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Clinical Testing of Omnipaque and Amipaque in External Carotid and Vertebral Angiography: Randomized Double-Blind Crossover Study

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Omnipaque, 300 mg I/ml, was compared with Amipaque, 300 mg I/ml, for cerebral angiography. Twelve patients were included in a randomized, double-blind, crossover study. Twenty comparisons were made in the external carotid and 21 in the vertebral artery. Both contrast media caused no or minor changes in blood pressure and heart rate. Good to excellent radiographic visualization of the cerebral arteries was obtained with both agents. The frequency of subjective reactions was almost equal, but the intensity of the reactions was less with Amipaque. No severe reactions were observed. Omnipaque is a more practical nonionic contrast medium than Amipaque because it is delivered in ready-to-use solutions.

Omnipaque (iohexol) is the second nonionic contrast medium developed by Nyegaard, Oslo, Norway. It is stable in solution and supplied ready-for-use in several concentrations. Amipaque, the first nonionic contrast medium, was earlier proven to be the best tolerated contrast medium in cerebral angiography [1, 2]. Comparative crossover and parallel studies of Omnipaque and ionic media, and Omnipaque and Amipaque for cerebral angiography have shown similar advantages for this new medium [3-8]. On the basis of these observations, a clinical trial was performed comparing Omnipaque with Amipaque for injection into two pain-sensitive vessels (external carotid and vertebral arteries). The investigation was carried out in the neuroradiologic section of the department of radiology, Aalborg Hospital, as a double-blind trial with the patient as his own control.

Subjects and Methods

Twelve patients were examined during the 1 month study period, yielding 41 comparisons. The median age was 41 years (range, 20-67). All studies were carried out under local anesthesia. All patients gave informed consent in accordance with the revised Helsinki Declaration and applicable government regulations in Denmark. None of the patients had electrocardiographic (ECG) abnormalities of clinical significance. No patients were excluded. All the angiograms were obtained by the same radiologist using the transfemoral Seldinger technique.

The patients were fasted and phenobarbital 100 mg and atropine 0.5 mg intramuscularly were used as premedication. After selective injection of contrast material, one to four comparisons were performed in each patient according to the diagnostic information needed. The contrast medium injected first was according to a random code prepared by Nyegaard. The injections were made with identical syringes, and the identity of the contrast medium was unknown to the radiologist and patient. Both contrast media had a concentration of 300 mg I/ml and were preheated to 37°C. The total median volume of contrast medium injected was 95 ml (range, 26-104 ml).

For selective injections in both arteries, 8 ml of contrast medium was injected at a rate of 8 ml/sec. The contrast injection and exposures were controlled by a punch-card system so that uniform conditions could be achieved.

A Mingograf 82 (Siemens-Eléma) was used to record the various parameters. The ECG was recorded, and injections and exposures were noted. The arterial blood pressure was

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TABLE 1: Sensation of Warmth during Contrast-Medium Injection

Artery: Contrast Medium	Reaction (No.)				Totals
	None	Mild	Moderate	Severe	
External carotid:					
Omnipaque	0	10	9	1	20
Amipaque	0	16	4	0	20
Vertebral:					
Omnipaque	4	11	6	0	17
Amipaque	4	15	2	0	17

TABLE 2: Discomfort/Pain During Injection of Contrast Medium

Artery: Contrast Medium	Reaction (No.)				Totals
	None	Mild	Moderate	Severe	
External carotid:					
Omnipaque	0	8	10	2	20
Amipaque	0	15	5	0	20
Vertebral:					
Omnipaque	7	6	7	1	14
Amipaque	10	9	2	0	11

recorded continuously via the catheter used for the injection from about 30 sec before up to 1 min after injection. The heart rate was determined by the R-R interval of the ECG.

A blind evaluation of the radiographic visualization of the pair of angiograms was performed using the following ratings: 0, no visualization; 1, poor; 2, good; and 3, excellent.

The patients were closely observed in the radiology department for any signs of reaction or adverse effects during and up to 30 min after the examination and were also questioned 24 hr after angiography. Sensation of warmth and discomfort/pain were asked for specifically. This was done in order to detect even small differences between the two contrast media. The intensity of the patient's reactions was graded as: 1, mild; 2, moderate; or 3, severe.

Data Processing and Statistical Analysis

The data were processed by the statistical department at Nye-gaard. For continuously recorded variables the median was used as an index of location, and the range or the interquartile range was used as an index of dispersion. In order to determine whether observed differences in location were statistically significant, a two-sided Wilcoxon signed rank test was used. For parameters recorded on a graded scale (e.g., subjective reactions and diagnostic information), the results were presented as frequencies, and the significance tests were carried out with correction for ties. The level of significance used was 5%. The contrast medium code was not broken until after completion of the tabulation and statistical analysis of the data.

Results

Forty-one comparisons were performed in 12 patients, four women and eight men. Twenty comparisons were made of external carotid artery studies and 21 of vertebral artery studies. The systolic and diastolic blood pressures and heart rate recorded during each injection showed no or minor transient changes. Small deviations in these physiologic parameters between the media compared were not found to be statistically different nor were the deviations between the before and the 1 min after observations. ECG changes were only observed in one patient. In this patient a few extrasystoles appeared after each injection with both contrast media. All the angiograms were judged to be good or excellent, and no difference in the radiographic visualization was demonstrated between Omnipaque and Amipaque.

The sensations of warmth after injection of contrast media

are stated in table 1. In both arteries the frequency of sensation of warmth after the injections was equal. The intensity of warmth was, however, smaller after the Amipaque injections, and the difference was found to be statistically significant ($p < 0.05$). As shown in table 2, the frequency of the immediate discomfort/pain reactions after the injections was about the same in both arteries for both media. Also in this comparison the intensity reaction was smaller after the Amipaque injections and the difference was statistically significant ($p < 0.05$).

All the subjective reactions were transient and serious reactions were not observed. No other contrast-induced adverse reactions were encountered up to 24 hr after angiography. Because of the small number of patients investigated, we could not assess the influence of age or of the order in which the agents were injected.

Discussion

The absence of serious reactions and the absence of differences between Omnipaque and Amipaque with respect to blood pressure, heart rate, and ECG confirmed earlier statements [3, 6-8] that both nonionic contrast media have good cardiovascular tolerance. While with both Omnipaque and Amipaque some warmth, discomfort, and pain followed administration of the contrast agent, the intensities of these sensations were significantly less for Amipaque in both arteries. This agrees with the tendency detected in an earlier study performed at Aalborg Hospital [7]. Contrary to this observation are the findings of two other centers [6, 8], in which no differences between the two media were demonstrated.

Omnipaque is easier to use than Amipaque because it is delivered in ready-for-use solution. In animal pharmacologic and toxicologic studies [9] Omnipaque was found to be better tolerated than Amipaque after intracisternal and intracerebral administration of small doses. Selective injections into the internal carotid artery of rabbits [9] showed that Omnipaque caused fewer injuries to the blood-brain barrier than did Amipaque. The above-mentioned advantages outweigh the small difference in minor subjective reactions. Omnipaque is considered a successful product of continued research for a better and more practical contrast medium for cerebral angiography.

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