THE COMBINED USE OF EPHEDRINE AND EPINEPHRINE IN SPINAL ANESTHESIA

A Preliminary Report

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In an article in this journal, Henderson (1) suggested the combined use of ephedrine and epinephrine in spinal anesthesia. The use of these drugs together is based on a recent theory advanced concerning the mode of action of ephedrine and its relationship to epinephrine.

In 1928 Schaumann (2) noticed that ephedrine had much less activity on isolated tissue than might have been expected from its action in the body; however, when epinephrine was added, the preparation became more sensitive to ephedrine. He observed in animals, as did Burn (3), that the pressor response to epinephrine was much greater if ephedrine were also present in the body. Csépai and Doleschall (4) accidentally produced similar results in the human while treating a patient with Addison's disease.

Recently Blaschko, Richter, and Schlossmann (5, 6, 7, 8, 9) found that extracts from mammalian tissue—liver, kidney, intestine, lung, and brain—contained an amine oxidase which oxidized epinephrine, but whose action was inhibited by ephedrine. Gaddum and Kwiatkowski (10), in working on the perfused vessels of a rabbit's ear, noted that ephedrine inactivated this amine oxidase, permitting epinephrine to act more effectively. In view of this and the above evidence, Gaddum (11) hypothecated that ephedrine is similar to eserine in its action. While eserine inactivates choline esterase, permitting acetylcholine to function, ephedrine inhibits amine oxidase, allowing epinephrine to work. However, Richter and Tingey (12), upon repeating Gaddum's experiments, did not arrive at the same conclusions.

We have observed clinically that there are some cases of high spinal anesthesia in which the fall in blood pressure cannot be elevated by one or more injections of ephedrine, additional oxygen or fluid therapy. From the experimental work, it seems probable that ephedrine inhibits the action of amine oxidase. It is possible, because of the blocking of most of the sympathetic secretory fibers to the adrenal glands, that there is a subnormal amount of epinephrine present in the circulation. Consequently, no pressor response is effected by ephedrine.

In 25 patients in whom 25–50 mg. of intramuscular ephedrine was ineffective in raising the blood pressure depressed by high spinal anes-

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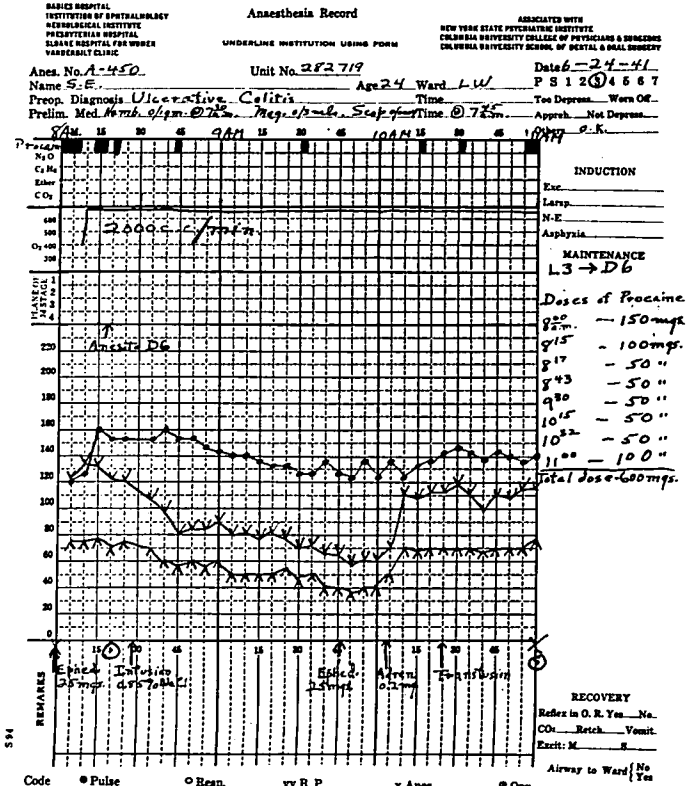

FIG. 1. This patient did not show any pressor response to the first or second intramuscular dose of ephedrine, to continuous oro-pharyngeal oxygen, or to an infusion of physiological saline. The intramuscular injection of epinephrine produced a prompt and sustained rise in the blood pressure, though the spinal was kept at a high level by additional doses of procaine. Spinal anesthesia was used so that the cautery knife could be employed.

thesia, 0.2 mg. (0.2 cc.) of adrenalin * was injected intramuscularly with the ephedrine or at various intervals up to fifty-five minutes after the ephedrine was administered. If the epinephrine were given with the ephedrine, a typical epinephrine rise and peak in the blood pressure resulted which was followed by a moderate fall and a leveling off at a higher systolic and diastolic pressure than was present at the time of injection. However, in the majority of our cases, the epinephrine was given fifteen to twenty minutes after the ephedrine, and a prompt rise in the blood pressure resulted, which was sustained for a considerable period of time. The chart below illustrates a typical reaction.

The patients should be selected when this procedure is used. It might prove harmful if used too often on the same patient, or if the patient has some cardiovascular disease, thyrotoxicosis, or diabetes. The epinephrine, in the dosage used, did not produce any untoward effects in any of our patients.

CONCLUSIONS

1. In cases of high spinal anesthesia with low blood pressure, when ephedrine, oxygen, and fluid therapy do not produce a pressor response, the addition of epinephrine fifteen to twenty minutes after the ephedrine has been injected will produce a satisfactory rise in the blood pressure.

2. The patients in whom this procedure is used should be carefully selected. No ill effects were seen with the amount of epinephine that was employed in this series.

3. It would seem that our results bear out the experimental proof that ephedrine inhibits an amine oxidase that oxidizes epinephrine.

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* Adrenalin 1:1000 solution; Parke, Davis & Co.