A Comparison of Iopamidol and Iohexol in Cerebral Angiography

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Iopamidol and iohexol, the new nonionic low-osmolality contrast agents, have both been shown to be safe, effective, and better tolerated than conventional ionic agents for cerebral angiography. In this randomized, double-blind study involving 40 patients, these two agents were compared for adverse effects, radiographic quality, and patient tolerance. No significant differences were observed in 220 injections.

Because we found iopamidol and iohexol to be equally safe and effective for cerebral angiography, the choice of which contrast agent to use should be based on other considerations.

Iopamidol and iohexol are two new nonionic, low-osmolality contrast agents that recently were approved for intravascular and intrathecal use in North America. Extensive research in Europe and North America has established the safety and efficacy of both agents [1, 2] compared with ionic contrast media. They have been shown to cause fewer adverse effects and less patient discomfort than ionic agents in cerebral angiography [3, 4]. No studies have directly compared these two agents in angiography, and our randomized, double-blind study was designed to compare and evaluate the patient tolerance, incidence of adverse reactions, and radiographic quality produced by iopamidol and iohexol in cerebral angiography.

Subjects and Methods

Forty patients undergoing routine cerebral angiography at our institution were admitted to the study. The patients were all 18 years old or older except for one who was 14 years old. Reasons for exclusion from the study included pregnancy, bleeding disorders, significant renal or hepatic dysfunction, abnormal fluid and electrolyte balance, severe debilitation, known hypersensitivity to contrast material, or prior administration of intravascular or cholangiographic contrast material within 3 days of the procedure. The patients were otherwise randomly selected from our inpatient population, and the clinical indications for angiography included atherosclerotic cerebrovascular disease, subarachnoid hemorrhage, aneurysms, arteriovenous malformations, and tumors. Informed consent was obtained in all cases. In this double-blind, parallel comparison study, patients were assigned to either the iopamidol or iohexol group in accordance with a predesigned, balanced random schedule.

Cerebral angiography was performed in the usual manner [5] by using the Seldinger technique from the right femoral artery in most cases. Usually 5-French catheters and occasionally 4-French catheters were used for selective injections into common, internal, and external carotid; vertebral; and subclavian arteries. In some cases 6.5-French Torcon catheters were used for selective injections and 6.3-French pigtail catheters were used for aortic arch injections. All patients were premedicated with 10 mg diazepam orally. Unless contraindicated (i.e., recent hemorrhage) an intraarterial bolus of 2000 U heparin was given at the beginning of the procedure and reversed with 20 mg protamine sulfate at the end. A combination of careful double-flush technique and constant heparinized saline infusion (3000 U/500 ml normal saline) was used.

A complete history was taken and a physical examination made of all patients within 24 hr before the procedure, and the neurologic examination was repeated 24–72 hr after the

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angiogram by the same examiner. Heart and respiratory rates, blood pressure, and temperature were measured just before the procedure, and repeat measurements were obtained at 1 and 5 min after each injection, 10 min after the last injection, and every hour for 4 hr after the procedure. Serum creatinine was measured before the study and 24–72 hr after angiography.

Objective determination of patient discomfort or distress was made after each injection as absent, mild, moderate, or severe. Film quality and contrast opacification were graded as superior, adequate, poor, or nonvisualization. Patients were observed for adverse reactions for 72 hr whenever possible. The nature and duration of the adverse effect and its relationship to the contrast medium were recorded. The severity of any adverse reaction was graded as (1) mild—disappearing spontaneously or no need for therapy, (2) moderate—necessitating therapy but responding immediately, or (3) severe—alarming or life-threatening, responding poorly or slowly to therapy.

Results

The 20 patients in each group were comparable statistically with regard to age, height and weight, gender, number of contrast injections, and total volume of contrast material administered (Tables 1 and 2).

Statistical analysis of physiologic data demonstrated no significant differences in vital signs or serum creatinine either before or after angiography in either group or between the two groups. There was no significant difference in radiographic quality between the two groups. Mild discomfort after contrast injection was experienced in three patients in the iohexol group (one left common carotid and two vertebral arteriograms) and in one patient in the iopamidol group (one right internal carotid injection).

Nine patients experienced adverse reactions, four in the iohexol group and five in the iopamidol group (Table 3). In the iohexol group, one patient developed mild generalized urticaria after the last injection that lasted 24 hr and responded slowly to oral antihistamines. This reaction probably was related to contrast administration; however, the relationship of the other three iohexol reactions was uncertain. One patient with a giant fusiform vertebrobasilar aneurysm developed moderate worsening of her preexisting respiratory difficulty after the procedure. This probably was related to brainstem compression by the aneurysm and she responded to oxygen by mask. Another patient being investigated for possible aneurysm experienced a 1-min loss of consciousness immediately after injection in the left vertebral artery. This resolved spontaneously, and the cause was uncertain, possibly vasovagal in origin. One patient experienced transient dizziness after a left vertebral artery injection that resolved spontaneously.

In the iopamidol group, there were five adverse reactions to angiography, two of which probably were unrelated to the contrast material. A 30-year-old patient with a large cerebellar hemangioblastoma experienced respiratory arrest about 8 hr after the procedure. This probably was related to changes in intracranial pressure caused by the mass effect of the tumor. The patient was successfully resuscitated. Another patient with a left thalamic arteriovenous malformation had tinnitus about 15 min after a right common carotid artery injection. It

TABLE 1: Summary of Variables in Patients Undergoing Routine Cerebral Angiography with Iohexol or Iopamidol

Variable	Iohexol (n = 20)	Iopamidol (n = 20)
Gender:		
Female	8	9
Male	12	11
Mean age (years)	48.6	48.8
Mean weight (kg)	68.5	68.4
No. of injections:		
Mean	5.6	5.4
Range	1–10	2–9
Volume of contrast material (ml):		
Mean	71.9	77.4
Range	9–127	16–137

TABLE 2: Vessels Injected and Contrast Material Used in Patients Undergoing Routine Cerebral Angiography

Artery	No. of Injections		
	Iohexol	Iopamidol	Total
Aortic arch	8	9	17
Innominate	0	3	3
Right common carotid	32	36	68
Left common carotid	33	28	61
Right internal carotid	2	5	7
Left internal carotid	0	6	6
Right external carotid	1	1	2
Left external carotid	0	4	4
Right subclavian	2	3	5
Left subclavian	0	1	1
Right vertebral	7	1	8
Left vertebral	26	12	38
Total	111	109	220

TABLE 3: Adverse Reactions in Patients Undergoing Routine Cerebral Angiography with Iohexol or Iopamidol

Adverse Effect	Iohexol[a]		Iopamidol[b]	
	Related	Uncertain	Uncertain	Unrelated
Dizziness	0	1	0	0
Syncope	0	1	0	0
Limb numbness (with transient ischemic attack)	0	0	2	1
Reversible ischemic neurologic deficit	0	0	1	0
Rash	1	0	0	0
Respiratory arrest	0	0	0	1
Respiratory difficulty	0	1	0	0
Tinnitus	0	0	0	1
Total	1	3	3	2

[a] No adverse reactions in this group were known to be unrelated to the contrast material.

[b] No adverse reactions in this group were found to be definitely related to the contrast material.

lasted 10 min and resolved spontaneously without treatment. Two patients developed transient sensory symptoms that probably were of embolic origin, although the exact relationship to the contrast material was uncertain. A 44-year-old woman being investigated for transient ischemic attacks (TIAs) noticed numbness in her left leg after a right common carotid artery injection. This lasted 1 min and resolved spontaneously. Another patient being investigated for TIAs experienced mild numbness in the left hand 5 min after a right common carotid arteriogram; this also resolved spontaneously after several minutes. Finally, a 55-year-old man with TIAs developed some numbness on the right side of his face after an arch aortogram, and 2 hr later he had a left hemisensory deficit; he completely recovered within 24 hr. This reversible ischemic neurologic deficit (RIND) was probably related to an embolic event or possibly transient hypotension, but the relationship to the contrast material was uncertain.

Discussion

The new generation of nonionic contrast agents has greatly benefited patients undergoing a variety of diagnostic procedures. Extensive research in Europe and North America has demonstrated the safety, diagnostic quality, and improved patient tolerance of the nonionic agents iohexol and iopamidol relative to ionic agents in peripheral arteriography [6–8], cardiac angiography [9, 10], myelography [11, 12], urography [13, 14], and cerebral angiography [3, 4, 15]. Iopamidol has been shown to cause less experimental neurotoxicity than meglumine iothalamate or meglumine diatrizoate [15] and less patient discomfort than Conray 60 [4, 16] for cerebral angiography.

In our study we wanted to know if any differences existed between the two major nonionic, low-osmolality contrast agents (iohexol and iopamidol) during cerebral angiography. Our results indicate no significant difference between the two agents in any of the measured physiologic or radiologic parameters. Patient tolerance to the two agents was comparable, and there were no significant differences in the incidence of adverse reactions, with only one case of urticaria in the iohexol group considered to be directly related to contrast material. The only other studies directly comparing these two agents similarly showed no significant differences in any of the measured parameters in 363 patients undergoing myelography [17, 18].

There were three cases of TIAs or RINDs in the iopamidol group, and their relationship to the contrast agent was uncertain in each case. Patients with atherosclerotic cerebrovascular disease are known to be at a higher risk during cerebral angiography [5, 19], and the need for a careful angiographic technique is well recognized. When using nonionic contrast material, the radiologist should be aware that spontaneous thrombus formation can occur if the contrast agent remains in contact with nonflowing blood in a syringe or catheter for more than a few minutes [20]. This is due to the absence of significant inhibition of the normal blood coagulation mechanisms by nonionic media. These media have less anticoagulative effect than ionic contrast media do, but neither has been shown to be actively thrombogenic in vivo. No cases of thromboembolic complications caused by nonionic contrast media alone have been discovered; however, one must be aware of this potential complication. Careful flushing of catheters and syringes with heparinized saline and minimal mixing of contrast material with blood is recommended [20].

The decision to use nonionic contrast agents for cerebral angiography is somewhat controversial, primarily due to the ten- to twelvefold cost increase over conventional ionic media [21, 22]. Some centers recommend using these media only in high-risk cases, in patients with prior reactions to contrast material, or for potentially painful injections [15]. Others recommend using the new media in all cases, citing the much lower incidence of adverse reactions and improved patient tolerance [23]. With time it is probable that these new agents will replace the older ionic media in most radiologic procedures.

Our blinded randomized study of 220 cerebral angiographic injections indicates that iopamidol and iohexol are equally safe and effective for cerebral angiography, and, therefore, the choice of one agent over the other should depend on price and service considerations.

REFERENCES

1. Dawson P. Chemotoxicity of contrast media and clinical adverse effects: a review. *Invest Radiol* **1985**;20:S84–S91
2. McClennan BL. Low-osmolality contrast media: premises and promises. *Radiology* **1987**;162:1–8
3. Kido DK, Potts DG, Bryan RN, et al. Iohexol cerebral angiography. *Invest Radiol* **1985**;20:S55–S57
4. Matozzi F, Turski PA, Gentry LR, Sackett JF. Cerebral angiography: clinical comparison of iopamidol and Conray-60. *Invest Radiol* **1984**;19:S219–S221
5. Dion JE, Gates PC, Fox AJ, Barnett HJM, Blom RJ. Clinical events following neuroangiography: a prospective study. *Stroke* **1987**;18(6):997–1004
6. Mills SR, Wertman ED, Heaston DK, et al. Study of safety and tolerance of iopamidol in peripheral arteriography. *Radiology* **1982**;145:57–58
7. Kallehauge HE, Praestholm J. Iopamidol, a new non-ionic contrast medium in peripheral angiography. *Cardiovasc Intervent Radiol* **1982**;5:325–328
8. Bettman MA. Angiographic contrast agents: conventional and new media compared. *AJR* **1982**;139:787–794
9. Newman TJ. Evaluation of iopamidol in peripheral arteriography and coronary arteriography with left ventriculography. *Invest Radiol* **1984**;19:S181–S186
10. Levarstad K, Simonsen S, Skrede O, et al. Tolerability and usefulness of iohexol in cardioangiography. An open multi-centre clinical trial. *Acta Radiol [Diagn]* (Stockh) **1982**;23:535–543
11. Burrows EH. Myelography with iohexol (Omnipaque): review of 300 cases. *AJNR* **1985**;6:349–351
12. Drayer BP, Warner MA, Sudilovsky A, et al. Iopamidol vs metrizamide: a double-blind study for cervical myelography. *Neuroradiology* **1982**;24:77–84
13. Thompson WM. Excretory urography; a comparison of iopamidol and meglumine diatrizoate. *Invest Radiol* **1984**;19:S229–S233
14. Rankin RN, Eng FW. Iohexol vs diatrizoate: a comparative study in intravenous urography. *Invest Radiol* **1985**;20:S112–S114
15. Pinto RS, Berenstein A. The use of iopamidol in cerebral angiography: initial observations. *Invest Radiol* **1984**;19:S222–S224
16. Drayer BP, Velaj R, Bird R, et al. Comparative safety of intracarotid iopamidol, iothalamate meglumine and diatrizoate meglumine for cerebral

angiography. *Invest Radiol* **1984**;19:S212–S218
17. Macpherson P, Teasdale E, Coutinho C, McGeorge A. Iohexol vs iopamidol for cervical myelography: a randomised double blind study. *Br J Radiol* **1985**;58:849–851
18. Lamb JT. Iohexol vs iopamidol for myelography. *Invest Radiol* **1985**;20:S37–S42
19. Earnest F, Forbes G, Sandok BA, et al. Complications of cerebral angiography: prospective assessment of risk. *AJNR* **1983**;4:1191–1197
20. Robertson HJ. Blood clot formation in angiographic syringes containing non-ionic contrast media. *Radiology* **1987**;163:621–622
21. White RI, Halden WJ. Liquid gold: low osmolality contrast media. *Radiology* **1986**;159:559–560
22. Wolf GL. Safer, more expensive iodinated contrast agents; how do we decide? *Radiology* **1986**;159:557–558
23. Hobbs BB. The use of low osmolality contrast agents. *J Can Assoc Radiol* **1986**;37:67–68