COMPARISON OF THE CARDIOVASCULAR EFFECTS
OF CONTRAST MEDIA IN CEREBRAL
ANGIOGRAPHY IN MAN*

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Cerebral angiographic contrast media recently have been compared on the basis of their cardiovascular effects after intracarotid injection in experimental animals. In the dog and cat abnormalities of cardiac rhythm and rate, arterial and venous blood pressure, and cardiac output were observed and related to the nature and the amount of the contrast material used. Three agents were tested in our laboratory. All three were triple-iodinated benzene-ring derivatives, varying in their side-chain structures. The methylglucamine salt of the diatrizoate compound (Cardiografin, Renografin) resulted in the fewest disturbances, the sodium salt of the diatrizoate compound (Hypaque) was intermediate in its effect and the acetrizoate compound (Urokon) produced the most apparent disturbances.

Although the differences in the observed responses of the laboratory animals to these compounds were quite definite, it was felt desirable to compare the reactions to the same agents during human cerebral angiography. The doses injected in the dog (0.15 and 0.30 ml./kg. of body weight) were higher than those used in a single injection in clinical angiography. A 7-ml. injection of contrast material in a 70-kg. patient represents 0.10 ml./kg. However, because of the differences in the relative calibers of the common, internal and external carotid arteries, the internal carotid artery of the dog received a smaller portion of the contrast media injected into the common carotid artery than the corresponding vessel of man. Since the lower incidence of experimental disturbances associated with sodium and methylglucamine diatrizoate led us to expect less morbidity, only these two agents were tested in our patients. In previously reported electrocardiographic studies following injection of sodium diatrizoate and methylglucamine diprotiztoate (Miokon) only electrocardiographic changes were found. These showed no qualitative or quantitative differences for the two compounds.

METHOD

The patients were unselected as to lesion, age and sex. There were 8 males and 3 females. The age range was 16 to 67 years. Angiography was indicated on the basis of the three following clinical diagnoses: Seizures, suspected brain tumor, and subarachnoid hemorrhage. All injections were done percutaneously into the common carotid artery, the patient lying supine. The technic was not varied except for change in position of the head as required by the radiographic examination.

Comparison was made between two injections of 6–10 cc. each into the common carotid artery. Each medium was used twice in each patient for a total of four injections. When more than four injections were made the additional injections were disregarded for purposes of this study. The sequence of injection of the two contrast solutions was randomized to exclude the effect of the order of injection. A 50 per cent solution of sodium diatrizoate (Hypaque) and a 60 per cent

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solution of methylglucamine diatrizoate were tested, since these two concentrations are equivalent in iodine content upon which their radiopacity depends. Renografin (60 per cent) was utilized as the methylglucamine compound. Although 13 per cent of its content consists of sodium salt, it was a preparation already available commercially and was considered of sufficiently high methylglucamine-salt content to be representative. To inject the somewhat more viscous Renografin, a stronger thrust of the syringe was used; otherwise the rate of injection was not controlled. Films were reviewed to insure comparable diagnostic quality from the two media. Arterial blood pressure was measured with a Statham strain gauge, connected to a needle inserted percutaneously into the right femoral artery. Blood pressure and a standard limb lead of the electrical potentials of the heart were recorded simultaneously with a Sanborn oscillograph.

**RESULTS**

Eight patients showed some changes in either arterial blood pressure or cardiac rate, or both. Among 43 separate injections, 15 “abnormal” responses were noted. Fall in blood pressure and slowing of the cardiac rate were observed in 11 instances, while change in cardiac rate alone was seen on 4 occasions. In general, these responses were minor and brief. The fall in systolic and diastolic arterial blood pressure, expressed as a fall in mean arterial pressure, was 10–20 mm. Hg, except in 1 instance, in which it measured 50 mm. (Fig. 1). The fall usually lasted for only 2 to 5 sec. However, in 3 instances it persisted for 15 to 20 sec. On 2 occasions, following recovery from the initial fall in blood pressure, a rise of 15 to 25 mm. Hg above the pre-injection level was seen.

The cardiac disturbances usually consisted of a transient slowing of rate and occasionally atrial premature beats. No other disturbance of cardiac mechanism was noted. The slowing in most instances lasted for only 2 to 5 sec.; however, in 2 instances a decrease in rate to 50 per cent of the pre-injection value persisted for 10 sec.

In 3 patients no change in either blood pressure or cardiac rate was observed. One of the 3 was operated upon during general anesthesia with methoxyfluorine without premedication; another, during general anesthesia with methoxyfluorine, premedicated by Demerol and scopolamine; and the third, during local anesthesia without premedication.

Of the 11 instances in which a fall in blood pressure occurred, 9 were considered to be “significant.” In 8 instances this fall was slight, and persisted for a short time only. In one instance, however, the fall was marked, and ocurred more slowly. The upper record in Fig. 1 (a) is the blood pressure curve of 1 patient during injection of 7 ml. of 50 per cent Hypaque. The pre- and postexamination diagnoses were intracranial aneurysm.

The upper record represents systemic arterial blood pressure; the lower record lead II of the electrocardiogram. One-sec. intervals are marked on the time line. Time of injection is indicated within the arrows.

With Hypaque (a) a fall of 50 mm. of systolic and 35 mm. diastolic blood pressure was recorded, and the cardiac rate slowed. Twenty sec. elapsed before recovery of pre-injection levels occurred. With Renografin (b) no significant changes in blood pressure and cardiac rate were recorded. [Both (a) and (b) are reproduced on same scale.]

![Image of blood pressure graph](image-url)
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pressure and slowing of cardiac rate appeared, 10 occurred with the sodium salt and only 1 with methylglucamine compound. With respect to change in cardiac rate, each compound accounted for 2 instances. The position of the head and the amount of injection did not appear to influence the number of positive responses. In no patient was a response to the methylglucamine but not to the sodium compound noted. Six patients reacted to the sodium salt, but not to methylglucamine. Two patients reacted to both compounds. The reactions proved to be slightly more severe to the sodium salt than to the methylglucamine.

Comparing the angiograms in lateral position in which first one and then the other agent was injected, the posterior communicating and posterior cerebral arteries were demonstrated in 5 patients. In the remaining 6 patients these vessels were not visualized. Four of the 5 patients with visualized posterior communicating and posterior cerebral arteries exhibited changes in the blood pressure and/or cardiac rate. Among these, 3 showed changes following injection of Hypaque and 1, after both Hypaque and Renografin.

Of the 6 patients in whom the posterior cerebral and posterior communicating arteries were not visualized, only 2 exhibited changes in blood pressure or cardiac rate. In both instances the abnormal response followed injection of Hypaque and not Renografin.

DISCUSSION

The lower incidence and the minimal nature of disturbances of cardiac rate and arterial blood pressure in the human do not strongly support a previously expressed suggestion that morbidity and mortality following cerebral angiography may result from these disturbances in vital functions. The evidence, however, does support the experiments on animals which demonstrated appreciable differences in the side effects of the different contrast agents.1,4 Even relatively small disturbances in functions of the body are useful as indicators of toxicity of the contrast agent, particularly when observed under clinical conditions of dosage and technic.

The effects on blood pressure and cardiac rate are considered to result from a direct action of the contrast medium on the brain,3,8 producing a vagal discharge with cardiac slowing.1,4 In the animal, the effects on blood pressure and cardiac rate can be abolished by sectioning the vagus. Similar abolition can be achieved by adequate atropinization. The responses in dogs and cats do not appear to be caused by physical or chemical stimulation of the carotid sinus.1,4 In man, protection from the circulatory disturbances might also be obtained with atropine blocking the vagal response; however, it must be anticipated that central stimulation nevertheless may occur.

A higher incidence of fall in blood pressure and slowing of cardiac rate was noted when the posterior communicating and posterior cerebral arteries were visualized on the angiogram than when these vessels were not visualized. This observation suggests the importance of flow of the contrast medium through vessels supplying the hypothalamus and midbrain in the production of changes in blood pressure and cardiac rate.

We believe the described disturbances in cardiac rate and blood pressure constitute useful peripheral indications of a toxic or irritative effect of the contrast media on the central nervous system. The disturbances caused by the sodium diatrizoate would be only infrequently of clinical significance; they should, however, be interpreted as signs of lesser tolerance of this agent by the brain than of the methylglucamine compound.

SUMMARY

Sodium and methylglucamine diatrizoates have been compared as to their capacities for disturbing cardiac rate and arterial blood pressure during standard carotid arteriography. Observed abnormalities were of relatively minor degree in both substances, but were regularly more frequent and of
greater magnitude with the sodium salt than with the methylglucamine. The significance of these data lies in interpretation of disturbances as a measurement of toxicity. On this basis, the methylglucamine salt appears to be less toxic than the sodium salt.

REFERENCES