



SAFETY CONCERNS REGARDING THE USE OF MODERN LIVER CONTRAST MEDIUM

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Abstract. The MRI is “the gold standard” to evaluate the nodular liver. A study made over a period of 22 months between 2009 and 2011 assessed the side effects of 2 types of contrast agents (SPIO and gadobutrol) administered to patients that underwent MRI investigations aimed to diagnose hepatic nodular lesions. 134 patients were examined and monitored. Gadolinium MRI contrast agents are much safer than the contrast used on CT, anaphylactic reactions being rare. None of the patients developed any clinical or biological side effects, contrast agents for magnetic resonance imaging being much safer than contrast used in computer tomography. Sex, age or associated pathology of the patients don't represent risk factors for the development of adverse reactions.

Keywords: liver, contrast medium, magnetic resonance

Introduction

The MRI is “the gold standard” to evaluate the nodular liver, having a high sensitivity and specificity. The contrast agents used for the magnetic resonance examination were evaluated to discover if they can determine some late adverse reactions.

In MRI evaluation of the liver, there are several categories of contrast agents that are being utilized: non-specific, which have extracellular distribution and are similar to those utilized in CT scans; hepatocyte-specific, which are partially excreted via the biliary tract; reticuloendothelial system-specific.

Non-specific gadolinium chelates are a variety of gadolinium chelates that have been universally adopted: gadopentetate dimeglumine-Gd-DTAPA, gadoteridol - Gd-HP-DO3A, gadodiamide-Gd-DTPA-BMA, gadoversetamide-Gd-DTPA-BMEA, gadobutrol - Gd-BT-DO3A, gadoterate meglumine -Gd-DOTA.

Liver-specific contrast agents with extracellular distribution are two types of contrast agents: gadobenatodimeglumine Gd-BOPTA and gadolinium acid etoxybenzylidietilenamina - Gd-EOB-DTPA.

Iron oxide particles can be classified in two categories: superparamagnetic iron oxide nanoparticles (SPIONs), with dimensions >50 nm and ultrasmall superparamagnetic iron oxide nanoparticles (USPIO-NPs), with dimensions < 50 nm.

When administered in I.V. bolus, gadolinium chelates shorten the T1 relaxation time. At the recommended dose of 0.1 – 0.3 mmol/kg, their effect consists in shortening the TR, which leads to a rise in local signal [1].

The main effect of SPIO is T2 relaxation and that is why is being used with T2 sequences [2,3]. The contrast uptake can also be visualized in T1 sequences, especially in the case of USPIO [4,5].

Objectives

The study intended to compare both the manners of hepatic lesions after administering the 2 types of contrast agents but also to trace the nature and seriousness of their side effects.

Materials and Method

A study made over a period of 22 months between 2009 and 2011 assessed the side effects of 2 types of contrast agents (SPIO and gadobutrol) administered to patients that underwent MRI investigations aimed to diagnose hepatic nodular lesions.

134 patients were included in the study, males

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and females, between 26 to 84 years old.

From the total of 134 patients, a group of 37 was examined by the double administration technique, thus having first been administered 1.4 ml SPIO (superparamagnetic iron oxide) followed by a 20-ml saline flush and then, after 15 minutes from the administration of the first agent, 0.1 mmol/kg b.w. SPIO, but without the saline flush.

The second groups, consisting of 97 patients were administered 0.1 mmol/kg b.w. of gadobutrol followed by a 30-ml saline flush.

Results

Overall, 134 patients were examined and monitored of which 86 did not present a history of hepatic disorders. The remaining 48 patients had been previously diagnosed with a hepatic disorder: cholelithiasis 26 patients, diffuse hepatopathies 18 patients and traumatic hepatopathies 4 patients.

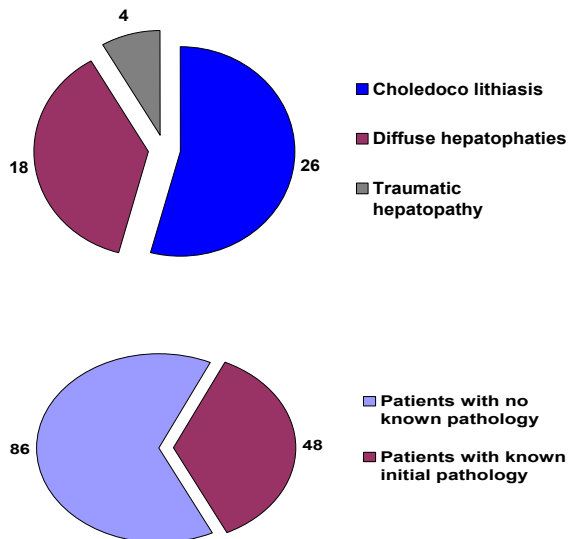


Figure 1. Pathology

From 134 patients 37 were examined with the monocontrast technique and the rest of 97 patients with the double contrast method.

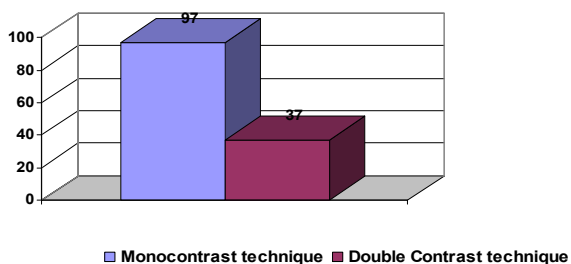


Figure 2. Number of patients for each of the two techniques

From the monocontrast method 52 were women and 45 men. In double contrast technique 21 patients were males and 16 females.

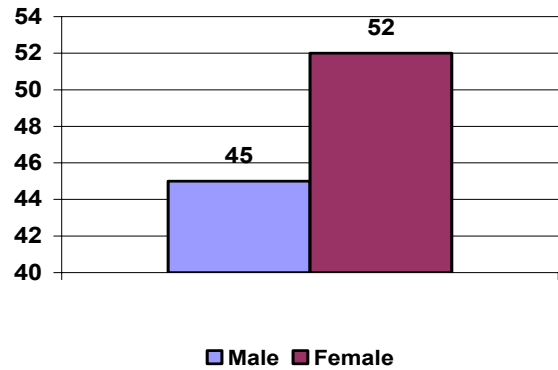


Figure 3. Monocontrast technique (sex distribution)



Figure 4. Double contrast technique (sex distribution)

Discussion

The MRI is “the gold standard” to evaluate the nodular liver, having a high sensitivity and specificity. The contrast agents used for the magnetic resonance examination are evaluated to find out if they can determine some late adverse reactions.

The study included only patients over 26 years old, none of the patients presenting alteration of renal or hepatic function; It was very difficult to follow-up all the patients from the study for a long period of time, because some of them died [5]; The other patients were evaluated periodically to follow the nodular lesions to see if their enhancement after contrast agent administration was modified or if they have grown. These patients were evaluated repeatedly renal and hepatic before the administration of contrast agents.

The protocol was with one contrast medium or with two contrast agents in the same time, so the risk of the adverse reactions was increased. It was also difficult to obtain accept from the patients because they were worried about the adverse effects.

The renal function of all patients was monitored

both before and after the administration of the contrast agent. No measurable alteration of any patient's renal function was detected. None of the patients developed any clinical or biological side effects.

The patient's age interval for both sexes was between 26-84 years, children not being included in the study.

Studies undertaken have showed that, compared to both gadolinium chelates and CT multislice exams, these contrast agents have a superior ability in detecting malignancy, having achieved a 27% and a 40% increase in sensitivity, respectively specificity [3,6,7,8,9].

In patients with renal disease severe complications may appear (Ex: nephrogenic system fibrosis) [10,11,12]. However no patient in our study developed this condition.

In November 2009 the World Organization restricted gadolinium contrast agents like Optimark, Omniscan, Magnevist, Magnegita and Gado-MRI radiopharm in patients with severe kidney problems, newborn babies up to four weeks of age and patients which are waiting or recently have received a liver transplant [13].

There is insufficient data about the possible late adverse effects in children < 2 years, therefore the administration is not recommended.

Conclusions

Gadolinium MRI contrast agents are much safer than the contrast used on CT, anaphylactic reactions being rare. There are reported in approx. 0.03-0.1% [14], in our study being none.

Sex, age or associated pathology of the patients does not represent risk factors for the development of adverse reactions. As a main disadvantage of the double contrast technique, is the utilization of two different contrast agents which increases the theoretical risk of adverse effects.

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