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Randomized Double-Blind Cross-over Study of Iohexol and Amipaque in Cerebral Angiography

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Iohexol was compared with Amipaque (metrizamide) in a double-blind study in one pair of injections in each of 20 patients referred for routine cerebral angiography. Catheter position, patient position, injection pressure, contrast medium volume, and concentration (300 mg I/ml) were the same in the two injections, with iohexol and Amipaque being used alternately. Except for these two injections iohexol was used throughout. The parameters studied included diagnostic information obtained (quality of the examination), circulation time, and comparison of patient reactions to the pair of injections (e.g., electrocardiogram, heart rate, and subjective reactions). The patients' reactions to the noncomparative part of the examination were evaluated also, and the patients were observed for possible adverse reactions after the examination. No difference could be detected between the two contrast media in this series. No serious adverse reactions occurred.

Amipaque (metrizamide) is better tolerated in the cerebral vessels than ionic contrast media [1, 2]. Iohexol, a new, nonionic contrast medium, has been found to be well tolerated in cerebral angiography [3-6]. From a practical point of view, iohexol would have advantages over Amipaque. Therefore, a comparison of the two contrast media was performed in a double-blind series in which the patient was his own control.

Subjects and Methods

The study was conducted as a double-blind randomized cross-over study where iohexol was compared with Amipaque (both 300 mg I/ml) in one pair of injections in each patient. Known iohexol was used on an open basis during the catheterization procedure and for all injections other than the pair in which the comparison was performed.

Twenty-three conscious and cooperative adult patients referred for cerebral angiography were admitted to the study. Emergency patients and patients in whom catheterization difficulties could be expected were not admitted. Three cases were excluded from the final evaluation. (Technical failure, which prevented adequate comparison of the injections, was responsible for these exclusions.) No reactions of any significance occurred in these three cases. The final data evaluated therefore consisted of 20 cases in which one comparison between Amipaque and iohexol injections was performed. There were 10 men and 10 women in this series, aged 36-38 years.

The patients were fasted, and, except in two cases where 0.6 ml atropine 1.0/0.0 was given subcutaneously before the examination, no premedication was given. Routine cerebral angiography with Seldinger technique by the femoral route was performed.

The contrast media for this comparison were delivered in identically coded vials, and the medium to be used first and second was randomized in each case. The hospital pharmacy was responsible for dissolving the Amipaque and for the delivery of the two contrast media. The contrast media were injected at room temperature. Iohexol and Amipaque (each 300 mg I/ml) were injected alternately in each patient with the catheter in the same position. The same volume of each medium was used. Films were exposed according to our standard routine, but detailed assessment of their quality was performed only for those in which the two contrast media were compared, using the subjective assessment of poor, good, or excellent.

The circulation time was measured from the appearance of contrast medium in the siphon to the filling of parietal veins, and was compared for the two contrast media. The overall quality of the whole examination was also recorded. The heart rate, obtained from the R-R interval of the electrocardiogram (ECG), was recorded just before, during, and just after both injections. Possible ECG changes were also recorded. The patients were closely observed in the radiology department for any signs of reactions or adverse effects during and up to 60 min after the examination. If indicated, the patients were also interviewed after 24 hr. A standardized pattern for asking the patients about possible subjective reactions was used. Adverse reactions were classified if possible as contrast medium-related, disease-related, or procedure-related. The intensity of the subjective reactions was graded as mild (1), moderate (2), or severe (3), and in the paired comparisons intermediate intensities (1.5 = mild to moderate, 2.5 = moderate to severe) were also used. In the paired comparison patients were also asked to state their preference for the first or the second injection.

The median and range or interquartile range were used as indices of location and dispersion. Range was used for age, weight, and volume injected, while interquartile range was used for all other parameters. In order to decide whether an observed difference between the two contrast media was statistically significant, a two-sided Wilcoxon signed rank test with correction for ties was used. This statistical method is based on the difference between pre- and postexamination values for each individual patient, not on the median values. A significance level of $p < 0.05$ has been used. No statistically significant differences were found.

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Results

In the 20 cases included in this study iohexol and Amipaque were compared in the common carotid artery in 15 cases, in the internal carotid artery in two cases, in the vertebral artery in two cases, and in the external carotid artery in one case. The median dose was 10 ml in the common carotid artery, 8 ml in the internal and external carotid arteries, and 9 ml in the vertebral artery for both contrast media. The total dose of contrast medium given to a single patient was 75–250 ml, the median total dose being 163 ml. It should be repeated that the total examination was performed with iohexol in all cases except for one injection of Amipaque.

The vascular visualization and the diagnostic information in the selective injections in which the two contrast media were compared were good in six cases and excellent in 14 cases for both iohexol and Amipaque. The median circulation time was 3.8 sec for iohexol and 3.7 sec for Amipaque. No statistically significant difference was found between the two media with respect to visualization or circulation time. No statistically significant difference in heart rate alterations between iohexol and Amipaque was found, nor were any ECG changes observed in any of the patients. No difference was found between the two media with respect to frequency or intensity of subjective reactions (e.g., sensation of warmth, bad taste, seeing "stars," salivation, feeling unwell, and pressure), and there were no serious adverse reactions.

The evaluation of the patient preference also showed that the two media were equally well tolerated. Nine patients stated better tolerance for the iohexol injection and eight for the Amipaque injection. Three patients found the two injections equal. Fifteen of the 17 patients who stated a preference preferred the first injection. Iohexol and Amipaque were both given as the first of the pair in 10 cases.

Patient reactions occurring during the noncomparative part of the examination were also evaluated. No adverse reactions occurred after the examination. The only kind of reaction during the examination with known iohexol was a sensation of warmth occur-

ring in all patients who received such injections. The sensation of warmth was short-lived in all cases. In most cases it was graded as mild, but three patients had a moderate sensation of warmth after one or more injections.

Discussion

The very small difference in patient reactions was obvious. The analysis of the results clearly indicates that no difference was detected between the two contrast media. Since Amipaque in previous studies has been proven to be an excellent contrast medium for cerebral angiography [1, 2], this comparative study indicates iohexol to be the same.

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