The role of ranitidine in the enhancement of imaging quality in magnetic resonance cholangiopancreatography*

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Abstract

Objective: To assess the impact of oral ranitidine on the imaging quality in magnetic resonance cholangiopancreatography (MRCP). Materials and Methods: Thirty-two patients underwent MRCP with 3D and 2D acquisitions, and three strategies for suppression of the gastrointestinal fluid signal: a) only at fasting; b) 12 hours after ingestion of 300 mg ranitidine; c) after oral administration of gadolinium solution. Three observers reviewed the images with a focus on the degree of visualization of the biliopancreatic tree. The interobserver agreement was evaluated with the kappa test. The difference between techniques and acquisition modalities were evaluated by means of average grading scores. Results: The three strategies for suppression of the gastrointestinal fluid signal presented high reproducibility. The results with suppression of the gastrointestinal fluid signal with ranitidine where similar to those obtained with fasting, and both were worse than those obtained with gadolinium solution. The 3D acquisitions surpassed 2D only in terms of visibility of the cystic duct and gallbladder, and were inferior or equivalent in the other biliopancreatic ductal segments. Conclusion: The use of ranitidine does not seem justified in the evaluation of the biliopancreatic tree at MRCP, since 2D MRCP with fasting allows the visualization of ductal structures with high quality and reproducibility in the majority of cases.

Keywords: Ranitidine; Diagnostic use; Magnetic resonance cholangiopancreatography; Contrast media; Bile ducts; Pancreatic ducts.

Resumo

Objetivo: Avaliar o impacto da ranitidina por via oral na qualidade do exame de colangiopancreatografia por ressonância magnética (CPRM). Materiais e Métodos: Trinta e dois pacientes realizaram CPRM com aquisições 3D e 2D, com três estratégias de supressão do sinal líquido gastrintestinal: a) apenas em jejum; b) 12 horas após ingerir 300 mg de ranitidina; c) após a ingestão de solução de gadolínio. Três observadores avaliaram os estudos, atentos para o grau de visualização da árvore biliopancreática. Foi medida a concordância interobservador com o teste kappa. A diferença entre técnicas e formas de aquisição foi avaliada pela média da soma dos escores de graduação. Resultados: As três estratégias de supressão do sinal líquido gastrintestinal apresentaram elevada reprodutibilidade. A supressão do sinal líquido gastrintestinal com a ranitidina foi semelhante ao jejum e ambas foram piores do que a solução de gadolínio. As aquisições 3D superaram a 2D apenas na visualização do ducto cístico e da vesícula biliar, sendo inferior ou equivalente nos demais segmentos ductais biliopancreáticos. Conclusão: O uso da ranitidina não parece justificado para aprimorar a avaliação da árvore biliopancreática em exames de CPRM. A CPRM 2D apenas em jejum permite a visualização ductal com elevada qualidade e reprodutibilidade na maioria dos casos.

Unitermos: Ranitidina; Uso diagnóstico; Colangiopancreatografia por ressonância magnética; Meios de contraste; Ductos biliares; Ductos pancreáticos.

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INTRODUCTION

The term magnetic resonance cholangiopancreatography (MRCP) can be extended to a number of imaging acquisition techniques whose main characteristic is exploring a long T2 relaxation time of the fluids contained within the biliopancreatic tree for the formation of the image. As a general rule, MRCP studies are performed both under breath-hold (2D MRCP) and with respiratory triggering (3D MRCP). This strategy seeks to combine the inherent advantages from each of the two modalities, such as the short acquisition time of the 2D sequence and the higher spatial resolution obtained with the 3D techniques.

On account of its projectional nature, the signal from the gastrointestinal fluid...
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Materials and methods

The present study was approved by the Committee for Ethics in Research of the institution. A term of free and informed consent was signed by all the individuals participating in the study.

A prospective, cross-sectional, observational and self-paired study was undertaken. The proposal for undergoing MRCP was opened to healthy and cooperative individuals aged above 18, who agreed in participating in the study. Any relative or absolute contraindication for MRI (for example: cardiac pacemaker, brain aneurism clips, cochlear implants, claustrophobia, previous history of allergy to the drug and use of synergistic drugs (for example: diazepam, ketoconazole, clarithromycin, phenytoin and warfarin) were considered as exclusion criteria.

The MRCP scans were performed in 32 volunteers, 12 women and 20 men, with ages between 27 and 63 years, mean age of 32 years. No exclusion was observed.

Patients preparation

The following steps were undertaken:  

First step – MRCP with no medication and after at least four-hour fasting, acquiring images with 2D and 3D techniques.

Second step – On the same day, MRCP after oral intake of negative contrast medium, acquiring images with 2D and 3D techniques. The negative contrast medium was a solution with 5 ml of gadolinium in 75 ml of water, as described in the literature.

Third step – MRCP under at least four-hour fasting and 12 hours after ingestion of 300 mg of ranitidine (peak of action) acquiring the images with 3D and 2D techniques. The mean time span between the first two steps and the third step was 30 days, ranging from 21 to 35 days.

Equipment and technique

All the scans were performed in a MRI equipment operating with a 1.5 T magnetic field, model Gyroscan Intera® (Release 13) (Philips Medical Systems; Best, The Netherlands) equipped with a synergy sense body coil for signal emission and reception.

The parameters for MRCP images acquisition were identical in the three steps, namely:

- 3D MRCP: repetition time (TR) = 1433; echo time (TE) = 650; NEX = 1; matrix = 256 × 205; slice thickness = 1.6 mm; gap = 0.8 mm with 80% overlap; turbo factor (TF) = 144; flip angle of 90 degrees; field of view (FOV) = 512 × 512; echo spacing = 9.9 ms; bandwidth = 723 Hz; and acquisitions during the final expiratory phase utilizing respiratory triggering (RT). The mean acquisition time was five minutes.

- 2D MRCP: TR = 8000; TE = 800; NEX = 1; matrix = 228 × 182; slice thickness = 4.0 cm; TF = 182; flip angle = 90 degrees; FOV = 380 × 380; bandwidth of 320 Hz; 6 radial coronal acquisitions centered on the bile duct, at an angle of 15 degrees and obtained with breath-hold. The time spent for each acquisition (slab of 4.0 cm) was 2 seconds, and for the entire sequence, less than 30 seconds.

Images evaluation

The images were independently and randomly evaluated by three different observers (observer 1, with 10-year experience in general radiology; observer 2, with 4-year experience in general radiology and 2-year experience in abdominal radiology; observer 3, with 4-year experience in general radiology). There was no consensual analysis in cases of interobserver disagreement.

The images were filed in DICOM format and were displayed on high-resolution displays utilizing the Osirix® platform. In order to avoid learning bias, the identification of patients and fluid signal suppression technique were replaced by codes.

The 3D MRCP images were initially evaluated, also utilizing the millimetric sections of the source images and multiplanar reconstructions with the MIP technique. The observers were totally free to perform reconstructions in other planes, change the imaging windows according to their preferences as well as changing the reconstruction thickness with the MIP technique. Each evaluation session was held at an interval of at least two weeks.

The 2D acquisition images were later evaluated. Similarly to the previous evaluation sessions, the observers were free to change the images parameters as they found convenient.

Evaluation parameters

The following ductal segments were evaluated:

- Main right hepatic ducts branch: defined as the segment interposed between the ductal hilar confluence and its first-order branching.
- Main left hepatic ducts branch: defined as the segment interposed between the ductal hilar confluence and its first-order branching.
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Statistical analysis

The sum of the scores assigned by the three observers for the visualization variable (ranging between 0 and 2), so as the score value was a minimum of 0 and a maximum of 6. The same was done to evaluate the degree of gastrointestinal fluid signal suppression (ranging between 1 and 4), where the sum of scores could range from 3 to 12. Such a method was applied for both image acquisition techniques (2D and 3D) and for the three gastroduodenal fluid signal suppression techniques (fasting, ranitidine and oral contrast).

The two-way analysis of variance (ANOVA) was utilized to verify significant differences between acquisition techniques (2D and 3D). In the case of statistical significance, the Tukey multiple comparison test was utilized.

The interobserver agreement was evaluated by means of the kappa ($\kappa$) test. Value of $\kappa$ lower than 0.4 indicate low agreement; values between 0.41 and 0.60 indicate moderate agreement; between 0.61 and 0.80 indicate substantial agreement; above 0.81 indicate excellent agreement.$^{[12]}$

The established significance level was $p > 0.05$.

RESULTS

Interobserver agreement

The interobserver agreement in relation to the degree of gastrointestinal fluid signal suppression was considered as being substantial, ranging between $\kappa = 0.63$ and $\kappa = 0.73$. For the qualitative assessment of the visualization of biliopancreatic duct segments, the interobserver agreement was moderate, ranging between $\kappa = 0.41$ and $\kappa = 0.48$. The images were considered as having diagnostic effectiveness when the biliopancreatic tree was partially or completely visualized (visualization score 1 and 2). On the other hand, images without diagnostic effectiveness were those where a determined biliopancreatic duct segment was not identified (score 0). As the images were grouped as “with diagnostic effectiveness” (visualization scores 1 and 2) and “without diagnostic effectiveness” (visualization category 0), the agreement about visualization of the biliopancreatic tree became substantial (Table 1). No statistically significant difference was observed in relation to the number of images with diagnostic effectiveness among the three techniques (fasting, ranitidine and oral negative contrast) (Table 2).

Gastrointestinal fluid signal suppression

The utilization of oral contrast agent was the strategy by which the highest suppression scores were achieved (Figures 1 and 2), and the difference with other gastrointestinal fluid signal suppression strategies (fasting and ranitidine) were statistically significant for any of the two acquisition techniques (2D × 3D) ($p = 0.02$). No statistically significant difference was observed between the scores obtained with ranitidine and fasting in both image acquisition techniques. The effect of the negative contrast on all segments is presented on Figure 3, where the scores for the three strategies for gastrointestinal fluid signal suppression with both acquisition techniques are represented.

Ten segments of the biliopancreatic tree were evaluated. All the 32 patients were evaluated six times (three times on 3D acquisitions and three times on 2D acquisitions). Thus, each observer performed 1,920 image analyses. The scores 1 and 2 (when the gastrointestinal fluid signal partially or totally impairs the biliopancreatic tree evaluation) occurred in only 3.2% of all evaluations, being most commonly observed in the analysis of the cystic duct on 2D acquisitions by the less experienced observers (Figure 4).

Degree of ductal visualization

The quality of ductal visualization kept a closer relationship with the acquisition technique (2D × 3D) than with the gas-
trointestinal fluid signal suppression strategy (Table 3).

For the right, left and common hepatic ducts, and the suprapancreatic segment of the bile duct, there was neither statistically significant difference between the acquisition techniques (2D × 3D) nor between the gastrointestinal fluid signal suppression strategies.

For the cystic duct and the gallbladder, the acquisitions with the 3D technique achieved higher visualization scores.

For the pancreatic segment of the bile duct, and for the entire extent of the pancreatic duct, the 2D acquisition surpassed the 3D acquisition technique, and such difference was statistically significant (Figure 5).

The evaluation of the gallbladder and cystic duct was significantly superior with ingestion of the gadolinium solution. In the remaining segments of the biliopancreatic tree the ductal visualization was similar among the three gastrointestinal fluid signal suppression techniques (Table 3).

For the three observers, in the majority of images, the 2D and 3D acquisition techniques presented similar performances in the visualization of the biliopancreatic tree (Table 4).

In all studied ductal segments, the gastrointestinal fluid signal suppression strategy with ingestion of ranitidine did not result in a better evaluation of the biliopancreatic tree as compared with the other two strategies, and there was no statistically significant difference in comparison with...
Figure 3. 2D sequence after fasting where, in spite of angled acquisitions, the cystic duct superposition persisted. Detail of small vesicular polyp on image D (arrow). E, stomach; d, duodenum.

Table 3  Values for statistical significance of gastrointestinal fluid signal suppression strategies and for the image acquisition techniques.

<table>
<thead>
<tr>
<th>p value</th>
<th>RHD</th>
<th>LHD</th>
<th>CHD</th>
<th>CD</th>
<th>GB</th>
<th>SBD</th>
<th>PD</th>
<th>HPD</th>
<th>BPD</th>
<th>TPD</th>
</tr>
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<tbody>
<tr>
<td>2D × 3D</td>
<td>0.054</td>
<td>0.71</td>
<td>0.15</td>
<td>0.001</td>
<td>0.001</td>
<td>0.15</td>
<td>0.01</td>
<td>0.02</td>
<td>0.006</td>
<td>0.02</td>
</tr>
<tr>
<td>Gd × R × F</td>
<td>0.13</td>
<td>0.41</td>
<td>0.41</td>
<td>0.68</td>
<td>0.04</td>
<td>0.99</td>
<td>0.53</td>
<td>0.09</td>
<td>0.25</td>
<td>0.01</td>
</tr>
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RHD, right hepatic duct; LHD, left hepatic duct; CHD, common hepatic duct; CD, cystic duct; GB, gall bladder; SBD, suprapancreatic bile duct; PD, pancreatic duct; HPD, head of the pancreatic duct; BPD, body of the pancreatic duct; TPD, tail of the pancreatic duct; Gd × R × F, gadolinium × ranitidine × fasting. Note: Bold numbers demonstrate statistical significance.

Figure 4. All segments of the pancreatic duct are identified at the 2D acquisition with gadolinium solution (arrows on A). At the 3D MIP sequence (B) only its cephalic segment is partially identified (arrow).

the scans performed after fasting only. In the evaluation of the tail of the pancreatic duct, a worse definition was observed on the images obtained after the utilization of ranitidine (Figure 6), as compared with the images obtained with other strategies for gastrointestinal fluid signal suppression (Table 3).
DISCUSSION

MRCP is the main non-invasive imaging method utilized in the evaluation of biliopancreatic disorders. Its accuracy is similar to that obtained at endoscopic retrograde cholangiopancreatography in the diagnosis of choledocholithiasis, biliary obstruction and sclerosing cholangitis\(^{13,14}\), without the potential risks involved in such invasive procedure\(^{15}\). In order to obtain such expected results, it is essential to assure a good imaging quality, which is expressed by the degree of ductal visualization\(^{16}\). The inappropriate characterization of the biliopancreatic tree ducts may originate from the presence of motion artifacts caused by peristaltic and respiratory movements and enteric fluid overlap\(^{17}\). In the present study, the authors have tried to demonstrate the results achieved in terms of ductal visualization at MRCP when different strategies are adopted, with the purpose of minimizing the superposition of gastrointestinal fluid over the biliary and pancreatic trees.

Among such strategies, the adoption of gadolinium solution in water was the best form to abolish the signal from the gastrointestinal fluid. As regards the pharmacological strategy utilizing oral ranitidine, the results of the present study were not similar to those reported by a previous study\(^{5}\). No significant difference was observed as regards reduction in signal between scans performed after fasting and after ingestion of 300 mg ranitidine. Ranitidine reduces the gastric acid secretion thanks to its action on the H2 receptors, reducing the hydrogen protons concentration in the gastric juice\(^{10}\). On their turn, gastric juices are utilized in the formation of the images at the MRI. There are studies demonstrating a linear relationship between the signal intensity measured by MRI and local concentration of hydrogen\(^{18,19}\). Probably, there was a difference in the concentration of such ions in the gastric juice as the patients underwent the scans after fasting and after ranitidine intake. However, such difference was not expressed in terms of amount of signal of the gastrointestinal fluid perceived by the observers. Another point to be considered is the effect of ranitidine on the gastric motility. According some authors, there is a prokinetic effect, accelerating the gastric emptying, while for others there is an opposed effect\(^{20-23}\), which can influence the results regarding the amount of fluid inside the gastric cavity. Such point is still controversial and should be further investigated in new studies about gastroduodenal motility. The ranitidine dose and its intake timing represent other issues which might have influenced its effectiveness in obtaining a more expressive reduction of gastric secretion. However such variables were compatible with those utilized in other studies and supported by their pharmacological action\(^{6,10}\).

A worsening in the visualization of the caudal segment of the pancreatic duct was observed with the utilization of ranitidine in both acquisition techniques (2D and 3D). Bowers et al. have also mentioned a non-significant reduction in the visualization of the pancreatic duct in their study, but those authors did not make any further comment on such a finding\(^{6}\). The present study authors’ hypothesis is that the basal gastric

Table 4  Frequency of similar performance (=) or different performance (> or <) in the biliopancreatic tree evaluations with 2D and 3D acquisition techniques, according to the three observers.

<table>
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<th>Observer 1</th>
<th>Observer 2</th>
<th>Observer 3</th>
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<tbody>
<tr>
<td>2D = 3D</td>
<td>78.9%</td>
<td>64.1%</td>
<td>64.2%</td>
</tr>
<tr>
<td>2D &gt; 3D</td>
<td>11.5%</td>
<td>15.9%</td>
<td>20.0%</td>
</tr>
<tr>
<td>3D &gt; 2D</td>
<td>9.5%</td>
<td>19.8%</td>
<td>15.7%</td>
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acid secretion maintains some stimulus over the exogenous pancreatic bicarbonate secretion, which would cause fluid to be present in the pancreatic ductal lumen, and consequent MRI signal on cholangiographic sequences. On the contrary, the gastric secretion suppression caused by ranitidine would limit such an effect.

Fluid superposition impairing the ductal visualization was not a frequent event, identified in only 3.2% of the scans. Such finding was more common for the cystic duct in 2D acquisitions. These scores were most frequently observed in the analyses undertaken by the less experienced observers. As far as one could observe, the present study is the first to identify the frequency in which the fluid superposition limits the ductal visualization, and also the first to relate it to the observers’ experience degree.

The visualization score was rather related to the acquisition modality and location of the evaluated segment. According to the present study results, the sequences obtained with the 3D and RT techniques improved the degree of visualization of the cystic duct and of the gallbladder. In the remaining segments, the visualization scores obtained with breath-hold sequences were equivalent or higher than those obtained with 3D sequences. Such aspect was mostly observed on the pancreatic duct images. According to some authors, there is superiority in the visualization of this segment as its anatomic plane is contained within the acquisition block, like in the 2D technique. Furthermore, reconstructions with MIP technique from images obtained with the 3D technique may exacerbate motion artifacts. Considering such aspects and the shorter acquisition time for imaging with the 2D breath-hold technique, it is justifiable to initiate the MRCP scan with this acquisition technique. In those cases where some ductal segment, crucial for diagnosis definition, is not appropriately represented with the 2D technique, the scan may be supplemented with images acquired with RT and the 3D technique. In cases where fasting alone was the strategy utilized for gastrointestinal fluid signal suppression, the use of negative oral contrast agent would have been necessary in three (9%) of the 32 cases for observer 1, in none for observer 2, and in five cases (15%) for observer 3. Gastrointestinal fluid signal suppression would be useful particularly in the evaluation of the cystic duct only in 2D acquisitions.

In summary, the three observers substantially agreed in relation to the fact that the signal from the enteric juice is rarely a factor which affects the biliarypancreatic tree visualization degree as the scan is performed after fasting. For that reason, the authors consider, similarly to other authors, that the utilization of negative contrast agent may be dispensable in MRCP scans. However, there is no consensus in the literature with respect to this theme. Some authors have put forward opinions which are based on their experience, rather than on hard evidences, indicating that the use oral contrast agent is not necessary. On the other hand, others have demonstrated the usefulness of such a strategy to improve the visualization of the biliarypancreatic tree. It is important to notice that the latter have not utilized the radial sequence in the 2D breath-hold acquisitions, or have not performed the 3D sequences with RT in the routine evaluation of the biliarypancreatic tree in their studies, contrarily to what was done in the present study, and which reduces the undesired superposition of the gastric juice with the biliarypancreatic ducts. That would explain the discrepancy obtained in the present study as compared with previous ones, towards considering the use of oral contrast unnecessarily, since the different angles of radial and volumetric acquisitions avoid the fluid superposition on the biliarypancreatic tree mapping.

The present study faced some limitations. The first one is the fact that patient fasting time was not controlled; only a minimum fasting time of at least four hours between the last meal and the scan was established; some patients may have fasted for longer than four hours, as it occurs in the daily practice. The second limitation was the fact that volunteers’ diet was not controlled. Some types of food can retard the gastric emptying, which may eventually reduce the efficacy of fasting as a strategy for reducing ductal superposition; however, limiting the intake of certain foods is not common in the patient preparation instructions for MRCP scans. The third limitation was the fact that no antiperistaltic drugs were utilized. Sodickson et al. report the finding of motion artifacts caused by peristaltic movements under the form of noise dispersed throughout the image on 3D MRCP acquisitions, leading to poor definition of ductal contours. This may have compromised image quality in 3D acquisitions; on the other hand, considering that some patients are sensitive to scopolamine, avoiding the utilization of such type of drug increases the tolerance to the procedure. Finally, the new respiratory-triggered techniques by means of diaphragmatic motion monitoring (PACE) seem to be superior to that utilized for the present study. This may have favored the 2D sequences in the present study, i.e., adopting more updated RT techniques might have improved the quality of the images obtained in 3D and make them better than those obtained with the breath-hold technique. On the other hand, it should be considered that new techniques for breath-hold acquisition might equally optimize results in the biliarypancreatic tree evaluation by MRCP.

In the evaluation of conditions affecting the pancreatic and biliary tract, MRCP has been playing an increasing role on account of its many advantages and complementarity with ultrasonography. Establishing a MRCP exam protocol that makes it simpler, faster and more efficient without impairing its diagnostic capability is important, and the present study is aimed at contributing in such sense.

Finally, the present study demonstrates that the utilization of oral ranitidine does not bring significant benefits to the image quality in MRCP studies. It is possible to perform the scan in a simplified way and with good quality by utilizing the breath-hold acquisition technique and after fasting. By dispensing with the use of time consuming acquisition sequences with RT and gastrointestinal fluid signal reduction strategies (either pharmacological or involving the use of oral contrast agents), and utilizing fast breath-hold sequences, one should save time and resources.

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