The Efficacy of Roselle (Hibicus Sabdariffa Linn.) Flower Tea as Oral Negative Contrast Agent for MRCP Study

Vithya Varavithya, MD*, Sith Phongkitkarun, MD**
Janjira Jatchavala, MD**, Supap Ngeonthom***,
Wutthi Sumetchotimaytha, MD****, Vichit Leelasithorn, MD*

** Department of Radiology, Faculty of Medicine, Srinakharinwirot University, Nakhon-Nayok*
*** Department of Radiology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University*
**** Prachachuen Imaging Center*
***** Section of Surgery, National Cancer Institute*

Objective: *To evaluate the efficacy of roselle flower tea (RFT) administration as oral negative contrast agent for MRCP study.*
Material and Method: *Roselle flower tea was prepared by packing 4,000 mg of dry ground roselle flower in a tea bag and soaked with 480 ml of hot distilled water. RFT was tested in phantom, volunteer subjects and was studied in patients for MRCP study. Quanlitative analysis was made by evaluation of the conspicuity of biliary system after RFT administration. Quantitative comparison was performed by comparing the contrast-to-noise ratio between each part of the biliary system with stomach and duodenum.*
Results: *Roselle flower tea can effectively reduce signal intensity of the stomach and duodenum. There was statistically significant ($p < 0.05$) improvement in conspicuity of the common bile duct. There was slight improvement of conspicuity of common hepatic duct, ampulla and main pancreatic duct. Contrast-to-noise ratios were all statistically significantly improved. RFT contains 0.6 mg of iron and 1.28 mg of manganese content.*
Conclusion: *Roselle flower tea is a very efficient oral negative contrast agent. It is natural, safe, inexpensive and palatable for oral administration.*

Keywords: *MRCP, Oral negative, Hetatobiliary*

J Med Assoc Thai 2005; 88(Suppl 1): S35-41
Full text. e-Journal: *http://www.medassocthai.org/journal*

Magnetic resonance cholangiopancreaticography (MRCP) is a noninvasive technique to evaluate pancreaticobiliary system. The recent development of fast 2D and 3D MRI technique, half-Fourier turbo spin echo (HASTE), provide promising image quality by minimized motion and respiratory artifact. Unfortunately, even though the scan technique has been improved, there is still a recognized limitation. The pancreaticobiliary system is usually obscured by residual high signal fluid in the stomach and small bowel. This artifact does frequently happen even in patients with adequate fasting period. This problem can be solved by using an oral negative contrast agent[1-3]. The agents, which have a high component of high molecular metal ion such as iron and manganese, will shorten T2 relaxation time of water and null bright, unwanted water signal[4,5]. Blueberry juice has been tested to be an effective oral negative contrast agent for MRCP study[3]. Roselle (Hibiscus sabdariffa Linn.) has been known as food, dye and herbal beverage in many countries. Because of its high mineral content, roselle has been on trial for treatment of a variety of diseases including hypertension and renal calculus[6,7]. The purpose of the present study was to investigate the efficacy of

Correspondence to : Varavithya V, Department of Radiology, Faculty of Medicine, Srinakharinwirot University, Nakhon-Nayok 26120, Thailand.

roselle flower tea as an oral negative contrast agent for MRCP study.

Material and Method

The study was divided into 3 parts; phantom study, volunteer human study and clinical study. All MR images were obtained with a 1.5 T MR machine (Magnetom Symphony; Siemens, Erlangen, Germany) with body phased array, multi-channel coil. Maximum gradient was 30 mT/m. Slew rate was 125 mT/m/s. MRCP was performed with half-Fourier acquisition single-shot turbo spin-echo (HASTE) sequence using multicoronal oblique projection along the pancreaticobiliary tract anatomy. The parameters were used as follows: Repetition time (TR), infinity; effective echo time (TE), 800-1000 ms; number of excitations, 0.5; matrix size, 256 x 256; field of view, 35 x 35. No fat saturation technique was applied. Slap thickness was 30-60 mm and acquisition time for each slap was 5 seconds. All images were acquired during inspiration. Overlapping anatomy by fluid containing structure, such as kidney and cerebrospinal fluid, were reduced by using various projections.

1. Phantom study

The phantom study was performed to select optimal concentration of roselle flower tea (RFT). RFT was prepared by packing 1,000 mg of dry ground roselle flower in a small tea bag. Phantom was composed of 6 plastic tubes (volume 20 ml) (Fig. 1). One bag of dry roselle flower was soaked with 240 ml of hot distilled water for 5 minutes. Ten milliliters of this RFT was filled in one tube. The other 4 tubes were filled with diluted RFT in different concentrations as follows; 80%, 60%, 40% and 20%. The last tube was filled with distilled water and acted as a control tube. All 6 tubes were scanned by using a head coil and HASTE technique with TE of 1000. Subsequently, the study was repeated with the same technique but with a different TE value at 500 and 300 ms to determine the effect of echo time on the RFT.

Signal intensity in each tube was measured and compared with background noise. Signal intensity of the tube with 100% RFT appeared equal to background noise in the standard MRCP technique (TE = 1000). Other tubes showed increased signal intensity as the concentration reduced (Fig. 2). When TE was decreased, all tubes showed slightly increased signal intensity. The authors concluded that the optimal concentration should be at least equal to 100% RFT (1 roselle flower tea bag in 240 ml of distilled water). This concentration was selected for clinical study.

Dry ground roselle flower was sent to the Laboratory of the Department of Chemical Engineering, King Mongkut's University of Technology Thonburi for iron and manganese content analysis by atomic absorption spectrophotometer.

2. Volunteer subjects

The purpose of volunteer subjects examination was to determine the optimal delay time between the RFT consumption and MRCP study. Because patients usually have preexisting fluid content in the stomach and duodenum, the RFT might be diluted and lose its property. The average adult stomach has a capacity of about 1,500 ml, the authors decided to increase the concentration and volume of the RFT to 4 bags (4,000 mg) soaked with 480 ml of distilled water[8]. Precontrast images were obtained before the RFT was administered to evaluate pre-existing fluid content in the stomach and duodenum. Subsequently, 480 mL of the RFT was given to volunteers orally through a straw to prevent alteration of the patient's position. MRCP studies were performed at 5, 10 and 15 minutes delayed time after consumption. The images were reviewed and showed that after 5 minutes, the RFT could eliminate most of the high fluid signal in the stomach and duodenum. There was no significant difference in images at 5, 10 and 15 minutes scan. Therefore, 5 minutes delayed time was selected for clinical study.

3. Patients study

There were 19 consecutive patients enrolled in the present study (13 male, 6 female, mean age = 54.5 years). All patients were suspected to have pancreaticobiliary diseases. Written consent was obtained from all patients. MRCP was performed with and without oral RFT administration and the data were recorded on a compact disc in Dicom format for analysis.

Statistic analysis

Qualitative analysis

The images were reviewed by 2 radiologists independently in computer without clinical history or other imaging findings. Pre and post RFT MRCP images were displayed side by side. The pancreaticobiliary system was divided into 7 segments; gallbladder (GB), cystic duct (CD), common bile duct (CBD), common hepatic duct (CHD), intrahepatic duct (IHD), ampulla and main pancreatic duct (MPD).

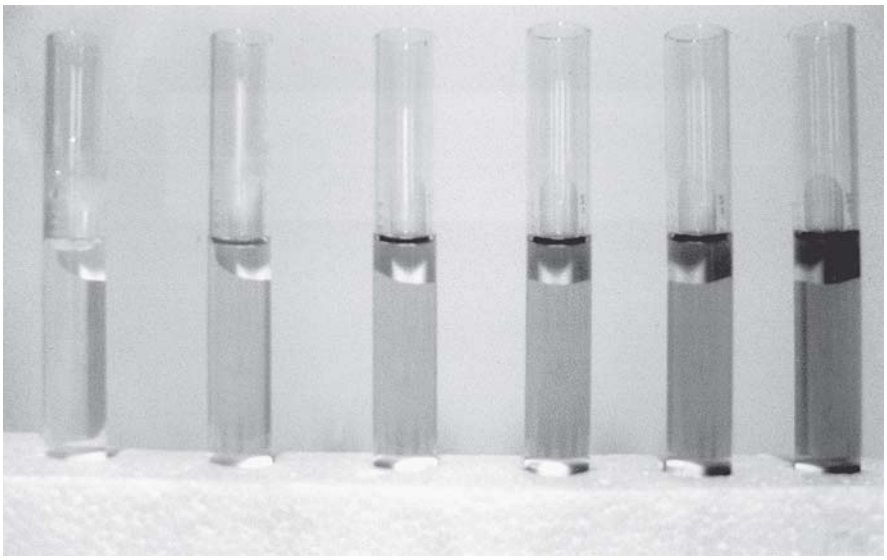

Fig. 1 Roselle flower tea (RFT) phantom. The far right tube is 100% concentration of RFT. The far left tube is distilled water. Other 4 tubes are RFA with diluted concentration of 80%, 60%, 40% and 20% from right to left, repectively

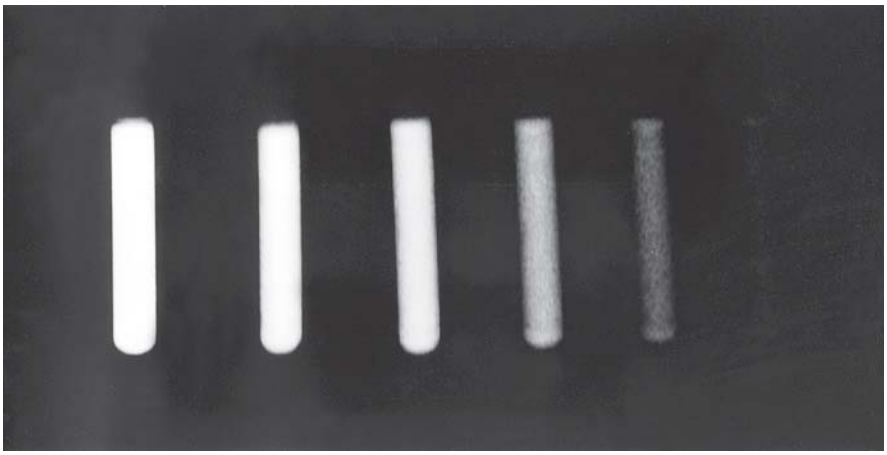

Fig. 2 Roselle flower tea (RFT) phantom was scanned with standard MRCP technique and showed that signal intensity of the tube with 100% RFT concentration appeared equal to the background noise. Other tubes shows increased signal intensity as the concentration reduced

The radiologists accessed the visualization of each segments in both pre and post RFT examination by using the 4 points scale: grade 0 = poor (anatomy was difficult to detect or no visualization of the segment); grade 1 = fair (anatomy was partly obscured); 2 = good (anatomy was well visualized with minimal obscuration); 3 = excellent (excellent depiction of anatomical structure).

All information was recorded on information data sheets for statistical analysis. If results from both radiologists were different in more than 1 point scale, the images were retrospectively reviewed and the final assessments were made by consensus.

Quantitative analysis

Signal intensity of CBD, CHD, MPD, GB, stomach, and duodenum was measured by placing spherical, 2 cm^2, region-of-interest (ROI) over these structures. The background noise was measured by placing the same size of ROI over the air outside the

human body. Contrast-to-noise ratio (CNR) between CBD and duodenum, CHD and duodenum, GB and duodenum, MPD and stomach in pre and post RFT administration were calculated.

McNemar test was used to assess statistical significant difference of conspicuity of various segments between pre and post RFT study. Inter-observer variation was calculated by using Kappa test. Wilcoxon signed ranks test was used to assess statistically significant difference of CNR between each pair. P-value less than 0.05 was considered as statistically significant.

Results

In 19 patients enrolled in the present study, there were 8 patients who had had cholecystectomy and were excluded from the statistical analysis. In observer 1, the conspicuity of post RFT study showed statistical significant improvement ($p < 0.05$) in CBD, ampulla and MPD. In observer 2, the conspicuity showed statistical significant improvement in CBD and CHD (Table 1).

There was no interobserver variation in most of the anatomical structures, except for CHD in the pre RFT study and ampulla in post RFT study (Table 2).

The quantitative comparison between contrast to noise ratio in pre and post RFT study showed statistical significantly improvement in CBD vs duodenum, CHD vs duodenum and MPD vs stomach (Table 3). The example of MRCP images in pre and post RFT administration are illustrated in Fig. 3 and 4.

The amount of iron and manganese were 0.15 mg and 0.32 mg, respectively, in 1,000 mg of dry ground roselle soaked with 240 mL of hot distilled water. Therefore, the total dose of iron and maganese for one patient (4,000 mg of dry ground roselle soaked with 480 mL of hot distilled water) was 0.6 mg for iron and 1.28 mg for manganese.

Discussion

Oral negative contrast agent is composed of a high concentration of high molecular metal ions such as iron or manganese. The paramagnetic and superparamagnetic property of these high molecular ions will increase magnetic susceptibility and shorten T2 relaxation time because of rapid T2 decay. This is responsible for nulling the bright unwanted-water signal. There are several negative oral contrast agent products on the market, such as GastroMARK (Mallinckrodt Inc, St. Louis, MO, USA) and Abdoscan

Table 1. Comparison between the conspicuity of different anatomic structure in pre and post roselle flower tea administration

Structure	Observer 1	Observer 2
	p value	p value
GB	0.999	0.999
CD	0.999	0.999
CBD	0.003*	0.002*
CHD	0.999	0.002*
IHD	0.289	0.375
Ampulla	0.022*	0.125
MPD	0.001*	0.065

GB, gallbladder; CD, cystic duct; CBD, common bile duct; CHD, common hepatic duct; IHD, intrahepatic duct; MPD, main pancreatic duct; *, if $p < 0.05$, conspicuity is significantly different between pre and post roselle flower tea administration

Table 2. Comparison between interobserver grading of conspicuity in pre and post roselle flower tea administration

Structure	Pre		Post	
	Agreement %	Kappa value	Agreement %	Kappa value
GB	72.22	0.44	72.22	0.40
CD	72.22	0.62	72.22	0.60
CBD	72.22	0.63	72.22	0.52
CHD	44.44	0.11*	77.78	0.50
IHD	55.56	0.24	72.22	0.55
Ampulla	55.56	0.35	38.89	0.11*
MPD	50.00	0.30	77.78	0.64

GB, gallbladder; CD, cystic duct; CBD, common bile duct; CHD, common hepatic duct; IHD, intrahepatic duct; MPD, main pancreatic duct; *, if $p > 0.05$ there is no interobserver variation

Table 3. Comparison between contrast-to-noise ratio in pre and post roselle flower tea administration

Structure	Pre		Post		p value
	Mean SI	SD	Mean SI	SD	
CBD vs duo	-8.06	17.48	10.95	10.07	<0.001*
CHD vs duo	-5.76	16.49	11.76	11.46	<0.001*
GB vs duo	12.87	28.88	31.95	23.75	0.007*
MPD vs stomach	-47.33	45.40	6.56	7.76	<0.001*

GB, gallbladder; CBD, common bile duct; CHD, common hepatic duct; MPD, main pancreatic duct; duo, duodenum *, if $p < 0.05$, there is significantly difference in contrast-to-noise ratio between pre and post roselle flower tea administration

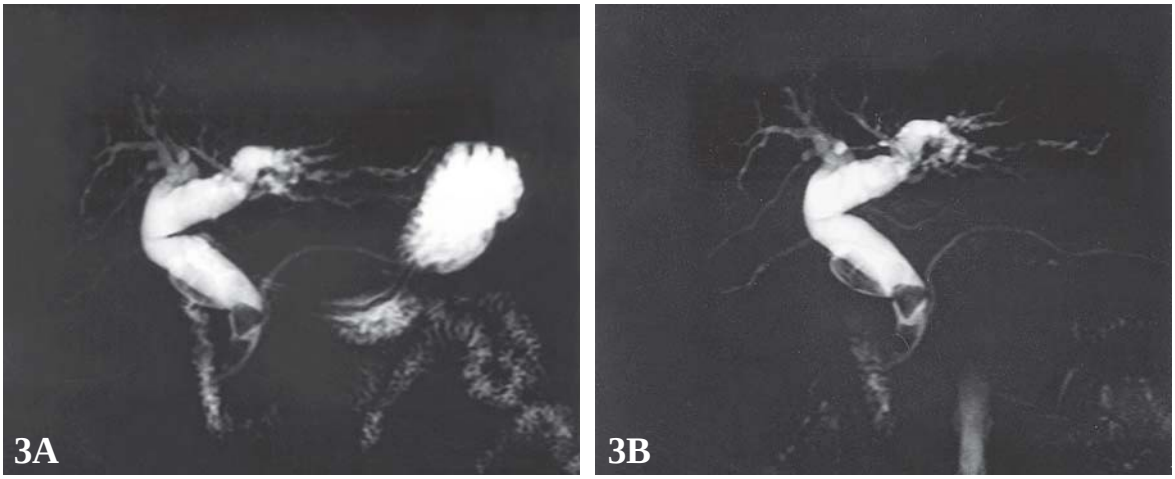

Fig. 3 A 68-year-old male, status post cholecystectomy, presented with recurrent jaundice

Fig. 3A Pre roselle flower tea (RFT) study shows high signal fluid in the stomach, duodenal bulb and duodenum C-loop. Signal of common bile duct (CBD) is obscured by the signal of duodenal bulb. There are several filling defects in CBD from CBD stone. Choledochoceles with stone is also presented

Fig. 3B Post RFT study shows absence of fluid signal in the stomach, duodenal bulb and duodenal C-loop. The CBD and main pancreatic duct are well visualized

(Nycomed SA, Oslo, Norway) and FerriSeltz (Otsuka Pharmaceutical, Tokushima, Japan). These contrast media are expensive and not widely available.

The present study used 480 mL of RFT as an oral negative contrast agent. Quantitative analysis showed that the conspicuity showed statistical significant improvement in CBD by both observers. CBD is the anatomical structure which has the most affect by fluid in duodenal bulb and duodenal C-loop. Therefore, unsurprisingly, CBD was clearly seen significantly by both observers after the RFT administration, which served the purpose of the present study. CHD, ampulla and MPD showed statistical significant improvement only in 1 observer and probably due to interobserver variation. This was graded as slight improvement.

The results of the present study correspond to the study by Chan et al[9] and Papanikolaou et al[4]. Chan et al used diluted gadopentetate dimeglumine with his MRCP studies in 23 patients with pancreaticobiliary disease and reported that diluted gadopentetate dimeglumine with a concentration of 1:15 can also be used effectively. Their results indicated that depiction of CBD and MPD was markedly improved. The depiction of GB and CD was slightly and moderately improved by oral diluted gadolinium. There was no evaluation of CHD, IHD and ampulla.

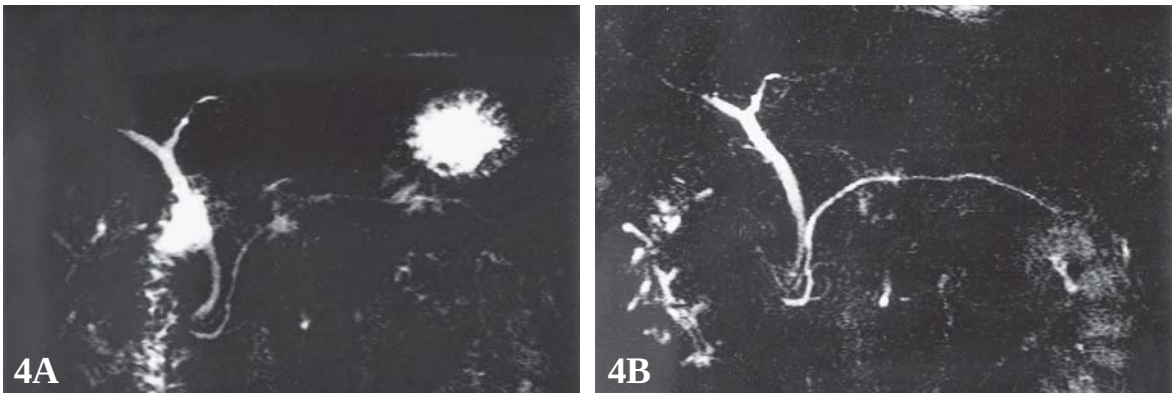

Fig 4. A 50-year-old male presented with abdominal pain and jaundice

Fig. 4A Pre roselle flower tea (RFT) study shows obscuration of common bile duct (CBD) and common hepatic duct (CHD) by high signal fluid in the duodenal blub. Part of the main pancreatic duct (MPD) is also obscured by residual high signal fluid in the body of the stomach (Gallbladder is not included in this projection)

Fig. 4B Post RFT study reveals total absence of high signal fluid in the stomach, duodenal bulb an duodenal C-loop. CBD, CHD and MPD are clearly seen

Papanikolaou et al performed MRCP study with 430 mL of blueberry juice in 37 patients suspected to have obstructive jaundice. They observed that CBD, CHD, ampulla and MPD depiction improved statistically significant. There was no statistically significantly difference in IHD.

Quantitative analysis in the present study showed significantly ($p < 0.05$) reduced CNR between CBD and duodenum, CHD and duodenum, GB and duodenum, MPD and stomach. The significant reduction in CNR between CBD and duodenum is similar to the Papanikolaou et al study.

Mineral component analysis by atomic absorption assay shows that the dose of iron and manganese for a patient is 0.6 mg and 1.28 mg. In the Papanikolaou et al study, the concentration of iron and manganese content in 430 ml of blueberry juice was 8.17 and 1.32 mg. The present data showed that RFT has much lower amount of iron and manganese concentration than blue berry juice but is still as effective.

There was one limitation in MRCP with oral negative contrast agent. It is inability to delineate ampullary region after RFT is given due to lack of contrast between high signal fluid in duodenum and ampulla. To solve this problem, MRCP is encouraged to be performed with and without the RFT administration. The alternative method is an additional 300 ml of water may be given after MRCP with RFT is done if pathology at ampullary region is suspected.

In conclusion, roselle flower tea is a very efficient oral negative contrast agent for MRCP study in reduction of high signal intensity fluid in the stomach and duodenum. It is natural, safe, inexpensive, palatable, and locally available.

Acknowledgement

The authors wish to thank Dr. Laiad Pengsopa and Dr. Jindarat Pimsamarn, Department of Chemical Engineering, King Mongkut's University of Technology Thonburi for RFT iron and manganese content analysis.

References

1. Hirohashi S, Uchida H, Yoshikawa K, Fujita N, Ohtomo K, Yuasa Y, et al. Large scale clinical evaluation of bowel contrast agent containing ferric ammonium citrate in MRI. Magn Res Imag 1994; 12: 837-46.
2. Hiraishi K, Narabayashi I, Fujita O, Yamamoto K, Sagami A, Hisada Y, et al. Blueberry juice: preliminary evaluation as an oral contrast agent in gastrointestinal MR imaging. Radiology 1995; 194: 199-23.
3. Papanikolaou N, Karantanas A, Maris T, Gourtsoyiannis N. MR cholangiopancreatography before and after oral blueberry juice administration. J comput Assist Tomogr 2000; 24: 2290-4.
4. Bernardino MR, Weinreb JC, Mitchell DG, William SC, Morris M. Safety and optimum concen-

tration of a manganese chloride based oral MR contrast agent. J Magn Res Imag 1994; 4: 872-6.
5. Schreiber WE. Iron, porphyrin and bilirubin metabolism. In: Kaplan LA, Pesce AJ, eds. Clinical chemistry: theory, analysis. St. Louis: Mosby, 1989: 496-511.
6. Kirdpon S, Nakorn SN, Kirdpon W. Changes in urinary chemical composition in healthy volunteers after consuming roselle (Hibiscus sabdariffa Linn.) juice. J Med Assoc Thai 1994; 77: 314-21.
7. Chewonarin T, Kinouchi T, Kataoka K, Arimochi H, Kuwahara T, Vinitketkumnuen U, et al. Effects of roselle (Hibiscus sabdariffa Linn.), a Thai medicinal plant, on the mutagenicity of various known mutagens in Salmonella typhimurium and on formation of aberrant crypt foci induced by the colon carcinogens azoxymethane and 2-amino-1-methyl-6-phenylimidazo [4, 5-b] pyridine in F244 rats. Food Chem Toxicol. 1999; 37: 591-601.
8. Carola R, Harley JP, Noback RC. The digestive system. Human anatomy and physiology. New York: McGraw-Hill, 1990: 680-728.
9. Chan JH, Tsui EY, Yuen MK, Szeto ML, Luk SH, Wong KP, et al. Gadopentetate dimeglumine as an oral negative gastrointestinal contrast agent for MRCP. Abdom Imaging 2000; 25: 405-8.

ประสิทธิภาพของน้ำกระเจี๊ยบในการเป็น oral negative contrast agent สำหรับการตรวจระบบทางเดินน้ำดีด้วย MRCP

วิทย์ วราวิทย์, สิทธ์ พงษ์กิจการุณ, จันจิรา ชัชวาลา, สุภาพ เงินถม, วุฒิ สุเมธโชติเมธา, วิชิต ลิละศิธร

วัตถุประสงค์: *เพื่อประเมินประสิทธิภาพของน้ำกระเจี๊ยบในการกำจัดสัญญาณน้ำในกระเพาะอาหาร และลำไส้เล็กส่วนต้น เพื่อการตรวจระบบทางเดินน้ำดีด้วย MRCP*

วัสดุและวิธีการ: *ชงน้ำกระเจี๊ยบโดยใช้ผงดอกกระเจี๊ยบจำนวน 4,000 มก. บรรจุในถุงชาแล้วจุ่มลงในน้ำร้อน 480 มล. นำน้ำกระเจี๊ยบมาทดสอบการทำ MRCP ในหลอดทดลอง อาสาสมัคร และในผู้ป่วยจริง การวิเคราะห์ในเชิงประสิทธิภาพกระทำโดยเปรียบเทียบความชัดเจนของภาพระบบทางเดินน้ำดี ก่อนและหลังดื่มน้ำกระเจี๊ยบ การวิเคราะห์ในเชิงปริมาณกระทำโดยเปรียบเทียบcontrast-to-noise ratio ระหว่างระบบทางเดินน้ำดี กระเพาะและลำไส้เล็กส่วนต้น ก่อนและหลังการดื่มน้ำกระเจี๊ยบ*

ผลการศึกษา: *ภาพของท่อน้ำดีร่วม (common bile duct) มีความชัดเจนขึ้นอย่างมีนัยสำคัญ ภาพของ common hepatic duct, ampulla และ main pancreatic duct มีความชัดเจนขึ้นบ้าง contrast-to-noise ratio ระหว่างระบบทางเดินน้ำดี กระเพาะอาหารและลำไส้เล็กส่วนต้นก่อนและหลังดื่มน้ำกระเจี๊ยบมีความแตกต่างอย่างมีนัยสำคัญจากการวิเคราะห์พบว่าน้ำกระเจี๊ยบที่ให้ผู้ป่วยดื่มมีธาตุเหล็กอยู่ 0.6 มก. และธาตุแมงกานีสอยู่ 1.28 มก.*

สรุป: *น้ำกระเจี๊ยบสามารถนำมาใช้เป็น oral negative contrast agent สำหรับการตรวจ MRCP เพื่อกำจัดสัญญาณน้ำในกระเพาะอาหารและลำไส้เล็กส่วนต้นได้อย่างมีประสิทธิภาพ ปลอดภัย และมีราคาถูก*