft injured tissue, normal organ and intra-abdominal masses from each other resulted in administration of GI contrast agents, which are divided into positive and negative contrast agents. To obtain qualified and favorable MRI images of some organs such as liver, pancreas, spleen, adrenal glands, stomach and intestines, contrast improvement is necessary, not only for visualizing the organ but also for suppressing one specific organ.

Positive oral GI contrast agents will enhance signal intensity within the bowel lumen and negative oral GI contrast agents will reduce the signal intensity within the bowel lumen. The positive contrast agents will result in bright areas in obtained T1-weighted MRI images by shortening the T1 relaxation time. Adversely, negative GI contrast agents lead to darken areas (lumen) in obtained T1- and T2-weighted images, which is due to the shortening of T2 relaxation time (4). It seems that the negative contrast agents reduce the motion artifact of images more than positive contrast agents.

Negative agents might be immiscible (only replace the bowel content) or miscible (mix with bowel content) and positive agents such as superparamagnetic agents (based on gadolinium-chelate or ferrous or manganese ions) are miscible. In this regard, the concentration of these agents might vary in different parts of GI. However, oil, fats, foods and liquid foods are immiscible and replace the bowel content. According to studies, perfluorochemicals and gases (air and carbon dioxide) are miscible types of negative agents while barium, particulate iron oxides, paramagnetic substances are immiscible ones, which replace the bowel content (3,5,6).

Several contrast agents such as clay suspensions, paramagnetic chelates and manganese chloride act as both positive and negative agents that are dependent on the pulse sequences and tend to decrease both T1 and T2; these agents are called biphasic types.

Perfluorooctyl bromide is known as the first oral contrast agents approved by the U.S. Food and Drug Administration (FDA), which is not extensively applied in clinical practices. This agent rapidly move through the GI tract without dilution and systemic absorption (7).

Based on literature, an ideal contrast agent should have some specific properties such as tolerability, availability, easily prepared, not stimulate peristalsis, homogenously distributed in GI, not absorb to the systemic circulation, stable characteristics of contrast effect, complete exertion, not associated with artifact, elevating the diagnostic sensitivity, cost effective and high safety. Generally, MRI imaging procedure is performed almost 50 minutes after oral administration of 600-900 ml (milliliter) of the oral contrast agent following at least 4 hours of fasting. In one study, intravenous application of glucagon or buscopan with negative or positive application of oral contrast agents was suggested to be the most beneficial method in increasing the imaging quality and reducing the artifacts produced by peristalsis movements (8).

In some studies, intravenous administration of gadolinium-chelate substances accompanied by the oral application of either positive or negative contrast agents was recommended to enhance the sensitivity of MRI imaging in GI, which is called double-contrast method. Performing this technique might have the most benefits during the diagnosis and staging of inflammatory or neoplastic process of bowels (9,10).

Natural oral contrast agents

Various artificial oral contrast agents (macroscopic magnetic particles) are proposed with beneficial effects in increasing the accuracy and quality of the MRI images, however there might be some associated adverse effects including toxicity, unpalatable, nausea, vomit, diarrhea, dysentery and not well tolerated by patients especially infants and small children (11).

Natural materials should be food and fruit pulps or tea, which have not shown the previous mentioned side effects. According to some reports, milk, vegetable oil, ice cream, green tea dilute with gadolinium-chelate. Blueberry juice is a natural food, which can be used for MRI imaging as positive oral contrast agents. However, application of these natural foods is not approved due to their signal intensity changes throughout the GI system (6,12-16).

Various experimental and clinical studies have been conducted to evaluate the efficacy of a variety of natural products to be used as contrast agents in increasing the quality of magnetic resonance cholangiopancreaticography (MRCP) for the evaluation of pancreaticobiliary system.

Due to the fluid collecting in stomach and duode-

Table 1. Application of natural oral contrast agent in magnetic resonance cholangiopancreaticography

Author Year Reference	**Oral contrast agent**	**MRI**	**Results**
Duarte 2012 [23]	180 ml of [1]pineapple juice with 1 ml of gadopentetate dimeglumine		Significant signal reduction of organs
Sanchez 2009 [18]	Euterpe olerácea (Acai) 200 ml per patients after 12 hours of fasting	[2]MRCP	Significant difference between signal intensity before and after the intervention (p<0.01)
Arrive 2007 [20]	[3]PJ compared with paramagnetic contrast (ferumoxsil-Lumirem)	MRCP	No significant difference between signal suppression and visualization contrast in the stomach, duodenum and proximal small bowel with PJ and ferumoxsil No significant difference in visualization contrast of pancreatic duct, intrahgepatic bile ducts and [4]CBD
Coppens 2005 [21]	180 ml of PJ/[5]Gd labeled with 1 ml of [6]Gd-DOTA	MCRP	Significant increase of complete visualization of the pancreaticobiliary ducts (p<0.01) and the MRCP image quality scores (p<0.05)
Varavithya 2005 [24]	Dry ground roselle flower (4,000 mg) in a tea bag soaked with hot distilled water (480 ml)	MRCP	Significant increase in visualization of common bile duct Significant increase of contrast-to-noise ratios
Riordan 2004 [25]	400 ml of pineapple juice	MRCP after 15 and 30 minutes following ingestion of juice	Significant improvement in the contrast after 15 and 30 minutes Significant improvement in contrast of Ampulla, CBD, [7]CHD and [8]IHD images before and 15 min after PJ administration
Ghanaati 2011 (26)	Three tea-bags of non-flavored black tea soaked in 300 mL of boiled water for 10 minutes	MRCP	Significant contrast increase of distal parts of CBD Significant reduction of signal intensity of stomach and duodenum

[1]Pineapple juice (PJ) solution labeled with a minimal gadolinium;[2]MRCP: magnetic resonance cholangiopancreatography;[3]PJ: Pineapple juice;[4]CBD: common bile duct;[5]GD: gadolinium;[6]Gd-DOTA: gadolinium- DOTA;[7]CHD: common hepatic ducts; [8]IHD: intrahepatic duct

num that reduces the clarity of pancreatic and biliary ducts, obtaining considerable images is difficult and needs contrast enhancement. In 2004, the efficacy of Euterpe Oleracea (Ac-ai) was evaluated in enhancing the contrast of GI images obtained through MRI and the content of iron, manganese, and copper were estimated as well. They showed a significant contrast enhancement by using Acai, a fruit, which is mostly found in Brazil. This natural material has shown a considerable advantage of Acai over artificial products (17). Another study demonstrated that the application of Acai could be highly effective in the diagnosis of different biliopancreatic diseases through MRCP imaging and significantly decreased overlapping of signals of the content of adjacent tissues over pancreaticobiliary tract structures (18).

Moreover, adequate dosage of blueberry juice has shown a considerable efficacy in increasing the contrast of MRI technique. Blueberry resulted in a considerable reduction of organ signals in T2-weighted images, which was due to the high concentration of manganese. Unfortunately, the natural form of blueberry is expensive with low availability that limits its application (19).

Pineapple juice (PJ) is a fruit that contains almost 2.76 mg/dl (milligram/deciliter) of manganese. It has shown that PJ had the ability to shorten the T2 relaxation time through in-vitro examination. A previous study, in 2007, showed a similar efficacy between PJ and paramagnetic materials regarding the signal suppression. Moreover, it was mentioned that different PJ available brands had variable concentrations of manganese (20). In another study, the significant efficacy of PJ labeled with gadolinium was shown to suppress the signal intensity of stomach and duodenum (21).

Based on Espinosa et al., in 2006, manganese is a responsible agent for signal reduction and PJ has also the highest amount of manganese (22). They measured the content of iron, manganese and copper in plum, blueberry, apple (red), pineapple, beet, grape, blackberry. They investigated the magnetic characteristic of these fruits pulps in vitro. They showed the efficacy of these fruits as natural oral contrast agents in MRI of GI just in one patient. They identified that iron content of these fruits were higher than the other estimated metals. According to the obtained results, blackberry had the greatest total paramagnetic metal content and the highest contrast enhancement in T1-weighted MRI images compared with other fruits. Therefore, blackberry is considered as a potential oral contrast agent (22). Table 1 summarizes the details of different studies conducted on patients undergoing MRI who consumed various natural oral contrast agents.

Conclusion

NO Adverse side effects have been reported in any of the conducted studies used natural oral contrast agents such as blueberry, mulberry, pineapple and acai juices, as well as water and tea. One important limitation of using natural materials as oral contrast agents is about their availability because some ingredients are only available in specific areas. Due to PJ availability in every region, it is studied extensively compared to other natural contrast agents.

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Conflict of Interest

The authors declare no conflict of interest.

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