

## USE OF MEPHENTERMINE AS A PRESSOR AGENT DURING SPINAL ANESTHESIA\* †

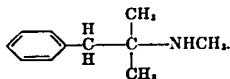
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THE use of vasopressors during spinal anesthesia represents a major advance in enhancing the safety of this type of anesthesia. Many of the drugs in current use have major disadvantages, and the search continues to obtain an agent as ideal as possible for the varying circumstances of hypotension. It appears that two mechanisms are involved in the production of hypotension: one concerns a decrease in peripheral resistance and the other a diminished cardiac output. Hence, vasopressor drugs with two general mechanisms of action are indicated for discreet treatment, and these drugs should be classified according to the dominant mode of action. The present report concerns the clinical experience with a relatively new vasopressor with predominantly peripheral action.

### PHARMACOLOGY SUMMARY

Chemically, mephentermine ‡ is N-methylphenyltertiary butylamine sulfate (1), and has the following structural formula



The molecule is composed of an aromatic ring attached to a tertiary butylamino compound. Thus, it differs from ephedrine by the presence of an additional methyl group on the alpha carbon atom of the aliphatic chain, and the absence of the hydroxyl group. It may be considered to be methylated desoxyephedrine (methedrine®).

Following intravenous administration, a significant pressor response occurs (3): there is an elevation in both systolic and diastolic pressure and the pulse pressure is increased; the mean pressure of the pulmonary artery is raised. Coronary blood flow is increased but cardiac output is unchanged; no significant electrocardiographic changes have been noted. Recent experiments indicate that there is an inotropic effect on the myocardium of dogs (4). Cerebral stimulant effects are minimal (5). A moderate degree of tachyphylaxis follow-

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‡ Mephentermine is available as wyamine®, Wyeth, Inc.

ing repeated administration has been observed and it has been suggested that this property is attributable to the presence of a methyl group on the alpha carbon (2, 6).

A mild, relaxing effect on smooth muscle in general occurs and there is mild bronchodilatation. A moderate increase in respiratory rate is also observed.

#### CLINICAL STUDY

The effect of administration of mephentermine was studied in 200 unselected patients undergoing major or minor surgical procedures under spinal anesthesia.

To prevent hypotension, the drug was given intramuscularly to all patients a few minutes before administration of the spinal anesthesia, utilizing procaine or pontocaine as agents according to accepted techniques (8). Blood pressure was determined by the auscultatory method at the brachial artery and recorded at five minute intervals; the first reading taken after the patient had been brought to the operating room was used as a control value. The age of the patients ranged from 15

TABLE 1

THE INCIDENCE OF BLOOD PRESSURE FALL OF 25 PER CENT OR MORE OCCURRING DURING SPINAL ANESTHESIA WITH AND WITHOUT VASOPRESSORS

	Incidence per cent
Ephedrine	16
Mephentermine	17
Controls	65

to 90 years and the percentage of males and females was approximately the same; no attempt was made to differentiate the results according to the type of anesthetic drug, the age or the initial blood pressures; only observations made during the first hour were considered in our study. After initial trials, 30 mg. was estimated to be an adequate intramuscular dose, and was used routinely. The cases were classified into two groups according to the level of anesthesia; the first group for low levels not reaching above the ninth thoracic segment comprised 104 patients or 52 per cent of the total; the second group, with levels extending anywhere from the first to the eighth thoracic segment, was composed of 96 patients or 48 per cent of the cases.

The effect of the vasopressor on the incidence of hypotension was determined by arbitrarily selecting a 25 per cent or greater fall in systolic pressure as being significant (Dripps) and comparing the number of cases in a control and in a treated group (table 1). It is readily seen that whereas 65 per cent of untreated patients have a pressure drop of 25 per cent or more, in the treated group, or those receiving a prophylactic dose of mephentermine, only 17 per cent had such a fall. This protective action is similar to that of ephedrine.

The extent of the decrease in blood pressure was also markedly diminished when mephentermine was given prophylactically (table 2). The average fall in systolic blood pressure was 9 per cent of the pre-anesthetic pressure for the patients who had low spinal anesthesia; this is contrasted with a 20 per cent fall in pressure in untreated controls. In the group of patients who had high spinal anesthesia who were prophylactically treated with mephentermine, at the time of administration of the spinal agent, the average fall was 15 per cent of the preanesthetic pressure level as compared with a 35 per cent fall in systolic pressure in the untreated controls. When both the two groups who had high and low level spinal anesthesia are combined—a total of 200 patients—the average fall in systolic pressure was 11.8 per cent as compared with a 28 per cent fall in systolic pressure for the untreated patients.

The onset of action after intramuscular injection is between five and eight minutes. Exaggerated increase in the blood pressure above control levels presumably from overdosage was never observed. The

TABLE 2

AVERAGE FALLS IN PERCENTAGE OF SYSTOLIC PRESSURE TABULATED ACCORDING TO LEVEL OF SPINAL ANESTHESIA AND TO THE VASOPRESSOR AGENT EMPLOYED

	T9 or Below,* per cent	T8 or Above,* per cent	All Levels, per cent
Mephentermine	9.2	15	11.8
Ephedrine	8.7	15.3	12
Controls	20	35	28

\* Note: An equal number of cases are analyzed in each spinal level group.

duration of action after intramuscular injection varied between forty-five and sixty minutes.

In cases in which the hypotension was allowed to occur or occurred despite prophylactic administration, an additional dose of 30 mg. was given intramuscularly. A response was usually observed in five minutes. When an immediate response was desired, the drug was given in continuous intravenous infusion. For this purpose a 0.1 per cent concentration in 5 per cent dextrose in water (1 mg. of mephentermine per cubic centimeter of solution) was used. The response to intravenous injection can be observed within one to two minutes.

Elevation of the systolic pressure was always accompanied by a rise in diastolic levels. The influence on the pulse rate and rhythm was minimal; as mentioned previously, a very moderate decrease in rate can be noted with rises in blood pressure and in no circumstances did arrhythmias ascribable to the drug appear. No respiratory changes or side effects of clinical significance, such as cerebral stimulation, nausea, pallor, pilomotor responses or sweating, were observed in connection with administration of mephentermine. However, some degree of tachyphylaxis appears after repeated injections.

To evaluate further the pressor activity of mephentermine, its action was compared to that of ephedrine administered under the same circumstances as mephentermine. In this parallel series of 200 unselected patients undergoing all types of surgical procedures, 50 mg. of ephedrine was administered prophylactically. The resulting data revealed that with ephedrine the average fall in systolic blood pressure was 8.1 per cent for the patients having an anesthesia level to the ninth thoracic segment or below and a fall of 15.3 per cent for the levels of the eighth thoracic segment and above. The average decrease for all the cases was 12 per cent; 16 per cent of the patients had a fall of 25 per cent or more.

### DISCUSSION

It has been conceded that pressor substances are of inestimable value in preventing and correcting the hypotension of spinal anesthesia. When no vasopressors are used, 65 per cent of all patients (half with levels above, and half with levels below, the ninth thoracic segment) have a decrease in systolic pressure of approximately 25 per cent (7).

The causes underlying hypotension during spinal anesthesia have been investigated by many workers (12-17). Two mechanisms appear to operate and, under varying circumstances, one or the other predominates. On the one hand, a decrease in total peripheral resistance occurs, presumably related to the removal of the normal influence of the sympathetic nerves on arteriolar tone; on the other hand, during spinal anesthesia there also occur a decrease in venous pressure, a prolongation in venous circulation time, and a decrease in cardiac output (15-16).

The various sympathomimetic amines available are capable of several actions on the cardiovascular system, with a resultant increase in blood pressure. The activity of these drugs may be brought about predominantly by one of three means: by a direct peripheral vascular stimulation (arteriolar or postarteriolar); by a simulation of the central vasomotor centers, and by a direct action on the myocardium. The effect of any specific vasopressor is usually brought about by one of these means predominating although, in general, a combination of actions is to be found (9, 10, 19, 21). There are, thus, many drugs from which to choose and most of these are useful in counteracting hypotension during anesthesia as well as during medical and surgical conditions accompanied by varying degrees of vascular collapse. A choice should be dictated by estimating which mechanism is predominantly operating to produce the hypotension and then selecting that vasopressor which pharmacologically is most suitable. In some cases, a purely peripheral acting compound might be advisable and in other circumstances a drug acting more specifically on the heart may be

indicated. In all cases and especially in cardiac patients, a drug producing a minimum of cardiac disturbance or other side reactions as previously enumerated is always desirable.

## SUMMARY

The effects of administration of mephentermine were observed in 200 patients who received spinal anesthesia. The number of cases exhibiting a significant fall in pressure was decreased from 65 per cent to 17 per cent. The average fall in systolic blood pressure was 11.8 per cent compared to that of ephedrine given to 200 patients under the same conditions, and with this drug the average fall in systolic blood pressure was 12 per cent. No cardiac arrhythmias or side effects ascribable to the drug were detected. Mephentermine appears to be a useful addition to the list of effective peripheral pressor substances.

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