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Comparison of Side Effects during Cerebral Computed Tomography with a Nonionic (Iohexol) and an Ionic (Metrizoate) Contrast Medium

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Cerebral computed tomography was performed in 60 patients referred for pre- and postcontrast scanning. The patients were randomly sampled with a nonionic contrast medium, iohexol, and an ionic contrast medium, sodium metrizoate. No complications were seen, and the adverse effects, usually a feeling of warmth, were very minor with both contrast media, but iohexol caused less discomfort than sodium metrizoate. A series of measurements of the attenuation values of well defined intracranial structures was performed and no difference in enhancement was found between the two contrast media.

Although the importance of intravenous injection of contrast media for enhancement of pathologic lesions in cerebral computed tomography (CT) has been documented in numerous publications, very few reports comparing the effects of various contrast media have been published [1]. No clinical study comparing nonionic and ionic contrast media in CT has hitherto been reported. One would not expect a priori to find differences in the enhancement properties of monomeric nonionic and ionic contrast media, since their molecules are of about the same size. However, the possibility cannot be excluded since minor differences were found in a recent experimental animal study comparing nonionic and ionic contrast media in CT of the liver in pigs [2].

The introduction of nonionic contrast media in myelography and angiography has reduced the frequency of adverse effects in these procedures [3–5]. Thus, one of the intentions with the present study was to find out whether the frequency of adverse effects was reduced after intravenous injections of a nonionic contrast medium.

Our study was performed as a double-blind clinical trial comparing the ionic contrast medium sodium metrizoate (Isopaque) with the nonionic compound iohexol (fig. 1) [6]. The recording of adverse effects was performed by using standardized questions in addition to careful recording of any signs caused by the contrast medium. To study the enhancement properties a series of measurements was performed in various well defined anatomic structures.

Subjects and Methods

We studied 60 consecutive patients (ages 19–79 years) referred for cerebral CT during ordinary working hours and scheduled for scanning pre- and postcontrast medium administration. Only co-operative patients were included and informed consent was required. The age and gender distribution of the patients is in table 1. The examination was performed with a Delta-50 body scanner (Ohio

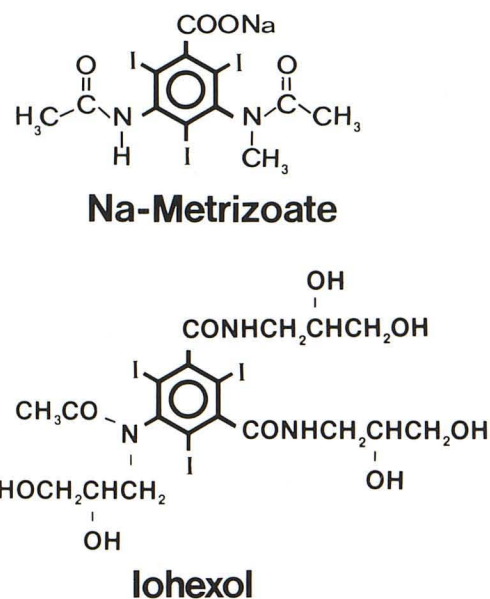


Fig. 1.—Structural formulas for sodium metrizoate (Isopaque) and iohexol.

Nuclear) using 13 mm slices angled 10° cranial to the orbitomeatal line, starting at the base of the skull. After the precontrast scan 80 ml of contrast medium with an iodine concentration of 350 mg/ml was injected intravenously, and the injection time was recorded. The patients were randomly chosen for one of the two contrast media, which were supplied in code-numbered vials so that neither the patients nor the staff knew which contrast medium was given. The first postcontrast scan was started 5 min after injection of contrast medium. At the end of the injection the patients were asked the following standardized questions: (1) "Did you feel anything?" If the answer was no, no more questions were asked. If the answer was yes, the next question was: (2) "What did you feel?" Then: (3) "Was it unpleasant?" and (4) "Was it painful?" In addition to the interview all adverse effects occurring during the examination were recorded.

The mean injection time for the two contrast media was the same, 88 sec for both. The examination time (from the first precontrast scan until the patient was removed from the scanner) was 27 min for the iohexol group and 28 min for the metrizoate group.

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TABLE 1: Gender and Age Distribution of Patients Studied with Iohexol and Metrizoate

Contrast Medium	Men	Women	<50 Years	>50 Years
Iohexol	18	12	14	16
Metrizoate	15	15	20	10
Totals	33	27	34	26

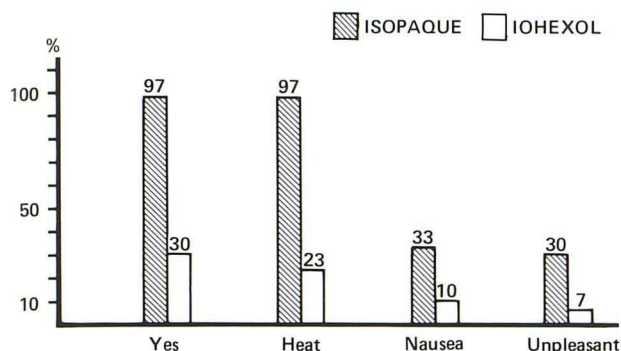


Fig. 2.—Adverse effects after intravenous injection of 80 ml contrast medium. Paired columns 1–4 represent percentages of patients who: (1) answered yes when asked, "Did you feel anything?," (2) and (3) answered heat, nausea, or both when asked, "What did you feel?," (4) answered yes when asked, "Was it unpleasant?" The differences in columns 1 and 2 are statistically significant ($p < 0.01$); the difference in column 3 is not significant, in column 4 significant at $p < 0.05$.

Attenuation measurements were performed in the following anatomic regions: (1) white matter in the centrum semiovale, (2) gray matter in the cortex away from the skull, (3) head of the caudate nucleus, (4) straight sinus in the confluens sinuum, and (5) falx cerebri. Measurements 1–3 were performed in a 52 pixel area and 4 and 5 in a 4 pixel area. The chi-square test was used for the statistical evaluations.

Results

No complications were seen and all the adverse effects were minor and would probably have escaped notice without the routine questioning of the patients. The results of the questioning appear in figure 2, which shows the kinds of reactions in those patients who felt sensations during the injection. In addition to these reactions one patient had a short period of dyspnea and one had palpitations, both after injection of metrizoate. Local pain at the site of injection occurred in another patient during injection of metrizoate and the injection was therefore stopped after 40 ml.

An abnormal CT scan was found in 10 patients, but the adverse effects in this group did not differ from those with a negative CT examination. The results of the attenuation measurements appear in table 2. No difference was found between iohexol and metrizoate.

Discussion

The adverse effects were very minor with both iohexol and metrizoate, but they were somewhat more prevalent with metrizoate. The clinical implication of these findings is not very impressive,

TABLE 2: Mean Attenuation Values before and after Intravenous Injection of 80 ml Contrast Medium with an Iodine Concentration of 350 mg/ml

Area: Time	Mean Hounsfield Units		
	Iohexol	Metrizoate	Totals
White matter:			
Before	28	28	28
After	28	29	28
Gray matter:			
Before	33	34	34
After	35	35	35
Caudate nucleus:			
Before	32	32	32
After	33	33	33
Straight sinus:			
Before	34	35	35
After	54	52	53
Falx cerebri:			
Before	36	37	37
After	47	48	48

Note.—There were 30 patients in each group.

since the discomfort experienced by the patients after injection of the ionic contrast medium was so minor that it would probably not justify the increased costs of a nonionic contrast medium. However, we do not answer the question whether nonionic contrast media might reduce the frequency of serious and fatal reactions. Such reactions are so rare, about one death/40,000 intravenous injections [7], that larger, multicenter studies will be necessary to solve this problem.

No differences in the frequency of adverse effects were seen between patients with a normal and a pathologic cerebral CT examination, but the number of patients was too small to draw any conclusions from this. The known reduction in toxicity in the non-ionic compounds may eventually prove to be of importance, since it has been shown that the prognosis of cerebral infarction is poorer in patients in whom postcontrast scans are obtained with a contrast medium (ionic) than in patients examined without contrast medium [8, 9].

No difference in attenuation measurements was found between ionic and nonionic contrast media. These results agree with those of Gado et al. [10], who found no significant enhancement of normal brain tissue and marked enhancement of the straight sinus after intravenous injection of 100 ml meglumine iohalamate 60% using a first-generation EMI scanner. It is unlikely that scanners more modern than the second-generation unit used in our study will alter our conclusions, since contrast resolution, which is the important quality factor in the present study, has not been improved with the third-generation scanners.

In conclusion, very minor adverse effects were recorded with both iohexol and metrizoate, but iohexol caused discomfort much less often than did metrizoate. No differences in enhancement of normal intracranial structures were found.

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