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AJNR Am J Neuroradiol 1986, 7 (2) 303-304

<http://www.ajnr.org/content/7/2/303>

This information is current as of July 10, 2025.

Omnipaque Vs. Hexabrix in Intravenous DSA of the Carotid Arteries: Randomized Double-Blind Crossover Study

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A randomized double-blind crossover study using Omnipaque 350 mg I/ml (iohexol) and Hexabrix 320 mg I/ml (ioxaglate) in 53 patients undergoing intravenous digital subtraction angiography of the carotid arteries revealed no significant differences in image quality. Some differences were found in subjective side effects that favored Omnipaque. Nausea was reported in four patients after injection of Hexabrix, and a metallic taste was significantly more frequent ($p < 0.01$) with this contrast medium. The patients' preference for Omnipaque was also statistically significant ($p < 0.01$). It was concluded that both contrast media are suitable for intravenous digital subtraction angiography.

Despite several limitations in the interpretation of intravenous digital subtraction angiography (IVDSA) [1, 2], there is a widespread acceptance of this imaging technique in patients with suspected carotid artery disease. To reduce the deterioration of image quality caused by swallowing and motion artifacts, some authors advocate nonionic rather than ionic contrast media [3–5]. Our study was undertaken to compare the nonionic monomeric contrast medium Omnipaque (iohexol) with the ionic dimeric Hexabrix (ioxaglate) with respect to subjective side effects and image quality and to try to derive useful guidelines for the choice of contrast media for IVDSA of the carotid arteries.

Subjects and Methods

IVDSA of the carotid arteries was performed in 53 patients, 21 women and 32 men 23–77 years old (mean, 56), with symptoms from the internal carotid arteries, especially transient ischemic attacks (TIAs). Only patients who were uncooperative or hypersensitive to iodine-containing agents were excluded from the study. No premedication was given. Informed consent was obtained from all patients.

The head and neck were fixed in a foam rubber device to restrict motion. After catheterization of the superior vena cava via an antecubital vein in 46 patients and transfemoral catheterization of the inferior vena cava in seven patients, 40 ml of contrast medium was injected each time. The injection rate was 15 ml/sec. A full examination of the extracerebral carotid arteries required four to five injections. Omnipaque 350 mg I/ml (osmolality 0.88 mol/kg H₂O) and Hexabrix 320 mg I/ml (osmolality 0.58 mol/kg H₂O) at body temperature were used in the first two injections performed as a double-blind crossover test under identical conditions with the patient in the right anterior oblique projection. There was a 5 min interval between injections of contrast agents. The code of the injection sequences was not broken until all 53 examinations were evaluated.

The evaluations of the subjective side effects were completed immediately after the injections using standard questions. The patients were asked to evaluate the intensity of pain, nausea, metallic taste, and other possible side effects as none, mild, moderate, or severe. After the last of the two blind injections a comparative evaluation was performed.

Standard procedure for postprocessing from the tape was performed to obtain the best possible image from each injection sequence. The image quality was evaluated independently by three radiologists. To evaluate the image quality, contrast medium density, superimposition, electronic noise, patient motion, swallowing, and motion from arterial wall calcifications were considered. The image artifacts from motion and swallowing were graded as none, slight, moderate, or severe. A Wilcoxon signed rank test was used for the statistical evaluation. The significance level was 5% ($p < 0.05$).

Received April 4, 1985; accepted after revision August 6, 1985.

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AJNR 7:303–304, March/April 1986

0195–6108/86/0702–0303

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TABLE 1: Evaluation of Subjective Side Effects (Crossover Testing)

	Omnipaque (n = 53)	Hexabrix (n = 53)
Heat:		
None	4	2
Mild	39	37
Moderate	10	13
Severe	0	1
Metal taste:		
None	52	39
Mild	1	13
Moderate	0	1
Nausea:		
None	53	49
Moderate	0	3
Severe	0	1*
Patient preference (%)	19 (35.8)	4 (7.5)

* This patient also experienced vomiting.

TABLE 2: Frequency and Severity of Artifacts (Crossover Testing)

	Omnipaque (n = 53)	Hexabrix (n = 53)
None	29	27
Slight	15	12
Moderate	9	12
Severe	0	2

Results

The frequency and intensity of subjective side effects appear in table 1 and the image quality with regard to artifacts in table 2. The slight differences in favor of Omnipaque with regard to heat reactions, nausea, and pain were not statistically significant. The metallic taste after Hexabrix injections in 14 patients was statistically significant ($p < 0.01$). The patients' preference in favor of Omnipaque was statistically significant as well ($p < 0.01$). Slightly fewer artifacts from motion and swallowing were found with Omnipaque; however, the difference was not statistically significant. Severe artifacts, that is, nondiagnostic images, occurred with Hexabrix in two patients.

In five elderly patients, the image quality was reduced with both contrast media due to slow cardiopulmonary circulation with loss of the bolus effect. The overall image quality with regard to all parameters tested did not reveal any statistically significant differences between the contrast media. The diagnostic efficacy was evaluated as excellent or good in 45 patients (85%) and poor in eight (15%).

Discussion

In our own experience and that of others [6], cardiac function and the ability to remain motionless during data acquisition are the two main factors that may impair image quality of IVDSA. The latter may be influenced to various degrees by the different contrast media. According to previous experience in comparative angiographic contrast media studies [5, 7, 8] the double-blind crossover technique with the patient acting as his own control seemed to allow the most accurate evaluation of the properties of these two new contrast media. A former study [5] demonstrated a significant improvement in both discomfort and image quality of IVDSA of the carotid arteries when Omnipaque was used instead of

the monomeric ionic Isopaque (meglumine metrizoate). The improvement is most striking in elderly or noncooperative patients.

Our study revealed only small differences between the nonionic monomeric Omnipaque and the ionic dimeric Hexabrix, although statistical significance in favor of Omnipaque was found with regard to patients' preference. Omnipaque, contrary to Hexabrix, is reported not to induce the so-called "hangover phenomenon," that is, an exacerbation of side effects in a subsequent contrast medium injection [9]. Consequently, the nausea and vomiting experienced with Hexabrix are probably related solely to the contrast medium itself. The higher frequency of side effects is probably related to the higher protein binding, the more extensive liberation of histamine, and the greater inhibition of enzymes by Hexabrix than by Omnipaque [10, 11]. Any effect of the small differences in iodine concentration, viscosity, and osmolality of the two contrast media are difficult to evaluate, but probably are without significance.

Although no statistically significant differences in image quality were found, the technical failures in two patients (4%) caused by motion artifacts with Hexabrix reflect the somewhat better tolerability of Omnipaque.

We conclude that both contrast media are well suited for IVDSA and that the selection of one or the other has no statistically significant major implication on the quality of the examination or on the subjective side effects related to the injections of the contrast media.

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