Determination of the safety of gadobenate dimeglumine in pediatric subjects referred for routine contrast-enhanced MR imaging procedures

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Purpose: Gadolinium-based MR contrast agents have long been considered extremely safe for routine diagnostic imaging. However, the advent of nephrogenic systemic fibrosis among certain patients with severe renal insufficiency has recently been brought the issue of safety into question. Nowhere is safety of greater concern than among pediatric patients who frequently require multiple contrast-enhanced MR examinations over an extended period of time. Gadobenate dimeglumine is a gadolinium-based contrast agent that has proven extremely safe among adult subjects for a variety of indications (1-4). Compared with other gadolinium agents, gadobenate dimeglumine has two unique features that make it advantageous for contrast-enhanced MR imaging of pediatric subjects; on the one hand it possesses increased relaxivity permitting the use of reduced doses to achieve comparable signal enhancement, and on the other hand it is partially eliminated by the hepatobiliary route rendering it suitable for both dynamic and delayed imaging of the liver. Although gadobenate dimeglumine is not yet approved in Germany for imaging of pediatric subjects, it is routinely used off-label at our center for this specific patient population because of these beneficial properties.

The present retrospective analysis was performed to determine the safety of gadobenate dimeglumine in pediatric subjects referred for routine diagnostic imaging for a variety of indications.

Methods and materials: A total of 201 pediatric subjects (age range: 0 years – 15 years) underwent CE MRI as part of clinical routine . Depending on the specific indication patients received a dose of either 0.05 mmol/kg bodyweight (liver, abdominal imaging, musculo-skeletal imaging, brain and other rare indications) or 0.1 mmol/kg bodyweight (cardio-vascular imaging, MR-urography). Very young patients underwent MR imaging either in sedation or general anesthesia, in case of MRA studies in congenital heart disease (CHD) patients below the age of 8 years generally underwent imaging in intubation with controlled ventilation. Since imaging was only performed in in-patients, monitoring for adverse events from the moment of injection of gadobenate dimeglumine in general was performed up to at least 24 hours post injection. Depending on the clinical necessity, laboratory measurements, and in some cases vital sign and ECG determinations were made before and after the contrast-enhanced examination. Determination of the safety of gadobenate dimeglumine was thereafter made by age-group, clinical indication and dose administered.

Age	Indications (all patients)					
	liver	cardiovascular	musculoskeletal	urography	abdomen	Misc.
0 – 6 months	5	11	4	4	18	5
0,5 – 1 year	1	2	1	-	8	3
1 – 2 years	-	3	-	1	17	10
2 – 5 years	-	9	11	-	35	11
5 – 12 years	2	35	2	5	42	8
12 – 18 years	4	28	1	4	22	4
0 – 18 years	12	88	19	14	142	41

Age	Dose (mmol/kg)	
	0.05	0.1
0 – 6 months	20	27
0,5 – 1 year	12	3
1 – 2 years	24	7
2 – 5 years	42	24
5 – 12 years	54	40
12 – 18 years	30	33
0 – 18 years	182	134

Results: No severe adverse events were noted in our patient series of 201 patients. Especially in the patient group with laboratory tests before and after injection of Gd-BOPTA no sign. changes of kreatinin and bilirubin levels were noted. However after 17 out of 316 studies performed, sign. lab value changes other than kreatinin and bilirubin were noted due to ongoing chemotherapy. These events were all rated as not related to contrast medium injection and both included sign. worsening as well as sign. improvement of lab values such as thrombocytes, liver enzymes, lactate dehydrogenase and others. A total of 48 subjects underwent 2 or more contrast-enhanced examinations while 15 underwent 3 or more, and one subject 10 examinations. Nevertheless, despite the relatively large cumulative dose of gadobenate dimeglumine in certain of these patients and the reduced renal function among the youngest patients, no detrimental effects of gadobenate dimeglumine were noticed and no patients exhibited symptoms of NSF. Image quality was excellent especially in patients that underwent CE-MRA for evaluation of CHD (Fig.1) and making use of the liver specific properties of Gd-BOPTA in follow-up imaging of patients with malignant tumors, hepatobiliary imaging allowed for differentiation between liver metastases and frequently observed regenerative liver lesions (Fig.2). The dose of 0,05 mmol/kg BW for imaging of the abdomen in patients with nephroblastoma, neuroblastom and other abdominal tumors was considered sufficient, similar to a dose of 0.1 mmol with standard extracellular Gd-agents.

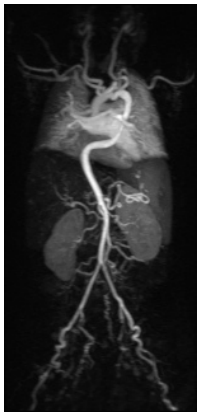

Fig. 1 CE-MRA in a 4 year old child with arterial tortuosity syndrome (0.1 mmol/kg Gd-BOPTA)

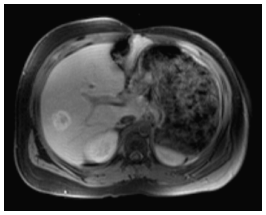

Fig.2 Regenerative hyperplasia of the liver in a 6 year old girl post chemotherapy for neuroblastoma. Hepatobiliary phase T1w fs image post 0.05 mmol/kg Gd-BOPTA

Conclusion: Based on the results of our retrospective analysis, Gd-BOPTA is a save and efficient contrast agent for imaging of pediatric patients. Both in CE-MRA with a dose of 0.1 mmol/kg BW and in abdominal and muscloskeletal imaging at a dose of 0.05 mmol/kg BW no severe adverse events were noted in a total of 201 patients and 316 studies. Especially with regard to the actual discussion on safety of Gd-based MR contrast agents, the lower dose of Gd-BOPTA in abdominal and vascular imaging seems to be beneficial.

References:

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