Scientific Paper

Signal suppressions of grape syrup and grape syrup/lemon aqueous solutions in magnetic resonance cholangiopancreatography using heavily T2-weighted pulse sequence

Mahdi ASGARI^{1,2}, Baharak DIVBAND^{3,4}, Nahideh GHAREHAGHAJI^{2,a}

¹*Molecular Medicine Research Center, Tabriz University of Medical Sciences, Tabriz, Iran*

²*Department of Radiology, Faculty of Paramedicine, Tabriz University of Medical Sciences, Tabriz, Iran*

³*Dental and Periodontal Research Center, Tabriz University of Medical Sciences, Tabriz, Iran*

⁴*Inorganic Chemistry Department, Chemistry Faculty, University of Tabriz, C.P. 51664 Tabriz, Iran*

^a*E-mail address: gharehaghaji@tbzmed.ac.ir*

(received 12 June 2019; revised 11 August 2019; accepted 12 August 2019)

Abstract

Signal suppression of the gastrointestinal tract fluids in magnetic resonance cholangiopancreatography (MRCP) has been performed using various natural and chemical substances with the different MRCP pulse sequences. This study aimed to investigate the signal suppressions of the grape syrup and the grape syrup/lemon aqueous solutions in MRCP using the heavily T2-weighted sequences. For this purpose, the potassium, iron and manganese contents of grape syrup were measured by atomic absorption spectroscopy. The grape syrup and the grape syrup/lemon solutions with the various grape syrup percentages were imaged using the heavily T2-weighted sequences of MRCP such as T2 HASTE thick slab and T2 SPACE. MRCP in the volunteers was performed before and 10 minutes after oral administration of the grape syrup solution. The concentrations of potassium, iron, and manganese in grape syrup were 34.8, 2.4 and 1 mg/l, respectively. The in vitro study showed significantly lower signal to noise ratio using the grape syrup samples comparing to the grape syrup/lemon. The effective signal suppression for the in vitro study and considerable enhancement of negative contrast in the post-contrast MRCP was obtained using a T2 HASTE thick slab sequence. As a conclusion, the grape syrup solution can be used for signal suppression of the gastrointestinal tract fluid in MRCP as an oral negative contrast material. A T2 HASTE thick slab sequence produces suitable contrast in MRCP images using the grape syrup solution.

Key words: signal suppression; pulse sequence; MRCP; grape syrup; lemon.

Introduction

Magnetic resonance cholangiopancreatography (MRCP) is a non-invasive choice procedure for imaging the pancreatobiliary system with anatomic details and detecting different pathologies with high sensitivity and specificity [1]. It can be used as an alternative to endoscopic retrograde cholangiopancreatography (ERCP) due to its role in the detection of many biliary disorders [2].

In MRCP, stationary or slow-moving fluids, bile, and pancreatic juices produce inherent contrast and are seen as high signal regions in the heavily T2-weighted images. However, the high signals from fluids in the gastrointestinal tract and other abdominal regions can overlap with the signals of the pancreatobiliary system and influence the diagnostic value of MRCP. Although using thin slices can partially help to solve the problem, due to the duodenum proximity to the pancreatobiliary system, the high signals may be problematic

to find pathologies [1]. To overcome this condition, negative contrast agents are orally administered for fasting patients to provide the T2 shortening effect and to suppress the high signals produced by the gastrointestinal tract fluids [3]. An ideal negative oral contrast agent should be nontoxic, easily accepted by the patient, homogeneously distributed through the gastrointestinal tract, not absorbed into the adjacent tissues, inexpensive, and possessing the capability of completely excreted from the gastrointestinal tract [4].

So far, the different chemical and natural materials have been used to improve MRCP image quality. As commercial chemical products, iron oxide based ferumoxsil [5], oral gadolinium-DTPA [6,7], and ferric ammonium citrate (FerriSeltz) [8] have been used for this purpose. Although ferumoxsil - superparamagnetic iron oxide nanoparticles with siloxane coating - is widely used for MRCP, its metallic taste limits patients' acceptance for ingestion of the required amount

of the agent [3]. Natural substances are more easily accepted by patients.

Various natural substances such as pineapple juice [9], blueberry juice [10], lemon/orange juice [11], date syrup [1], Açai pulp and juice [12,13] black tea [14], and bananas [15] have been investigated for MRCP. The high concentrations of manganese and iron are responsible for the T2 shortening effect of oral negative contrast materials in MRCP [3]. In some cases such as banana, the high percentage of potassium leads to the T2 shortening effect and the subsequent signal suppression [15]. Combination of a natural substance with the gadolinium chelate has also shown efficiency for MRCP [16,17].

Carbon dioxide was introduced as a negative contrast agent for MRCP. The results of the study showed a decrease in the fluids of the antrum and the duodenal bulb, which in turn led to a decrease in the signal overlapping with the common bile duct. However, the tolerability of the bad smell and side effect of carbon dioxide made the patients uncomfortable [18].

Of various negative oral contrast agents, ferumoxsil, ferric ammonium citrate, and pineapple juice are among the most commonly used substances for MRCP [3]. However, less palatability of ferumoxsil [19], mild diarrhea with ferric ammonium citrate [8], and lower suppression of fluid signal in the gastrointestinal tract by pineapple juice comparing to ferumoxsil [1] are the problems with these contrast materials for MRCP. Therefore, investigation of the natural substances with potential for negative oral contrast agent can be conducted in order to improve the quality of MRCP images. As a low-cost substance readily acceptable by patients, grape syrup contains the T2 shortening elements such as potassium, iron, and manganese. Based on our knowledge, the capability of the grape syrup solution for signal suppression of the gastrointestinal tract fluids in MRCP has not been investigated.

The aim of this study was to investigate the in vitro signal suppression of the grape syrup solution using heavily T2-weighted pulse sequences of MRCP and to evaluate the negative contrast enhancement in MRCP of the volunteers. For this purpose, the potassium, iron and manganese contents of grape syrup were determined by atomic absorption spectroscopy. Since the previous study using lemon/orange juice [11] had shown the substance effect on dilatation of the pancreatic duct, the impact of adding lemon juice to grape syrup on the signal suppression was also investigated.

Materials and methods

Quantitative analysis of grape syrup

The measurements of potassium, iron, and manganese concentrations of the commercially available grape syrup were carried out using atomic absorption spectroscopy (Analytik Jena, novAA® 400P, Germany). A pH meter was used to measure the pH of the different percentages of the grape syrup and the grape syrup/lemon solutions.

In vitro study

The grape syrup was diluted with water to prepare 10, 20 and 30% solutions. The second series of the samples were prepared by adding 5 ml lemon juice to the grape syrup solutions. Besides, two other glass tubes were filled with water and the water/lemon juice as the control samples. All samples were placed in a glass phantom and the collection was set out in the center of the flexi large Timcoil. MRCP was performed using a 1.5 T clinical MRI scanner (Siemens, Magnetom Avanto, Germany) with the following pulse sequences and the imaging parameters:

- The T2-weighted “Half Acquisition Single-shot Turbo spin Echo” (T2 HASTE) with thick slab: TR = 6000 ms, TE = 757 ms, flip angle = 150°, average = 1, turbo factor = 269, slice thickness = 40 mm, FOV read = 350 and FOV phase = 100%.
- The T2-weighted “Sampling Perfection with Application optimized Contrasts using different flip angle Evolution” (T2 SPACE) 3d iso trigate: TR = 2500 ms, TE = 707 ms, flip angle = 140°, average = 1.4, turbo factor = 245, slice thickness = 1 mm, FOV read = 380 and FOV phase = 100%.

The images were prepared in a coronal orientation with an iPAT of GRAPPA accel factor of 2 (pe = 2).

The signal intensities were measured by placing a circular region of interest (ROI) over the samples of each image using a Siemens workspace. The standard deviation of the background noise was obtained from the average signals of the three circular ROIs in the background. The signal to noise ratio (SNR) was calculated by dividing the mean signal to the standard deviation of the background noise.

Statistical analysis

SPSS software (version 18) was used for the statistical analysis. The mean and the standard deviation of the measured SNRs were calculated. The normality of the grape syrup and the grape syrup/lemon groups was considered using a Kolmogorov-Smirnov test. A parametric independent t-test was conducted for the data that follow a normal distribution; otherwise, a Mann-Whitney nonparametric t-test would be used to determine the statistical difference between the two groups. The difference with p-value < 0.05 was considered significant.

MRCP in volunteers

The healthy volunteers including one female and two males were referred for MRCP with a 30% grape syrup solution. There was no history of diabetes mellitus and gastrointestinal diseases. A pre-contrast MRCP was performed in fasting status with similar pulse sequences and imaging parameters of the in vitro study using the same MR scanner. For preparing the T2 HASTE thick slab images, the coronal oblique planes were arranged on the axial section so that they radiated from an anterior aspect of the portal vein bifurcation. Additionally, the images were acquired during breath-hold with 12 radial 40

mm/15° slabs. Respiratory gating was used for preparing the T2 SPACE images.

The post-contrast MRCP images were acquired 10 minutes after oral administration of 100 ml of grape syrup 30% solution. The circular ROIs were drawn on the stomach and the adjacent soft tissue in the pre- and post-contrast images. Then the three other ROIs were drawn on each image background to determine the standard deviation of the noise. The SNR of the ROIs were calculated and the CNR amounts for the stomach and the adjacent soft tissue in the pre- and post-contrast images were obtained from the differences between the SNRs.

Results and discussion

Quantitative analysis of grape syrup

The potassium, iron and manganese concentrations in the grape syrup solution were 34.8, 2.4 and 1 mg/l, respectively. The results showed potassium is the main T2 shortening element in the grape syrup solution. In the study of Mikkelsen et al. [15], the high amount of potassium in banana was also the factor for T2 shortening in MRCP.

Adding 5 ml lemon juice to the grape syrup solution 10, 20 and 30% was led to pH reduction of 20.78, 20.44 and 20.29%, respectively, compared with the similar grape syrup contents.

In vitro study

For both series of the grape syrup and the grape syrup/lemon samples, decreasing the signal intensity as a function of the grape syrup percentage was seen in the images acquired with both sequences. **Figure 1** shows the image prepared by use of a T2 HASTE thick slab pulse sequence. The most pronounced T2 shortening effect and consequently the darkest areas of the contrast distribution were seen in the samples with the highest grape syrup percentage. This is due to the increasing contents of potassium, iron, and manganese in the samples with an increasing percentage of grape syrup. This, in turn, enhances the T2 relaxation and leads to signal suppression.

The comparison between the signal intensity of water and the water/lemon samples showed a slight signal change for the water/lemon. The grape syrup and the grape syrup/lemon samples showed a significantly lower signal than those of water and the water/lemon juice, respectively. However, in the similar grape syrup percentages, the signal suppression (image darkness) for the grape syrup samples was much higher than that of the grape syrup/lemon (**Figure 1**). Lemon juice contains a little amount of iron which is in ion form due to the acidic property. Hence, the water/lemon solution shows only a slight signal change comparing to that of water. On the other hand, heating grape syrup during preparation process leads to the production of the oxide form of the potassium, manganese, and iron. Therefore, the susceptibility effect and the T2 shortening appear in the T2-weighted images. Adding lemon juice to the grape syrup solution leads to the reduction in pH, which results in the conversion of some of the magnetic oxides into ionic

forms. The process which in turn reduces the magnetic susceptibility. Therefore, in similar grape syrup percentages, the grape syrup/lemon solutions produce lower signal suppression than what grape syrup does.

The SNR of grape syrup, the grape syrup/lemon, and the control samples for both heavily T2-weighted sequences is demonstrated in **Figure 2**. The grape syrup/lemon samples showed significantly higher SNR for both sequences ($p < 0.05$) especially for the T2 HASTE thick slab in similar grape syrup percentages. Besides, the T2 HASTE thick slab showed a higher SNR than the T2 SPACE in all samples. This finding is related to each pulse sequence properties and the imaging parameters. The main factor which causes the high SNR difference between the two sequences is a very thick slice thickness (40 mm) of the T2 HASTE thick slab. Moreover, this sequence as a heavily T2 pulse sequence uses a high TR and TE. The high TR increases the SNR while the high TE decreases the signal intensity. However, a high TR has a dominant effect on the SNR. Although the T2 SPACE is also a heavily T2 pulse sequence, the lower TR leads to the lower SNR than that of the T2 HASTE thick slab. Using thin slices (1 mm) in this sequence is another factor which affects the SNR.

Figure 1. Image of the different percentages of the grape syrup and the grape syrup/lemon solutions prepared using the T2 HASTE thick slab pulse sequence. The grape syrup solutions are seen darker than the grape syrup/lemon samples in similar percentages.

Figure 2. SNR of the grape syrup and the grape syrup/lemon solutions (10, 20 and 30%), and the control samples

As it is seen in **Figure 2**, despite the high signal of the T2 HASTE thick slab, the SNR of the samples were dramatically dropped comparing to the control samples so that the signal suppressions for the grape syrup 30% and the grape syrup 30%/lemon solutions were 96.43% and 77.51%, respectively. For the T2 SPACE sequence, the signal changes from the lowest to the highest percentages of grape syrup were 93.10% and 66.53% for the grape syrup 30% and the grape syrup 30%/lemon solutions, respectively. The results revealed more effective signal suppression using the T2 HASTE thick slab than the T2 SPACE sequence.

Most studies in the field of new MRCP contrast agents have been focused on the clinical aspects of using the agent in MRCP procedure. However, there are a few in vitro studies which can be comparable with the results of the present study. In the study by Govindarajan et al. [1] with date syrup, despite the higher T2 effect resulted from the imaging parameters of the single-shot radial sequence, the SNR change of date syrup relative to water is similar to the signal suppression by grape syrup 30% for both sequences in our study. The finding shows the high efficiency of grape syrup for contrast-enhanced MRCP. Moreover, the results of the present study for grape syrup 20% and the T2 HASTE thick slab sequence is comparable with the study using FerriSeltz (a contrast agent containing ferric ammonium citrate) and the single-shot fast inversion recovery (SSFIR) pulse sequence at an inversion time of 150 ms [8].

MRCP in volunteers

Figure 3A and **3B** show the pre- and post-contrast MRCP images prepared with the T2 HASTE thick slab. The pre-contrast image (**Figure 3A**) shows high signal region in the fundus of the stomach that was suppressed following consumption of the grape syrup solution (**Figure 3B**). The pre- and post-contrast MRCP images for the T2 SPACE sequence are shown in **Figure 3C** and **3D**. The signal voiding in the gastric folds is seen in the post-contrast image (**Figure 3D**). The differences in the contrast between the various regions depended on the times of imaging for the sequences used. The preparation of a thick slab image is a time-consuming procedure during which the grape syrup solution is replaced from the stomach while a little amount of it still remains in the gastric folds. Therefore, fewer signal suppressions are observed when the T2 SPACE sequence is performed.

Although signal suppression in the duodenum was not completely captured in this study due to the limitation of volunteers' numbers, the observation of signal loss in the stomach confirmed the capability of grape syrup for suppressing the signal from the gastrointestinal tract fluids.

Since the fat content in grape syrup is low, the peristaltic reactions did not occur during contrast-enhanced MRCP which confirms another advantage of grape syrup for MRCP. No adverse reactions were recorded during and after the examination. However, application of the grape syrup solution is limited in diabetic patients.

Figure 3. Pre- and post-contrast MRCP images prepared with the T2 HASTE thick slab (A and B), and the T2 SPACE (C and D). The signal suppressions in the fundus of the stomach (B) and the gastric folds (D) are seen in the post-contrast images.

Figure 4 shows the CNR between the stomach and the adjacent soft tissue using the T2 HASTE thick slab and the T2 SPACE sequences for the pre- and post-contrast images. Comparing the two sequences showed a considerable CNR difference between the pre- and post-contrast images using the T2 HASTE thick slab. The adjacent soft tissue showed a low SNR in the heavily T2-weighted images indicating a short T2 relaxation time. The SNR of the adjacent soft tissue did not change in the pre- and post-contrast images for each one of the sequences, but it was higher for the T2 SPACE due to the lower T2 effect. The high SNR was measured for the stomach in the pre-contrast images for both sequences because of its fluid content which has a long T2 relaxation time. Despite the strong T2 effect of the T2 HASTE thick slab, the 40 mm slab led to a higher SNR for this sequence. Therefore, a high CNR was calculated between the stomach and the adjacent soft tissue for the pre-contrast T2 HASTE thick slab. On the other hand, the sequence showed significant SNR reduction for the stomach in the post-contrast images so that a considerable drop of CNR has occurred. This finding is related to the presence of grape syrup as a T2 oral contrast agent in the stomach and heavily T2 effect of the T2 HASTE thick slab that strongly suppress the stomach fluids signal and reduce the SNR changes between the stomach and the adjacent soft tissue. Although the CNR decrease was also seen for the post-contrast T2 SPACE images, it was much lower than that of the T2 HASTE thick slab (38% CNR reduction for the T2 SPACE versus 88% for the T2 HASTE thick slab). These findings show a significant effect of the T2 HASTE thick slab sequence on the signal suppression and the contrast improvement in MRCP.

MRCP images have been acquired using different pulse sequences in different studies [2,20,21]. In the present study, T2 HASTE thick slab and T2 SPACE were used as heavily T2-weighted sequences for the investigation of the signal suppression resulted from the grape syrup solution. This selection was based on the advantages of each sequence. T2 HASTE thick slab benefits from a very strong T2 effect which produces a suitable signal suppression for MRCP. Depiction of the entire pancreatobiliary system is possible with this sequence and image post-processing is not required [2]. On the other hand, since the sequence is performed during breath-hold, it is problematic for uncooperative patients [22]. However, respiratory gating in T2 SPACE sequence can solve the problem. In spite of using thin slices in T2 SPACE, 3D technique leads to high SNR of the images. Besides, using isotropic voxels for image acquiring provides image post-processing with multi-planar reconstruction (MPR) and maximum intensity projection (MIP) [2]. Another advantage of T2 SPACE is a high spatial resolution of the images due to low slice thickness.

Figure 4. CNR of the pre- and post-contrast images for the stomach and the adjacent soft tissue using the T2 HASTE thick slab and the T2 SPACE sequences

Conclusions

In this study, the signal suppressions in MRCP caused by the grape syrup and the grape syrup/lemon solutions were investigated in vitro and in volunteers. The T2-weighted MRCP sequences, such as T2 HASTE thick slab and T2 SPACE were used. As revealed from the in vitro results, the magnetic resonance signal suppression was higher for the higher grape syrup percentages. The effect was stronger for the T2 HASTE thick slab sequence. The grape syrup/lemon solutions showed much lower signal suppression than that of the grape syrup. The results of MRCP in the volunteers revealed a strong signal suppression in the post-contrast images, especially for the T2 HASTE thick slab. This sequence also showed a considerable CNR difference between the stomach and the adjacent soft tissue in the pre- and post-contrast images. This study suggests that the grape syrup solution can be used as an oral negative contrast material for MRCP. Since the study was focused on the image quality aspects of the heavily T2-weighted pulse sequences of MRCP, further investigations with the grape syrup solution in the high number of volunteers and then in patients can be done.

Acknowledgments

This study was conducted as MSc thesis and financially supported by Molecular Medicine Research Center, Tabriz University of Medical Sciences (Grant number: 1397.180).

References

- [1] Govindarajan A, Lakshmanan PM, Sarawagi R, Prabhakaran V. Evaluation of date syrup as an oral negative contrast agent for MRCP. *Am J Roentgenol*. 2014;203(5):1001-1005.
- [2] Griffin N, Charles-Edwards G, Grant LA. Magnetic resonance cholangiopancreatography: the ABC of MRCP. *Insights Imaging*. 2012;3(1):11-21.
- [3] Frisch A, Walter TC, Hamm B, Denecke T. Efficacy of oral contrast agents for upper gastrointestinal signal suppression in MRCP: A systematic review of the literature. *Acta Radiol Open*. 2017;6(9):1-7.
- [4] Giovagnoni A, Fabbri A, Maccioni F. Oral contrast agents in MRI of the gastrointestinal tract. *Abdom Imaging*. 2002;27(4):367-375.
- [5] Chavhan GB, Babyn PS, Manson D, Vidarsson L. Pediatric MR cholangiopancreatography: principles, technique, and clinical applications. *Radiographics*. 2008;28(7):1951-1962.
- [6] Chan JHM, Tsui EYK, Yuen MK, et al. Gadopentetate dimeglumine as an oral negative gastrointestinal contrast agent for MRCP. *Abdom Imaging*. 2000;25(4):405-408.
- [7] Gong J, Zhao H, Liu T, et al. Value of MRCP using oral Gd-DTPA as negative contrast materials in diagnosis of atypical juxtaepapillary duodenal diverticulum. *Clin Imag*. 2009;33(5):361-364.
- [8] Kato J, Kawamura Y, Watanabe T, et al. Examination of intra-gastrointestinal tract signal elimination in MRCP: Combined use of T1-shortening positive contrast agent and single-shot fast inversion recovery. *J Magn Reson Imaging*. 2001;13(5):738-743.
- [9] Riordan RD, Khonsari M, Jeffries J, et al. Pineapple juice as a negative oral contrast agent in magnetic resonance cholangiopancreatography: a preliminary evaluation. *Br J Radiol*. 2004;77(924):991-999.
- [10] Papanikolaou N, Karantanas A, Maris T, Gourtsoyiannis N. MR cholangiopancreatography before and after oral blueberry juice administration. *J Comput Assist Tomogr*. 2000;24(2):229-234.
- [11] Chu ZQ, Ji Q, Zhang JL. Orally administered lemon/orange juice improved MRCP imaging of pancreatic ducts. *Abdom Imaging*. 2010;35(3):367-371.
- [12] Sanchez TA, Elias Jr J, Colnago LA, et al. Clinical feasibility of Acai (*Euterpe oleracea*) pulp as an oral contrast agent for magnetic resonance cholangiopancreatography. *J Comput Assist Tomogr*. 2009;33(5):666-671.
- [13] Pinho KEP, Pinho AC, Pisani JC, et al. Açai juice as contrast agent in MRCP exams: qualitative and quantitative image evaluation. *Braz Arch Biol Technol*. 2019;62:e19160697.
- [14] Ghanaati H, Rokni-Yazdi H, Jalali AH, et al. Improvement of MR cholangiopancreatography (MRCP) images after black tea consumption. *Eur Radiol*. 2011;21(12):2551-2557.
- [15] Mikkelsen D, Watson J, Vallø J. The use of banana in MRCP. *Acta Radiol*. 2005;46(2):215-216.
- [16] Coppens E, Metens T, Winant C, Matos C. Pineapple juice labeled with gadolinium: a convenient oral contrast for magnetic resonance cholangiopancreatography. *Eur Radiol*. 2005;15(10):2122-2129.
- [17] Duarte JA, Furtado AP, Marroni CA. Use of pineapple juice with gadopentetate dimeglumine as a negative oral contrast for magnetic resonance cholangiopancreatography: a multicentric study. *Abdom Imaging*. 2012;37(3):447-456.
- [18] Chen CW, Liu YS, Chen CY, et al. Use of carbon dioxide as negative contrast agent for magnetic resonance cholangiopancreatography. *World J Radiol*. 2011;3(2):47-50.
- [19] Bittman ME, Callahan MJ. The effective use of acai juice, blueberry juice and pineapple juice as negative contrast agents for magnetic resonance cholangiopancreatography in children. *Pediatr Radiol*. 2014;44(7):883-887.
- [20] Kinner S, Dechêne A, Ladd SC, et al. Comparison of different MRCP techniques for the depiction of biliary complications after liver transplantation. *Eur Radiol*. 2010;20(7):1749-1756.
- [21] Nakaura T, Kidoh M, Maruyama N, et al. Usefulness of the SPACE pulse sequence at 1.5 T MR cholangiography: Comparison of image quality and image acquisition time with conventional 3D-TSE sequence. *J Magn Reson Imaging*. 2013;38(5):1014-1019.
- [22] Kim JH, Hong SS, Eun HW, et al. Clinical usefulness of free-breathing navigator-triggered 3D MRCP in non-cooperative patients: comparison with conventional breath-hold 2D MRCP. *Eur J Radiol*. 2012;81(4):e513-518.