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Less is better? Intraindividual and interindividual comparison between 0.075 mmol/kg of gadobenate dimeglumine and 0.1 mmol/kg of gadoterate meglumine for cranial MRI

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ABSTRACT

Purpose: To retrospectively compare a reduced dose (RD) (0.075 mmol/kg) of gadobenate dimeglumine (RD-gadobenate) with standard single dose (SSD) (0.1 mmol/kg) of gadoterate meglumine (SSD-gadoterate) for cranial MRI.
Materials and methods: Thirty-one patients (12 males; aged 52 ± 16 years) underwent cranial MRI with SSD-gadoterate and repeated the examination with RD-gadobenate after a median interval of 10 months. Signal-to-noise ratio (SNR) was obtained on contrast-enhanced images for enhancing lesions ($n = 10$) as well as for right and left transverse venous sinuses, internal carotid arteries, and parotid glands. Moreover, a consecutive series of 100 cranial MRI with SSD-gadoterate (49 males; aged 51 ± 19 years) was compared with a consecutive series of 100 cranial MRI with RD-gadobenate (45 males; aged 54 ± 18 years). Two blinded neuroradiologists (R1, R2) judged contrast enhancement as sufficient, good, or optimal. Wilcoxon, Mann–Whitney, χ^2, and Cohen κ statistics were used.
Results: At intraindividual analysis, median SNR ranged 57–88 for SSD-gadoterate and 79–99 for RD-gadobenate, the latter being systematically higher, the difference being significant for both transverse venous sinuses ($p \leq 0.011$), not significant for both internal carotid arteries and both parotid glands, and enhancing lesions ($p \leq 0.101$). The two series of interindividual analysis were not significantly different for gender/age ($p > 0.415$). Contrast enhancement was optimal in 59% (R1) and 76% (R2) of patients using RD-gadobenate, in 39% (R1) and 49% (R2) of patients using SSD-gadoterate ($p \leq 0.016$), with substantial reproducibility ($\kappa \geq 0.606$).
Conclusion: Both analyses showed an equal or better contrast enhancement when using RD-gadobenate compared to SSD-gadoterate for routine cranial MRI. The high relaxivity of gadobenate allowed for a 25% dose reduction.

1. Introduction

Gadolinium-based contrast agents (GBCAs) are used for cranial magnetic resonance imaging (MRI) mainly to detect the presence of injuries of the blood–brain barrier as well to detect and characterize enhancing lesions, such as primary or secondary neoplasms or inflammatory lesions [1,2]. Moreover, GBCAs are also used to evaluate perfusion within focal lesions and normal or abnormal (e.g. ischemic) brain parenchyma [1].

Although rare, GBCAs can induce adverse events but these are seldom severe [3]. Moreover, studies have demonstrated a probable association between GBCA injection and the onset of nephrogenic systemic fibrosis in patients affected with acute or chronic renal disease [4]. Finally, the administration of GBCA is associated with a not negligible cost. Thus, strategies could be adopted in order to reduce the contrast dose without affecting contrast enhancement.

One of the most commonly administered GBCA for cranial MRI is gadoterate meglumine (Gd-DOTA, Dotarem, Guerbet, Paris, France), usually dispensed at a standard single dose (SSD) of

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0.1 mmol/kg bodyweight [5]. This contrast material has a longitudinal relaxation rate similar to that of other standard-relaxivity GBCAs. In recent years, gadobenate dimeglumine (Gd-BOPTA, MultiHance, Bracco Imaging SpA, Milan, Italy) has been increasingly applied for routine MR exams thanks to its roughly two-fold higher longitudinal relaxivity compared to the other GBCAs [6,7]. This characteristic is due to a weak binding to plasmatic proteins, leading to a significantly higher reduction of T1-relaxation time compared with that of standard relaxivity GBCAs [2].

In 2002, Schneider et al. [8] demonstrated that for liver MRI a dose of 0.05 mmol/kg of gadobenate dimeglumine provides similar diagnostic information when compared with a standard dose of 0.1 mmol/kg of gadopentetate dimeglumine. In a recent review, Giesel et al. [2] reported that a standard single dose (0.1 mmol/kg) of high-relaxivity contrast material provides greater contrast enhancement of brain lesions compared with equal doses of conventional standard-relaxivity contrast materials. Moreover, they suggested that the greatest advantage of high-relaxivity contrast materials could be the ability to lower the dose injected without sacrificing image quality or diagnostic confidence [2]. On the other hand, in a comparison of 0.05 mmol/kg of gadobenate dimeglumine and 0.1 mmol/kg of gadodiamide for the detection of brain metastasis only one out of two blinded readers demonstrated the same diagnostic performance, however, this was an inter-individual comparison rather than an intra-individual comparison and was therefore subject to differences between treatment groups in terms of patient and lesion characteristics [9].

At our institution, 0.1 mmol/kg of gadoterate meglumine had been used for cranial MRI up to February 2011. Knowing that the same dosage of gadobenate dimeglumine would have resulted in a higher contrast enhancement of brain lesions [2,10] while a half dose may have resulted in lower diagnostic performance [9], we hypothesized that a 25% dose reduction may be at least equivalent to a full single dose of gadoterate meglumine. Thus, since March 2011, we have adopted an injection protocol adopting a reduced dose (RD) of 0.075 mmol/kg of gadobenate dimeglumine for routine cranial MRI.

The aim of the current study was to compare the contrast enhancement obtained using 0.075 mmol/kg of gadobenate with that obtained using 0.1 mmol/kg of gadoterate for routine cranial MRI, using an intraindividual and interindividual retrospective design.

2. Materials and methods

2.1. Study population

The local Ethics Committee approved this retrospective study.

For the intraindividual comparison, we identified 31 consecutive patients (aged 52 ± 16 years, mean ± standard deviation; 12 males and 19 females) in our database who underwent cranial MRI twice, before and after the change of contrast material (February 2011), without any relevant clinical or imaging changes between the examinations, with a median interval between the two examinations of 10 months (interquartile interval 5–12 months). The first examination was performed using 0.1 mmol/kg gadoterate, while the second examination was performed using RD-gadobenate.

For the interindividual comparison, we identified 100 consecutive patients (aged 51 ± 19 years; 49 males and 51 females) who underwent cranial MRI before February 2011 with SSD-gadoterate and 100 consecutive patients (aged 54 ± 18 years; 45 males and 55 females) who underwent a cranial MRI after February 2011 with RD-gadobenate.

2.2. Imaging protocol and image analysis

All examinations were performed using a 1.5-T scanner (Magnetom Sonata Maestro Class, Siemens Medical Solution, Erlangen, Germany) and a volumetric head coil. Apart from the contrast material regimen, the imaging protocol did not differ among groups. All 231 patients were imaged at 4–5 min after contrast injection, as per our routine cranial MRI protocol, using axial T1-weighted spin-echo sequences (TR 500–750 ms; TE 8–20 ms; pixel size 0.81 mm^2; 1 excitation).

For the intraindividual quantitative comparison, a circular region of interest (ROI) was placed on the following anatomical structures:

- enhancing intracranial lesions (if any);
- right and left transverse sinuses;
- right and left internal carotid arteries (ICA) at the infra-petrosal level;
- right and left parotid glands;
- 10 enhancing lesions (two meningiomas and one for each of the following: rhabdomyosarcoma, pituitary macroadenoma, aneurysm of the internal carotid artery, demyelinating lesion, schwannoma of the eighth cranial nerve, radiation necrosis, metastasis from breast cancer, pineal cyst).

Measurements were performed by a final year medical student, after a 3-month training period by a neuroradiologist with 3 years of experience. Circular ROIs were adapted in order to measure the signal intensity of the most enhancing part of the vascular or parenchymal site, using a ROI not smaller than nine pixels (7.29 mm^2). A further ROI of the same size was placed in the air surrounding the patient's head in a site free from artifacts along the phase-encoding axis. Each ROI was accurately placed in a homogeneous area avoiding image artifacts. The signal-to-noise ratio (SNR) of each site was calculated as the ratio between the signal intensity of that site and the standard deviation of the noise.

For the between-group qualitative analysis, two independent neuroradiologists with three (R1) and eight (R2) years of experience, blinded to the contrast regimen and demographics, subjectively evaluated all images. They assigned a quality score to the contrast enhancement of the structures mentioned above as sufficient, good, or optimal.

2.3. Statistical analysis

For intraindividual quantitative analysis, the median SNR obtained with the two contrast regimens were compared using the Wilcoxon signed-rank test. Data were expressed as median and interquartile interval.

For interindividual qualitative analysis, age distribution was compared using Mann–Whitney *U* test. For each reader, the score assigned to the two patient groups was compared using the χ^2 test. Inter-reader reproducibility was estimated using the Cohen κ statistics.

3. Results

3.1. Intraindividual quantitative analysis

At intraindividual quantitative analysis, the median SNR ranged from 57 to 88 for SSD-gadoterate and from 79 to 99 for RD-gadobenate (Table 1). The SNR was systematically higher for all measured structures using RD-gadobenate, the differences being significant for the two transverse venous sinuses ($p \leq 0.011$). Examples of the two contrast regimens are shown in Figs. 1 and 2.