Safety of Gadobenate Dimeglumine and Other Gadolinium Contrast Agents in Intraindividual Crossover Studies

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Purpose: To summarize safety results from 5 prospective, randomized, intraindividual crossover comparison studies of gadobenate dimeglumine (Gd-BOPTA; MultiHance) with gadopentetate dimeglumine (Gd-DTPA; Magnevist), gadoterate meglumine (Gd-DOTA; Dotarem), and gadodiamide (Gd-DTPA-BMA; Omniscan) for magnetic resonance imaging (MRI) of the central nervous system (CNS).

Materials and Methods: All enrolled patients were scheduled to undergo 2 identical MRI examinations within 48 hours to 2 weeks, one with 0.1 mmol/kg bw gadobenate dimeglumine (n=375) and the other with an equal dose of comparator (gadopentetate dimeglumine [n=224], gadodiamide [n=125], or gadoterate meglumine [n=28]) (Table 1),. A total of 381 patients completed at least 1 of the MRI examinations and thus were included in this safety analysis (total of 752 examinations). Safety monitoring included vital signs, laboratory values, and adverse events (AEs). All patients were monitored for AEs from the time informed consent was obtained until 24 hours after administration of the first contrast agent, and then again from the time the second agent was administered until 24 hours after administration. Adverse events were classified as either serious (death, life-threatening, or requiring or prolonging hospitalization) or not serious (rated as mild, moderate, or severe), and the perceived relationship to the contrast agent was noted as probable, possible, not related, or unknown.

Results: In all individual trials, all contrast agents were well tolerated. Changes in vital signs and lab values were considered unremarkable and were similar in all contrast agent groups. Overall, 45 potentially-related AEs were reported following a total of 752 total examinations (6.0%). The most commonly reported AEs with all agents included nausea/vomiting, headache, dizziness, hypoesthesia, injection site reaction/pain/hemorrhage. No statistically or clinically significant differences between gadobenate dimeglumine and comparators were noted in any of the 5 studies (Table 2). No serious AEs considered related to contrast administration were reported. Most AEs were mild and self-resolving, with the exception of 6 instances in which the AEs with a possible relationship to CM were considered moderate (1 each of nausea, headache, pruritus, rash, epistaxis, and ear discomfort).Of these 6 moderate AEs, 5 (1.3%) occurred after Gd-BOPTA and 1 after Gd-DTPA (0.4%).

Table 1. Design of CNS Crossover Studies

	N	Magnet Strength	Comparator
1	28	1.0T or 1.5T	Gd-DOTA
2	27	1.5T	Gd-DTPA
3	156	1.5T	Gd-DTPA
4	126	1.5T	Gd-DTPA-BMA
5	44	3T	Gd-DTPA

Table 2. Incidence of AEs (All p=ns)

Ref	N	Gd-BOPTA	Comparator	Comparator Incidence
1	28	3/28 (10.7%)	Gd-DOTA	2/28 (7.1%)
2	27	1/27 (3.7%)	Gd-DTPA	1/27 (3.7%)
3	156	14/153 (9.2%)	Gd-DTPA	114/156 (9.0%)
4	126	4/126 (3.2%)	Gd-DTPA-BMA	1/125 (0.8%)
5	44	3/46 (6.5%)	Gd-DTPA	0/46 (0.0%)

*All p=ns

Conclusions: Based on intraindividual crossover comparisons involving over 380 patients, the safety of gadobenate dimeglumine is comparable to that of other gadolinium agents used for contrast-enhanced MRI of the CNS. Due to the higher relaxivity of gadobenate dimeglumine, this agent has demonstrated improved efficacy at comparable single 0.1 mmol/kg bodyweight doses.[1-5] Therefore, it may be possible where clinically appropriate to use lower doses of this agent compared to other Gd agents, with possible benefits in terms of patient safety and reduced costs.

References

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