PENTOCAINΕ-DEXTROSE-EPHEDRINE FOR SPINAL ANESTHESIA *

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In the latter part of the nineteenth century epinephrine had been extracted from the suprarenal glands of animals, and its pressor effect had been described. Early in 1900 Heinrich Braun (1) realized the value of this effect in local anesthesia. He found that when the drug was applied to an anesthetized area its vasoconstrictor action caused a decrease in the flow of blood to that region and slowed absorption of the anesthetic agent, thus prolonging its effect and decreasing its systemic toxicity. Subsequent investigation and clinical experience have demonstrated the value of the use of vasoconstrictors in local anesthesia.

Largely as a result of the work of the German investigators, Bier, Donitz, Braun and Klappe, in the early part of the twentieth century, the use of epinephrine in spinal, as well as in local, anesthesia became widespread. The efficacy of injecting epinephrine into the subarachnoid space with the spinal anesthetic, however, became a matter of controversy, and the method fell into disuse. In recent years several investigators (2, 3) have again called attention to the value of adding epinephrine to the spinal anesthetic. The most recent report was made by Cullen and his associates (4), who found that the use of epinephrine with procaine definitely prolonged the duration of spinal anesthesia. At the present time there is little general interest in this method of increasing the effectiveness of spinal anesthesia, one of the principal reasons being the possibility of damage to the spinal cord by vasoconstrictor drugs, either by direct action on the nerve tissue itself or by decreasing the effective blood supply to the cord. To the best of our knowledge there is no good clinical evidence that the injection of epinephrine in proper concentrations into the spinal fluid is a dangerous practice. Although epinephrine has been the vasoconstrictor drug most widely used for this purpose, the present discussion will be limited to the subarachnoid injection of ephedrine.

The amount of recorded experimental work on the effect of ephedrine injected into the subarachnoid space has been very limited. The epinephrine-like sympathomimetic action of ephedrine had been described by Chen and Schmidt in 1924 (5). Investigation had shown it to have a less powerful local effect than epinephrine, to be more easily

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absorbed, and less easily destroyed by the liver. Thus, since the systemic effects of ephedrine are more pronounced than its local action, it is less suitable than epinephrine for use as a vasoconstrictor in local anesthesia. Burch and Harrison (6), in 1931, reported upon the intraspinal injection of the drugs in dogs. They found that 2 to 5 mg. of ephedrine per kilogram of body weight produced a marked rise in blood pressure. In 1927, Read and Lin (7) showed that ephedrine potentiated the effect of procaine in blocking motor nerves. In 1940, Schultz (8) demonstrated that ephedrine itself has an anesthetic effect. Injected intracutaneously in man in concentrations of 0.1 per cent or greater, it produced local anesthesia. In the frog, 5 per cent solutions were found to be capable of blocking the sciatic nerve, while intraspinal injections produced anesthesia of the extremities. The minimal dose for spinal anesthesia was found to be 0.1 mg. per gram of body weight, as compared to 0.015 mg. per gram of body weight for procaine. These effects of ephedrine were completely reversible.

After being virtually abandoned for many years, the question of the possible use of vasoconstrictors in spinal anesthesia was reopened in 1932 when Jianu (9) referred to the addition of ephedrine to spinal anesthetic agents. In the following year Jianu and Moisescu (10) reported that they had obtained prolonged anesthesia for operations above the diaphragm by the subarachnoid injection of very small doses (as little as 2 mg.) of nupercaine to which was added 1 cc. of cardiazol-ephedrine. By varying the site of injection they were able to obtain satisfactory anesthesia in every part of the body. It was their opinion that the addition of cardiazol-ephedrine to nupercaine provided better analgesia and eliminated many of the disturbances ordinarily encountered during spinal anesthesia. In 1943, Romberger (3) reported that in 108 cases in which 0.5 to 1 cc. of 5 per cent ephedrine was added to procaine injected intraspinally, the duration of anesthesia was increased 40 to 50 per cent.

Since 1943 we have employed ephedrine in combination with pontocaine hydrochloride for spinal anesthesia in over 2,500 cases. The method used in this report was to mix equal parts by volume of 1 per cent pontocaine, 10 per cent dextrose and 5 per cent ephedrine. This resulted in a 0.3 per cent solution of pontocaine, which was injected into the subarachnoid space without further dilution. The average dose of pontocaine varied between 4 and 8 mg. Rarely was more than 10 mg. used. It was found that, compared to pontocaine-dextrose alone, approximately 30 per cent less pontocaine was required to obtain anesthesia of a similar degree and duration. It has not been determined as yet whether other concentrations of ephedrine are more or less effective in potentiating the spinal anesthetic properties of pontocaine. Our use of ephedrine intraspinally has rarely exceeded 50 mg. and no untoward effects have been observed. The usual systemic effects produced by the subcutaneous or intravenous injection of ephedrine do not seem to
occur when it is deposited in the subarachnoid space. Patients known to be sensitive to vasoconstrictor drugs, such as those having hyperthyroidism, were not affected by pontocaine-dextrose-ephedrine spinal anesthesia. The occurrence of complications ordinarily seen during or following spinal anesthesia, such as nausea, vomiting, headache, circulatory and respiratory depression, was not increased by using ephedrine with the pontocaine and dextrose. Aside from headache there were no neurologic complications or deaths attributable to the anesthesia. In all cases in which ephedrine was mixed with the spinal anesthetic the need for a subcutaneous injection of 50 mg. of ephedrine to maintain the blood pressure level was not decreased. As Lundy and Essex (11) have demonstrated, this dosage of ephedrine usually compensates for the fall in blood pressure from a moderate dose of spinal anesthesia.

<table>
<thead>
<tr>
<th>TABLE 1</th>
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<tbody>
<tr>
<td><strong>COMPARATIVE DOSAGE OF PONTOCAINEx IN SPINAL ANESTHESIA WITH AND WITHOUT EPHEDRINE</strong></td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th></th>
<th>No. of Cases</th>
<th>In Percentage of Cases, Milligrams Pontocaine</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>2 or less</td>
</tr>
<tr>
<td>Hemorrhoidectomies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without Ephedrine</td>
<td>154</td>
<td>8</td>
</tr>
<tr>
<td>With Ephedrine</td>
<td>154</td>
<td>9</td>
</tr>
<tr>
<td>Cystoscopies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without Ephedrine</td>
<td>271</td>
<td>3.5</td>
</tr>
<tr>
<td>With Ephedrine</td>
<td>271</td>
<td>11</td>
</tr>
<tr>
<td>Vaginal Plastics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without Ephedrine</td>
<td>40</td>
<td>2.5</td>
</tr>
<tr>
<td>With Ephedrine</td>
<td>40</td>
<td>5</td>
</tr>
<tr>
<td>Inguinal Herniorrhaphies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without Ephedrine</td>
<td>70</td>
<td>2</td>
</tr>
<tr>
<td>With Ephedrine</td>
<td>70</td>
<td>1</td>
</tr>
<tr>
<td>Operations on Extremities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without Ephedrine</td>
<td>22</td>
<td>4.5</td>
</tr>
<tr>
<td>With Ephedrine</td>
<td>22</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 1 illustrates the dosage of pontocaine required to obtain anesthesia of comparable extent with and without ephedrine. Each group is composed of a consecutive series of cases. When ephedrine was not used, the anesthetic solution consisted of one part by volume of 1 per cent pontocaine and 2 parts of 10 per cent dextrose. When ephedrine was used, equal parts of 1 per cent pontocaine, 10 per cent dextrose, and 5 per cent ephedrine were mixed. Proportionate amounts of this mixture were given to obtain the selected dose of pontocaine, e.g., 1.5 cc. contained 5 mg. of pontocaine, 25 mg. of ephedrine and 0.5 cc. of 10 per cent dextrose.

In 80.5 per cent of the cases in which hemorrhoidectomy was performed without ephedrine it was necessary to give 8 mg. or more of
pontocaine, while with ephedrine 82.5 per cent of the patients were
given 5 mg. or less of the anesthetic drug. Anesthesia has been satis-
factory, and duration similar to that obtained when pontocaine was
employed alone. It was our impression that in some cases pontocaine
with ephedrine provided anesthesia of longer duration than even larger
doses of pontocaine and dextrose alone. With pontocaine and dex-
trose, 76 per cent of the patients who had cystoscopies were given 8 mg.
or more of the drug. When ephedrine was added to the anesthetic solu-
tion 74.5 per cent of the patients received 5 mg. or less. Before the em-
ployment of ephedrine in our solutions for operations upon the vaginal
canal, including vaginal hysterectomy, 85 per cent of the patients re-
ceived 8 mg. or more of pontocaine. With ephedrine, satisfactory anes-
thesia was obtained with 6 mg. or less of the anesthetic drug in 82.5 per
cent of the cases. In 87 per cent of the cases in which inguinal hernior-
rhaphy was performed without the use of ephedrine, 10 mg. or more of
pontocaine was given. When ephedrine was added to the solution 70
per cent were given 7 mg. or less. When ephedrine was not used 87 per
cent of the patients received from 10 to 15 mg. of the anesthetic drug,
as compared to 23 per cent when the vasoconstrictor was employed.
The results were similar for operations of the extremities. Without
ephedrine, 8 mg. or more of pontocaine was administered in 90 per cent
of the cases, while with ephedrine 6 mg. or less of the drug gave com-
parable anesthesia in 91 per cent of the cases.

In one respect the results obtained by the use of ephedrine in com-
bination with pontocaine to produce sensory and motor anesthesia have
been impressive. It has been possible to use smaller doses of the anes-
thetic drug. Prior to the use of ephedrine, we only occasionally used
less than 8 mg. of pontocaine, while now with ephedrine, it is common
practice to use 5 mg. in the types of operations listed in the table. We
have further noted that very small doses, i.e., 3 or 4 mg. of pontocaine
with ephedrine, give satisfactory anesthesia in selected cases. It has
been our impression that the size of the dose is an important factor in
the safety of spinal anesthesia. It remains to be determined, however,
whether the decrease in dosage reported here represents an actual ad-
vantage in so far as the margin of safety of pontocaine spinal anes-
thesia is concerned.

Inasmuch as it has been suggested that ephedrine possesses anes-
thetic properties, we omitted the anesthetic drug on several occasions
and injected only the dextrose and ephedrine mixture in the usual
amount. In none of these cases was there any evidence that it pro-
duced anesthesia or muscular relaxation.

The mode of action of ephedrine in altering the anesthetic effect of
pontocaine in the subarachnoid space is unknown. It may be reasoned,
however, that ephedrine causes vasoconstriction of the blood vessels,
thereby prolonging the time required for the absorption of the anes-
thetic drug from the spinal fluid. This is evidenced clinically by the
increased length of time that the level of anesthesia can be influenced by gravity. With small doses of pontocaine (5–10 mg.) and dextrose, we have noted that it is rarely possible to change the level of anesthesia by gravity after a period of five minutes. When ephedrine is added to the pontocaine-dextrose solution the time interval during which the height of anesthesia can be increased by lowering the patient’s head is usually doubled.

**Summary**

The addition of vasoconstrictor drugs to local anesthetic agents has proved to be an effective method of decreasing the toxicity and prolonging the duration of the anesthesia. This is accomplished by delaying the absorption of the anesthetic drug. This same principle has been applied in spinal anesthesia, with encouraging results. Attention is called to the fact that vasoconstrictors were used in this manner principally during the first decade of spinal anesthesia, before sufficient experience had been obtained to clarify the basic principles of this method of anesthesia. It is suggested that the use of vasoconstrictors in spinal anesthesia be reinvestigated in the light of present day knowledge, and a scientific appraisal of their possible value be made.

A comparative report is made of 1,114 cases, in half of which pontocaine-dextrose-ephedrine and in the other half pontocaine-dextrose was given. It was observed that the addition of ephedrine increased the effectiveness of pontocaine as a spinal anesthetic. With the use of a constant technic of administration, smaller doses of pontocaine than those employed without the addition of ephedrine were found to give comparable anesthesia. It was our impression that the duration of anesthesia was increased and that the anesthetic was not absorbed or "affixed" as rapidly when ephedrine was used.

No systemic effects were observed from the subarachnoid injection of ephedrine in quantities up to 50 mg. To maintain circulation, additional subcutaneous injections of ephedrine, usually 50 mg., were routinely given before spinal anesthesia was induced. No unusual or serious complications attributable to the use of pontocaine-dextrose-ephedrine were noted.

**References**


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PROGRAM FOR THE ONE HUNDREDTH ANNIVERSARY OF THE FIRST ADMINISTRATION OF ANESTHETIC ETHER

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