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Optimization of Low-Osmolality Contrast Media for Cranial CT: A Dose Comparison of Two Contrast Agents

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A prospective, randomized, double-blind comparative study of 200 patients was made to examine the image quality, safety, and costs of 100 ml of ioversol-320 (32 g iodine) and 150 ml of iohexol-300 (45 g iodine) in patients undergoing cranial CT. We found no statistically significant difference in image quality between the two low-osmolality, nonionic contrast agents at these doses. There was a statistically significant ($p = .02$) difference in the occurrence of minor to mild adverse effects caused by ioversol ($n = 0$) as compared with iohexol ($n = 5$). No patient in either group experienced any major contrast-induced reactions. Contrast media costs were 34% less in patients receiving 32 g of iodine as compared with those receiving 45 g of iodine.

This study demonstrates that high-quality cranial CT scans are possible even with a reduced volume of low-osmolality contrast medium, and that the potential cost savings are significant.

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The advent of nonionic contrast media has brought about significant increases in patient safety and comfort. Approximately 10 million intravascular injections of contrast media are administered annually in the United States. Until recently, only high-osmolality contrast media were used. Although the use of low-osmolality, nonionic agents is associated with a reduction in toxicity, their costs have been a major deterrent to their widespread use. It has been thought that, in the United States, use of the newer low-osmolality contrast media might result in a cost increase of 12- to 15-fold as compared with the high-osmolality contrast media.

This study was designed to compare two low-osmolality, nonionic contrast agents and doses for use in cranial CT scanning on the basis of image quality, safety, and cost considerations.

Materials and Methods

Two hundred consecutive patients referred for cranial CT scanning were eligible for participation in this randomized, double-blind study. A medical history and signed informed consent for administration of contrast medium was obtained from all patients before the procedure. Eligible patients weighed greater than 50 kg and had not received any intravascular or intrathecal contrast medium during the previous 48 hr.

One hundred patients received 100 ml of ioversol (Mallinckrodt Medical, Inc., St. Louis, MO) (320 mg I/ml) and 100 patients received 150 ml of iohexol (Winthrop-Breon Laboratories, New York, NY) (300 mg I/ml). In each patient, one half of the volume of contrast medium was administered as an IV bolus and the remaining volume was infused in a drip fashion over 5 to 10 min. Cranial scanning utilizing a General Electric 9800 CT scanner (General Electric Co., Milwaukee, WI) began at the base of the skull at approximately 1 to 2 min after bolus administration of the contrast medium. All patients were closely monitored for untoward effects.

The neuroradiologists (blinded to which agent was used) reviewed the quality of the scans and rated them on a four-point grading system as: excellent (4), good (3), fair (2), or poor (1).

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Chi-square analysis was used to compare contrast media groups with respect to adverse effects and image quality. The unit dose cost of the contrast medium used was recorded.

Results

A total of 200 patients, 100 in each contrast medium group, completed the study. Both patient groups were comparable in age, sex (Table 1), and distribution of clinical diagnoses (Table 2).

None of the patients receiving ioversol experienced adverse reactions. Five patients (5%) receiving iohexol experienced minor to mild adverse effects, including dyspnea ($n = 1$), urticaria ($n = 1$), pain at the injection site ($n = 2$), and the sensation of heat ($n = 1$). The difference in frequency of adverse effects between the contrast media treatment groups was statistically significant ($p = .02$).

All contrast-enhanced cranial CT studies were determined to be diagnostic (Table 3). The difference in image quality between ioversol (mean value, 3.69) and iohexol (mean value, 3.59) was not statistically significant ($p = .5$).

The unit dose cost for patients receiving ioversol was $87 as compared with a unit dose cost of $131 for patients receiving iohexol.

TABLE 1: Patient Demographics

	Ioversol	Iohexol
Number of patients	100	100
Age range (years)	9–89	16–93
Mean age (years)	58.3	57.7
Sex		
Female	53	53
Male	47	47

TABLE 2: Distribution of Clinical Diagnoses Among Patients

Clinical Diagnosis	Ioversol	Iohexol
CVA/TIA	21	23
Confusion/dementia	11	11
Metastases	8	10
Headache	7	9
Trauma	9	5
Vertigo	5	7
Seizure	4	5
Syncope	5	4
Psychiatric disorder	3	6
Hearing problem	5	2
Glioma	3	3
Encephalitis/abscess	4	1
Meningitis	3	2
Hemorrhage	2	3
Aneurysm	2	2
Coma	1	2
Movement disorder	1	1
Meningioma	1	1
Miscellaneous	5	3
Total	100	100

TABLE 3: Rating of Diagnostic Quality of CT Scans

Rating	Point Scale	Ioversol (%)	Iohexol (%)
Excellent	4	74 ($n = 74$)	65 ($n = 65$)
Good	3	21 ($n = 21$)	29 ($n = 29$)
Fair	2	5 ($n = 5$)	6 ($n = 6$)
Poor	1	0 ($n = 0$)	0 ($n = 0$)
Total		100 ($n = 100$)	100 ($n = 100$)
Cumulative average point scale		3.69	3.59

Discussion

Choosing between high-osmolality contrast media that cost significantly less and low-osmolality contrast media that have significantly fewer adverse physiological effects presents a difficult choice. Evaluation of image quality, patient safety, and tolerability as well as cost and dose must be compared not only between high- and low-osmolality agents but also among the available low-osmolality agents. Many experts advocate the use of low-osmolality agents for a variety of reasons [1–3]. The challenge then becomes to identify the most diagnostically efficacious and cost-effective way to use low-osmolality agents.

Many European and American comparative studies of high- vs low-osmolality contrast media demonstrate essentially equal efficacy in generating diagnostic studies [3]. Our study confirmed the good image quality achievable with low-osmolality agents.

Currently in the United States, 45 g of iodine is a common dose for cranial CT scanning. However, a study in 1978 [4] that compared different total iodine doses to determine the minimal dosage requirements for clinically diagnostic cranial CT scans found that only 28–42 g of iodine were optimal for clinically diagnostic results. The authors, using a first-generation EMI scanner, suggested that even less contrast medium may be needed as the resolution capability of future CT scanners improves. Our study corroborates this speculation, showing that with present-generation CT scanners, less contrast medium is required and that 32 g of iodine is an effective, diagnostic dose of a low-osmolality agent.

Most prior guidelines for the use of contrast material have been determined empirically in regard to dose, method of administration, and the time to scan [5]. Past recommendations have called for the use of doses as high as 80 g of iodine for head CT scans [6, 7]. Such high doses were found to be most useful as a follow-up examination in patients with multiple enhancing lesions in order to identify every lesion or in cases of equivocal enhancement. High doses of contrast media were also found to be useful in the CT evaluation of temporal lobe or posterior fossa lesions. Cranial MR imaging now usually replaces high-dose contrast CT for these purposes.

Besides cost, several factors that affect safety and efficacy should be considered when evaluating a dose. Adverse effects such as renal dysfunction may be dose-related [5]. The

neurotoxicity of contrast material has been related to destruction of the blood brain barrier; the use of less contrast material is preferable in these cases [8]. A fogging effect, caused by excess contrast medium may occur, making the visualization of infarcts more difficult [9]. Each of these effects may be reduced by lowering the total dose of contrast medium.

A study in Japan by Katayama and co-workers [10] on the safety of contrast media concluded that severe reactions associated with low-osmolality contrast agents were only one sixth that associated with conventional high-osmolality agents. This poses important medical, ethical, and legal questions, based mostly on economic issues. Since the potential increase in health costs from a change in practice to the universal use of low-osmolality contrast agents would be tremendous, the need to effectively control and minimize this fiscal predicament is urgent.

One way of conserving costs is to administer the minimal effective dose of contrast medium. Our study found that a total iodine dose of 32 g (as ioversol) was just as effective and resulted in a 34% reduction in cost compared with a total iodine dose of 45 g (as iohexol).

Thirty-two grams of a low-osmolality contrast agent may not be the absolute minimal effective dose. Future investigations may show that even less than that amount may be effective for cranial CT as faster scanners with ever greater contrast resolution become available. Alternative methods of contrast delivery, such as power injectors, and additional work in determining the optimal scanning time during contrast infusion may also contribute to dose reduction.

Identifying the minimum effective dose of a low-osmolality contrast medium is important to maintain diagnostic image quality while conserving costs. This study indicates that 32 g of nonionic contrast medium provides high-quality diagnostic images at a considerably lower price than does 45 g of contrast medium. The reduced cost may make the broader use of low-osmolality, nonionic contrast media more feasible.

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The reader's attention is directed to the commentary on this article, which appears on the following pages.