Contrast-Enhanced MR Imaging of the Central Nervous System in Children: Evaluation of Gadobenate Dimeglumine

M. J. Kuhn[1], P-Y. Gao[2], C. Fonda[3], E. Cianciulli[4], and M. Pasowicz[5]

[1]Radiology, Southern Illinois University, Springfield, IL, United States, [2]Radiology, Beijing Tian Tan Hospital, Beijing, China, People's Republic of, [3]Radiology, Anna Meyer Pediatric Hospital, Florence, Italy, [4]Radiology, "Santobono Pausillipon" Children's Hospital, Naples, Italy, [5]John Paul II Hospital, Krakow, Poland

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Purpose: To evaluate the safety and efficacy of the high-relaxivity contrast agent gadobenate dimeglumine (Gd-BOPTA or MultiHance) in children using an open label, multicenter, phase-III study design.

Methods: *Patient Population*: Children (ages 2- <18 years) referred for cranial or spinal contrast-enhanced MR imaging for known or highly suspected CNS disease were enrolled at one of 26 centers in North America, Europe, and China.

Study Protocol: Patients underwent contrast-enhanced MR imaging of the brain or spine with Gd-BOPTA (MultiHance, Bracco) administered intravenously at a dose of 0.1 mmol/kg dose (0.2 mL/kg) at a rate of ≤2 mL/s (manually or by power injector) followed by normal saline flush. Complete precontrast T1wSE, T2wFSE, and FLAIR sequences and postdose T1wSE sequences acquired between 3 and 10 minutes after contrast injection were performed. Brain images were acquired in either axial or coronal projections, and spine images were acquired in either axial or sagittal projections. Optional sequences were performed at the discretion of investigator.

Safety Assessment: Safety monitoring included assessment of clinical history, physical examination, pre- and post-examination monitoring of vitals signs, serial 12-lead electrocardiograms (ECG), and evaluation of pre- and post-examination blood and urine samples. Patients were monitored for adverse events for 72 hours and followed up at 30 days to determine final diagnosis.

Table 1. Safety Assessments

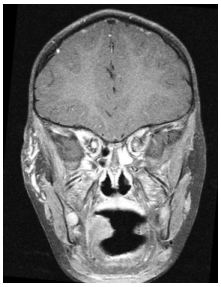
Parameter	Test	Timing
Urinalysis	Basic metabolic panel	24-hr pre- and 24-hr postcontrast
Blood	Complete blood count	24-hr pre- and 24-hr postcontrast
AE Monitoring	---	72-hr + 30-day follow-up
Vital Signs	BP, heart rate, and respiration rate	Within 1-hr pre- and 1-, 2-, and 24-hr postcontrast
Lead ECGs	---	1-hr pre- and 1-, 2-, and 24-hr postcontrast

Efficacy Assessment Pre- and postdose images were evaluated to assess the efficacy of Gd-BOPTA in terms of lesion contrast enhancement, lesion border delineation, and visualization of internal lesion morphology.

Results: *Patient Population:* Seventy one children met the inclusion criteria and were enrolled in this study to date; results are available for 41 children, (21 boys and 20 girls; mean age: 10.1 years [range: 2 – 17.4 years]). MRI was indicated for worsening symptoms, postoperative follow-up, or follow-up of untreated lesions. The mean dose of contrast was administered was 8.1 mL.

Safety Assessments: Gd-BOPTA was well tolerated by all children enrolled. Four mild adverse events have been reported to date (drowsiness, vomiting, 2 headaches). No clinically significant or serious adverse events have been reported. No clinically meaningful changes in laboratory parameters and ECGs have been observed during the study period. Modest vital sign changes (both increases and decreases) were recorded, but none of any clinical significance.

Efficacy Assessment: Pathologies studied included: malignant and benign neoplasms (eg, germ cell tumor, high-grade glioma, medulloblastoma, primitive neuroectodermal tumor, pineal cyst, pilocytic astrocytoma, fibrous meningioma, and neurofibromatosis); vascular malformations (AVM & aneurysms); and other conditions (eg, demyelinating processes, hemangiomas, pseudotumors). In all patients with enhancing lesions, assessment of lesion border delineation, definition of disease extent, visualization of lesion internal morphology, and lesion contrast enhancement were considered good to excellent with gadobenate dimeglumine. In these patients, gadobenate dimeglumine provided clinically significant information which led to a greater understanding of the disease processes found on pre-dose images.



Coronal, fat suppressed T1 weighted image through the orbital apices in a 2.5 y old boy. Image following 0.1 mmol/kg gadobenate dimeglumine shows thickening and prominent enhancement of both optic nerves, right greater than left, consistent with bilateral optic gliomas

Conclusion: Gadobenate dimeglumine a dose of 0.1mmol/kg was well tolerated by all subjects and provided excellent enhancement of enhancing brain or spine tumors. The clinical advantages of greater signal intensity with gadobenate dimeglumine in children may include: improved detection and/or diagnosis of small or poorly enhancing tumors; more precise definition of tumor borders and the extent of disease; better visualization of vascular malformations; and improved evaluation of the relationship between adjacent neurovascular structures and the neoplasm itself.

References

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