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# The efficacy of manganese sulfate as a negative contrast agent for magnetic resonance cholangiopancreatography

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## Abstract

The current study aims to find an alternate oral contrast media for use in magnetic resonance cholangiopancreatography (MRCP) that satisfies the following criteria, the greatest imaging quality safety, no or few side effects, and low cost. The present study created an oral contrast agent sample (solution) by dissolving a one tablet of manganese sulfate supplement (taken daily dose) in 200 ml of distilled water. Thirty-three volunteers assessed the sample using MRCP examine pre and post contrast. By evaluating the signal intensity to compute contrast (C), signal to noise ratios (SNR), and contrast to noise ratio (CNR), the resulting MR images were quantitatively evaluated. And the radiologist examined the MRCP questionnaire, which was used for the qualitative evaluation. The results indicated substantial differences before and after manganese sulfate supplement consumption, as well as enhanced quality of images following manganese sulfate consumption of the biliary systems.

## Keywords

MRCP, Contrast agent, Oral contrast agent, Magnetic Resonance Imaging, Safe contrast agent.

RESEARCH PAPER

# The Efficacy of Manganese Sulfate as a Negative Contrast Agent for Magnetic Resonance Cholangiopancreatography

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**Abstract**

**The current study aims to find an alternate oral contrast media for use in magnetic resonance cholangiopancreatography (MRCP) that satisfies the following criteria, the greatest imaging quality safety, no or few side effects, and low cost. The present study created an oral contrast agent sample (solution) by dissolving a one tablet of manganese sulfate supplement (taken daily dose) in 200 ml of distilled water. Thirty-three volunteers assessed the sample using MRCP examine pre and post contrast. By evaluating the signal intensity to compute contrast (C), signal to noise ratios (SNR), and contrast to noise ratio (CNR), the resulting MR images were quantitatively evaluated. And the radiologist examined the MRCP questionnaire, which was used for the qualitative evaluation. The results indicated substantial differences before and after manganese sulfate supplement consumption, as well as enhanced quality of images following manganese sulfate consumption of the biliary systems.**

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## 1. Introduction

The Magnetic Resonance Cholangiopancreatography is the preferred non-invasive imaging method for assessing the pancreaticobiliary system using heavily T2-weighted sequences. Even in fasting individuals, the accuracy of diagnostic imaging can be considerably decreased by the great signal strength of fluids in the stomach, pancreatic, and biliary ducts [1]. Many articles have been published to solve this problem in medical imaging; some of them studied natural materials as oral contrast agents, such as Grape syrup, grape syrup-lemon solutions in water [2], Pineapple juice, date syrup [3], oolong tea [4,5], jasmine tea, green tea [6], Black tea [7,8], and acia juice [9]. The other articles examined some medicines to reduce the signal intensity of the upper gastrointestinal system such as Ranitidine [10], hematinic syrup [3], Iron supplements [11], and manganese supplements (as tablets of manganese citrate). The use of natural components is beneficial because they contain manganese element, but it doesn't completely reduce the signal intensity of fluid in the gastric tract [12,13]. Also, the concentration of manganese in natural sources varies greatly depending on the food type and preparation, resulting in inconsistent imaging results. Manganese sulfate tablets, on the other hand, provide a higher, more standardised, and more regulated manganese content. This allows for more predictable luminal signal suppression and better repeatability, which are the fundamental reasons for suggesting this approach as an alternative oral negative contrast agent.

This study aims to assess manganese sulfate supplement as an oral contrast agent on heavily T2-weighted sequences in MRCP. The manganese supplement solution acts as negative contrast that are caused by a shorter T2-relaxation period, leading to reduced signal strength from the manganese sulfate solution compared to gastric tissues on T2-

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weighted scanning. The manganese ion works as tiny magnet that accelerates the movement of hydrogen in water. Due to their five unpaired electrons, manganese ions ($Mn^{2+}$) have a significant paramagnetic effect. On T2-weighted MRI sequences, these unpaired electrons produce local magnetic field fluctuations that speed up the transverse (T2) relaxation of adjacent hydrogen protons, causing signal loss.

Manganese sulfate is one type of manganese supplement essential for developing erythrocyte cells and the structural fraction of enzymes [14]. A safe manganese sulfate dosage was employed in this investigation, and no adverse effects were seen [15].

## 2. Materials and methods

### 2.1. Quantitative analysis of manganese sulfate solution

The oral contrast agent solution was obtained by dissolving one tablet of manganese sulfate supplement (the daily dose) in 200 ml of distilled water. This amount of contrast solution is enough for one volunteer.

The manganese supplement pill (contains 132 mg of manganese sulfate, the Daily Value (DV) for elemental manganese = 6.600%).

It is completely safe for adults (Needed daily = 1.8−2.3 mg of manganese) [15]. The amount of manganese in pill that is used in this study = 0.15 mg (very mild). The volunteer could take this daily without any toxicity. The side effects of manganese supplement such nausea, headache, and dizziness that appear when taken in high doses (typically>11 mg/day) [14,15].

The concentration of manganese in contrast media solution equals 25 ppm which is measured by SPECTRO ARCOS (Made in Germany).

### 2.2. MRCP exam protocol

The images of scans have been processed using an MRI device (Siemens-1.5 T), and the imaging parameters are illustrated in Table 1.

*Table 1. Characteristics of the abdominal MRI and MRCP procedure.*

| Sequence | The abdominal MRI | MRCP |
|---|---|---|
| The pulse sequence | Single Shot Fast Spin Echo | Fast Recovery Fast Spin Echo |
| Time repetition (TR) | 2400ms | 3680 |
| Time echo (TE) | 600 ms | 700 |
| Field-of-view (FOV) | 250 mm | 250 |
| Slice thickness | 60 mm | 60 |
| Matrix | 320 × 224 | 320 × 224 |

### 2.3. MR imaging in volunteers

This was a prospective research that took place between January and September 2025 on 33 healthy volunteers at Imam Al Hassan Al Mujtaba Teaching Hospital in Karbala, Iraq. All of the volunteers appear to be healthy, with no biliary system problems. Volunteers who showed incidental signs of claustrophobia were eliminated. Individuals with contraindications such as metal implants, cardiac pacemakers, dentures, cochlear implants, or pregnancy were not allowed to participate.

This study's participants were healthy adults between the ages of 20 and 49 with a normal body mass index (BMI) is between 19.3 and 25.9 kg/m$^2$. The sample number was 33 Individuals who completed an MRCP routine preparation for each fasting 6 h before the exam. This article required administering a manganese sulfate supplement dissolved in 200 mL of distilled water. The scan intervals used were 10 min. The MRCP image information was then analyzed before and after administering an oral manganese sulfate supplement solution, to determine the optimal scanning duration for improving the MRCP image.

### 2.4. Statistical analysis

The data was analysed using SPSS (Statistical Package for Social Science) version 26.0. The statistical data was evaluated using the mean and standard deviation. When using the t-test to assess differences between two sets of quantitative data, a P-value of 0.001 on both sides was deemed statistically significant.

### 2.5. Quantitative analysis of images

The proton relaxation process is affected by the contrast media used in MRI, which raises informative value and image contrast [16]. The anatomical contrast-to-noise ratio (CNR), signal-to-noise ratio (SNR), and contrast values were computed in order to objectively evaluate the images. We determined signal intensities ($I_A$) by creating a 200 mm$^2$ area of interest (ROI) in each image of the participant's stomach before and after administration of an oral manganese sulfate supplement solution. And also determined signal intensities ($I_B$) by creating a 200 mm$^2$ area of interest (ROI) on the stomach wall. Than calculated contrast-to-noise ratio (CNR), signal-to-noise ratio (SNR), and contrast.

The signal-to-noise ratio (SNR) is a measure of the level of signal intensity (SI) acquired in the ROI when compared to the standard deviation (SD) of signal intensity in a particular area outside of the item being scanned [6]. This formula is used to calculate SNR.

$$SNR = \frac{(SI) of\ solution - (SI) of\ background}{(SD) of\ background} \quad (1)$$

The term "contrast" describes the variation in signal intensity between two nearby places, such as between tissues or between the surrounding tissues and contrast agents. This formula is used to calculate it.

$$C = SI_A - SI_B \quad (2)$$

$SI_A$, $SI_B$ are signals from two neighbouring the contrast agent and surrounding tissues [17]. The contrast to-noise-ratio (CNR) is calculated with the following formula [18].

$$CNR = \frac{SI_A - SI_B}{standard\ deviation (SD) of\ background} \quad (3)$$

### 2.6. Qualitative analysis of images

The MRCP images were qualitatively evaluated by radiology professional examined who has 13 years of expertise in *MR* Imaging using a questionnaire. The following Likert scale, shown in Table 2, was used to administer questionnaires on the biliary system's contrast and the strength of the stomach and duodenal signals.

## 3. Results and discussion

Thirty-three volunteers (20 males and 13 females) aged 20 to 35 years participated in this study with an average age of 26.696 years and a BMI of 25.25 kg/m$^2$, ranging from 21.5 to 27.9 kg/m$^2$. Each volunteer underwent two MRI exams: one before and one after drinking the manganese solution after an 8-h fast.

Before and after taking a drink of the oral contrast solution (one tablet of manganese sulfate supplement was dissolved in 200 mL of water), Fig. 1 shows a comparison between MRI images of an empty stomach and one filled with a manganese solution. The MRCP scanning is performed before and 10 min after the manganese supplement solution administration. The two images illustrate the effect of the manganese supplement solution in reducing a signal intensity in the stomach. The results of the MRCP imaging pre and post contrast administration of the manganese sulfate solution be seen in Fig. 2. The biliary system appears more clearly and in better detail in image B due to the manganese supplement solution's effect on concealing the signal intensity of the fluids in the stomach and duodenums.

In two tests, the images quality of MRI has been evaluated by signal intensity (SI), contrast-to-noise ratio (CNR), contrast (C), and signal-to-noise ratio (SNR) for each participant. We determined signal intensities by creating a 200 mm$^2$ area of interest (ROI) in each image of the participant's stomach. Data was collected and computed for 33 people pre and post they consumed a manganese sulfate solution. The data was analysed with the SPSS application. To analyse quality differences, the mean and standard deviation of quantitative values were determined, and the t-test was used to compare quantitative data in two sets. Both sides' P-values have to be 0.001 or less to be deemed statistically significant. Table 3 displays the statistical

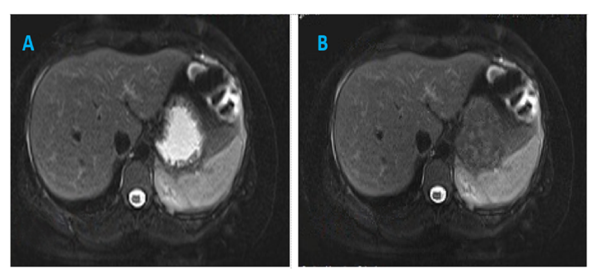


*Fig. 1. MRI transverse slice of the abdomen (T2-weighted) during imaging circumstances: single-shot fast spin-echo. (A)pre-contrast (B) post-contrast.*

*Table 2. The assessment criteria for gastric tract intensity and biliary system visibility.*

| Gastric system | Biliary system |
|---|---|
| Scale 1 = poor (both the duodenum and the stomach looked to have significant signal intensity and interfered with reading images). | Scale 1 = poor (it was challenging to locate seen or visualized information since the biliary system's and the bile's anatomical wall's structure and boundary were not distinct, bright, and firm). |
| Scale 2 = sufficient (Although the duodenum and stomach seemed to have high signal intensities, this did not affect the image's clarity). | Scale 2 = sufficient (the bile's and the biliary system's anatomical wall's structure and borders were quite distinct, firm, and bright, but not as distinct as those with score 3). |
| Scale 3 = good (The duodenum and stomach signals were barely noticeable on the image). | Scale 3 = good (the bile and biliary system anatomy seemed very firm, bright, and transparent). |

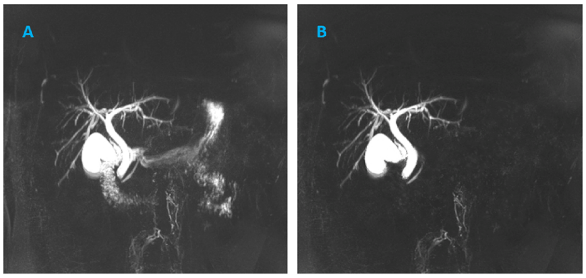


*Fig. 2. MRCP longitudinal slice of the abdomen (T2-weighted) during imaging circumstances: fast-recovery fast spin-echo transverse oblique 3D respiratory triggered. (A)pre-contrast (B) post-contrast.*

*Table 3. The quantitative parameter values for abdominal MRI. P-values ≪0.001 was considered statistically significant.*

| Quantitative parameters | Pre-contrast | Post-contrast | P-value |
|---|---|---|---|
| $SI_{mean}$ ±SD | 560.43 ± 26.18 | 322.40 ± 12.40 | $1.04 \times 10^{-12}$ |
| $SNR_{mean}$ ±SD | 254.88 ± 11.91 | 134.57 ± 5.30 | $3.57 \times 10^{-17}$ |
| $C_{mean}$ ±SD | 276.43 ± 27.00 | 37.40 ± 12.00 | $6.92 \times 10^{-14}$ |
| $CNR_{mean}$ ±SD | 149.42 ± 14.49 | 29.77 ± 9.87 | $3.56 \times 10^{-19}$ |

data from thirty-three volunteers for abdominal MRI with region of interest equals 200 $mm^2$. While Table 4 displays the statistical data from MRCP with region of interest equals 30 $mm^2$.

Oral contrast agents are preferred in MRCP standardized assessment methods. Oral signal suppressors improve the representation of the pancreatobiliary duct system by lowering the superimposed fluid signal from the upper GI tract.

In Tables 3 and 4, the manganese supplement solution acts as negative contrast that are caused by a shorter T2-relaxation period, leading to reduced signal strength from the manganese sulfate solution compared to gastric tissues on T2-weighted scanning. The manganese ion works as tiny magnet that accelerates the movement of hydrogen in water. P-values ≪0.001 was considered statistically significant.

The graphs in Figs. 3 and 4 depict the radiologist judgment of the bile tract and gastric tract scan. In that figures, the most of the biliary tract had a bad value before to manganese supplement administration, however a dominating value of excellent was achieved following manganese supplementation.

*Table 4. The quantitative parameter values for MRCP. P-values ≪0.001 was considered statistically significant.*

| Quantitative parameters | Pre-contras | Post-contrast | P-value |
|---|---|---|---|
| $SI_{mean}$ ±SD | 268.3 ± 17.06 | 328.4 ± 15.90 | $3.33 \times 10^{-27}$ |
| $SNR_{mean}$ ±SD | 91.03 ± 6.32 | 125.66 ± 6.38 | $6.13 \times 10^{-28}$ |
| $C_{mean}$ ±SD | 243.3 ± 16.07 | 310.4 ± 14.91 | $2.96 \times 10^{-27}$ |
| $CNR_{mean}$ ±SD | 93.57 ± 6.56 | 137.58 ± 7.04 | $5.84 \times 10^{-25}$ |

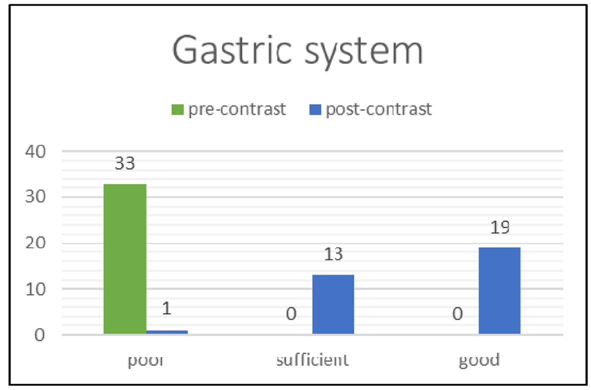


*Fig. 3. A comparison of MR images pre and post the administration of a manganese sulfate supplement was performed on thirty three participants and examined by a professional radiologist.*

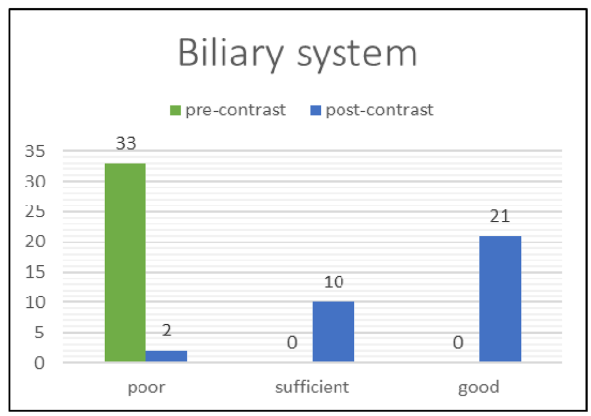


*Fig. 4. A comparison of MRCP images pre and post the administration of a manganese sulfate supplement was performed on thirty three participants and examined by a professional radiologist.*

On T2-weighted scanning, the manganese sulfate supplement solution shows less intensity of signal than stomach contents due to a shorter T2-relaxation period, The enhanced signal suppression found with the manganese supplement solution might be attributed to its greater and more standardized manganese content than that reported for natural compounds such as green, oolong, or jasmine teas. Manganese sulfate supplementation is more soluble in water and less absorbed in the intestines than manganese citrate [19]; therefore, manganese sulfate supplementation is more effective as a contrast agent and has less of an effect on the human body.

The manganese supplement tablet contains 132 mg of manganese sulfate; the Daily Value (DV) for elemental manganese is 6.600%. It is perfectly safe for adults (the recommended daily dose is 1.8-2.3 mg of manganese [15]. The manganese content of the tablet utilized in this investigation was 0.15 mg (extremely weak). The patients with biliary dysfunction tht might take this on a daily basis without risk of toxicity. Side effects of manganese supplements include nausea, headaches, and dizziness when used at high amounts (usually >11 mg/day) [14,15].

When used as a negative oral contrast agent in MRCP, manganese sulfate has a number of useful benefits over naturally made solutions such fruit juices or herbal teas [1−9]. Manganese sulfate, in contrast to natural products, offers a calibrated and well regulated manganese content, guaranteeing reliable and constant suppression of the strong T2 signal from the duodenum and stomach. In ordinary clinical practice, this standardization improves reliability and lowers inter-examination variability. Manganese sulfate is also cheap, an acceptable test, easier to store and prepare in a hospital setting, has a longer shelf life, and doesn't need to be refrigerated or made fresh. These elements reduce batch-to-batch inconsistency, seasonal variations, and unpredictability associated with natural product composition while increasing workflow efficiency. Manganese sulfate may therefore be a more workable and repeatable substitute for standard MRCP imaging.

Manganese sulfate was shown to reduce gastric/duodenal SNR significantly while improving biliary CNR, indicating successful background signal suppression. When compared qualitatively to previous findings on pineapple juice and black tea, the degree of suppression found in our group looks higher and provides greater uniformity owing to increased and controlled dosage.

## 4. Conclusion

The magnetic resonance cholangiopancreatography with oral contrast is very important to diagnose rare cases, for example, a choledochocele wandering in the duodenum lumen [20].

A manganese supplement works effectively as a substitute for a negative oral contrast agent when taken 10 min before a scan. It can increase anatomical information about the biliary system, as well as CNR quality and contrast (C) on MRCP images, by reducing the strength of the stomach and duodenal signals. Future research should include MRCP studies using manganese supplementation as a negative oral contrast media for individuals with specific biliary system symptoms or diseases.

## Ethics approval

- The research was conducted in accordance with the guidelines of the Research Ethics Committee at the College of Applied Medical Sciences, University of Karbala. The committee approval letter reference number is (MPAMSKU/2). The study adhered to the Declaration of Helsinki (as amended in 2013).
- The Ethics Committee of the Medical Research Committee, Training and Human Development Center, Karbala Health Department, Iraqi Ministry of Health, authorized the research, and the approval letter number is 2022020/Karbala
- Before the work was done, the volunteers gave their approval, and their data was handled completely confidentially and kept private.

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## Conflict of interest

The authors declare no conflicting interests.

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