INTRACAROTID INJECTION OF PAPAYERINE IN CASES OF CEREBROVASCULAR THROMBOSIS*

PRELIMINARY REPORT

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It is the purpose of this paper to report our clinical observations on the effect of injection of a known vasodilating agent directly into the common carotid artery in cases of thrombosis of cerebral blood vessels and ischemic cerebral infarction. This constitutes a preliminary report of a study concerned with the effect of intracarotid administration of vasodilating drugs upon the cerebral circulation in man.

The literature concerned with the treatment of patients with ischemic cerebral infarction has been replete with paradoxical statements and contradictions. Such basic considerations as the anatomic and physiologic arrangement of terminal vessels, the occurrence or nonoccurrence of angiospasm of intracranial blood vessels, the role of the autonomic nervous system in regulation of caliber of intracranial arteries and arterioles, the objective results of stellate ganglion block in the treatment of cerebrovascular disease, and the clinical effect of vasodilating drugs on the cerebral circulation of man are not yet clearly understood nor has agreement among authorities been reached on any of these issues. One of the most lucid essays on this subject is that of Schmidt. He says that while the possibility of cerebral angiospasm from sympathetic impulses in man can be neither affirmed nor denied, at present the preponderance of the evidence is against it. Our own clinical experience with stellate ganglion block in cases of cerebral vasoconstriction has thus far borne out this statement. Moreover, Schmidt has pointed out that the physiologic basis for failure of the commonly employed vasodilating agents to be clinically effective in increasing cerebral circulation is the apparent lesser sensitivity of intracranial vessels to vasodilator agents as compared with the sensitivity of the extracranial vessels. Hence a vasodilator agent, such as papaverine, when administered orally or parenterally in sufficient concentration to act all over the body, may bring about a redistribution of blood at the expense of the brain, plus a decrease in peripheral blood pressure and an actual decrease rather than the desired increase in cerebral blood flow.

Our investigation is ultimately concerned with several questions that bear upon the treatment of ischemic infarction of the brain. These questions are: (1) How can selective vasodilatation of the intracranial arteries and

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arterioles in man be best accomplished? (2) Under what conditions is such vasodilatation accompanied by increased cerebral blood flow? (3) What consideration must be given to the changes in the peripheral blood pressure, cardiac rate and output, and respiratory rate which are side effects produced by certain vasodilating agents? (4) If cerebral vasodilatation and increased cerebral blood flow can be accomplished in cases of ischemic brain infarction, will it prove to be clinically beneficial, or will reactive edema, increased intracranial pressure, and later angiospasm mitigate any possible benefits?

The phase of this study with which we are concerned in this preliminary report is the effort to produce selective dilatation of intracranial vessels. The basis for attempting to accomplish this by the intracarotid injection of papaverine is simply the rationale of delivering a vasodilating agent directly into the vessels to be dilated. Mufson\(^9\) has based his treatment of peripheral obliterator arterial disease on the same rationale. We wish to report certain of our clinical observations following the intracarotid injection of papaverine in 6 patients with complete hemiplegia caused by ischemic infarction of the brain, and in 10 additional patients in whom injection was carried out for its vasodilating effect during cerebral angiography. An evaluation of these early observations will not be attempted by us in this preliminary report, and only unequivocal objective findings will be reported.

Single and multiple intracarotid injections of papaverine, in dosage varying from 0.5 to 1.5 grains, were made in 6 patients demonstrating complete hemiplegia. In each patient the hemiplegia had been present for 72 hours or more. In each case a clinical diagnosis of cerebrovascular thrombosis with ischemic infarction of the brain had been arrived at independently by several examiners on the basis of mode of onset and development of the hemiplegia, neurologic examination, and absence of red blood cells from the cerebrospinal fluid. Each injection was made into the common carotid artery that was contralateral to the hemiplegic extremities. In 2 cases a single injection was made, in 2 cases two injections were made, and in 2 cases three injections were made. Four of the patients demonstrated an objective change in the paralyzed extremities within 60 seconds after the initial injection. Two demonstrated no observable change. Brief summaries of these clinical investigative procedures follow.

**CASE REPORTS**

Case 1. A.S., a 52-year-old white male, a known hypertensive, noted onset of weakness of the right extremities. This progressed to complete right hemiplegia within 24 hours. Neurologic examination revealed complete flaccid paralysis of the right extremities, sensory type aphasia, deviation of eyes to the right, and a positive response to the Babinski test on the right. The pupils were equal and reacted well to light.

On the second day after admission 0.5 gr. of papaverine was injected into the left common carotid artery.

Two days later another injection of 0.5 gr. of papaverine was made. During the next 10 minutes the patient moved his right arm spontaneously and on command.