NUPERCAINE IN DILUTIONS GREATER THAN 1:1500 FOR SPINAL ANESTHESIA *

A. J. Fisher, M.D.† and R. J. Whitacre, M.D.

East Cleveland, Ohio

Received for publication on April 7, 1947

The introduction of the synthetic quinoline derivative, nupercaine, for spinal anesthesia by W. Howard Jones (1) has resulted in considerable use of this drug. The principal advantage of nupercaine is that it is the most potent of all spinal anesthetic agents, even when the dose is corrected to make allowance for the greater toxicity of the drug. The effectiveness of nupercaine as an anesthetic drug has led to the clinical use of this agent in concentrations less than the 1:1500 dilution ordinarily recommended for spinal anesthesia. Dodd and Hunter (2), using 1:2000 solutions of nupercaine in an effort to decrease the toxicity of the drug, failed to note any decrease in the incidence of circulatory depression. In contrast, Fairlie (3), after investigating the 1:2000 and 1:2500 dilutions, was of the opinion that there was less danger in using the more dilute solutions. Wilson (4) used 1:2500 nupercaine in a small series of babies with satisfactory results.

In an effort to evaluate the clinical effects of nupercaine in dilutions greater than 1:1500, concentrations varying from 1:2000 to 1:10,000 were used in 1124 cases, of which all but 61 involved intra-abdominal operations. It was desired to determine the weakest effective dilution necessary to produce anesthesia, and to observe whether high dilutions decreased the toxicity of nupercaine. To carry out this investigation it was necessary to use minimal doses of the drug. The total amount of nupercaine injected in any one case rarely exceeded 5 mg. except when the continuous spinal technic was used.

Jones, using a hypobaric solution of nupercaine, recommended that the patient be placed in the ventral decubitus position so that the anesthetic solution would come in contact with the posterior or sensory nerve routes. If this was not done, sensory anesthesia was often incomplete. In this series, in order to eliminate the necessity of turning the patient, the nupercaine solutions were made definitely hyperbaric by the use of dextrose, and the patients were placed in the dorsal position immediately after the subarachnoid injection. With this technic the anesthetic would presumably come in contact with and exert its greatest effect on the posterior spinal nerve roots.

* From the Department of Anesthesia, Huron Road Hospital, East Cleveland, Ohio.

† Now with the Youngstown Hospital Association, Youngstown, Ohio.

The hyperbaric solution was prepared by diluting the 1:200 solution of nupercaine with 10 per cent dextrose. The single injection technic with the patient in the lateral position, was employed in the majority of lower abdominal operations. In many of the upper abdominal and in selected lower abdominal procedures, the continuous or serial method was used. Because sensory anesthesia was usually incomplete, light first plane cyclopropane anesthesia was routinely administered as a supplement. With this depth of general anesthesia, it could readily be determined whether relaxation of the abdomen was obtained from the spinal anesthesia. Fifty mg. of ephedrine was administered subcutaneously before the spinal tap.

The 1:10,000 dilution of nupercaine (1 mg. in 10 cc.) was used in 34 cases, of which 31 were lower abdominal and 3 were upper abdominal operations. The continuous method was used 6 times. Due to the large volume of fluid necessary to make this dilution, the amount of drug that could be injected into the subarachnoid space at one time was necessarily limited: the average dose was 2 mg. Abdominal relaxation was obtained with the 1:10,000 dilution, although it was not satisfactory in all cases. The duration of relaxation was about sixty minutes. Partial sensory anesthesia was occasionally obtained, but the predominant effect was on the motor nerves as evidenced by the degree of abdominal relaxation. This dilution did not prevent circulatory depression. Mild circulatory reaction occurred in 2 cases (5.8 per cent) and severe depression was observed in one instance (2.9 per cent). Circulatory depression was classified as severe when there was a fall of 40 per cent or more in systolic blood pressure, or when the systolic blood pressure fell to 80 mm. of mercury or less.

A dilution of 1:6000 (1 mg. in 6 cc.) was used in 257 lower abdominal, 46 upper abdominal, and 10 extra-abdominal operations. The dose varied from 2 to 4 mg. (12 to 24 cc.), the average being 20 cc., or 3.3 mg. of nupercaine. An exception was made in cesarean sections, where 6 cc., or 1 mg. of the drug, was not exceeded. When the continuous technic was used for upper abdominal operations, the initial dose was 3.3 mg. Subsequent injections of 1 or 2 mg. were made at thirty to sixty minute intervals. In the majority of cases, the 1:6000 dilution produced satisfactory relaxation, but sensory anesthesia was incomplete. The duration of relaxation varied between sixty and ninety minutes. Circulatory reactions not requiring active therapy occurred in 55 cases (17.5 per cent); severe reactions occurred in 10 cases (3.2 per cent).

Forty-six operations were performed with a 1:5000 dilution of nupercaine. The average dose was 4 mg. The anesthesia and relaxation produced with this concentration did not differ appreciably from that obtained with the 1:6000 dilution.

A 1:4000 dilution was used in 177 cases, including 147 lower abdominal and 25 upper abdominal procedures. The dose varied from

2 to 5 mg., with an average of 4 mg. Satisfactory relaxation was produced, and occasionally there was sufficient sensory anesthesia to permit surgery without supplemental anesthesia. This was believed to be due to the tendency to use slightly larger doses as the concentration of nupercaine was increased. The duration of anesthesia was sixty to ninety minutes. Twenty-five patients (14 per cent) had mild circulatory reactions, and severe reactions occurred in 6 cases (3.3 per cent).

Nupercaine in a dilution of 1:3000 was used in 361 lower abdominal, 64 upper abdominal and 41 extra-abdominal procedures for a total of 466 cases. The average dose was 15 cc., or 5 mg. of the drug. Mild circulatory depression was observed in 68 cases (14.5 per cent), and severe depression in 22 (4.7 per cent).

Seventy-eight lower abdominal, 7 upper abdominal and 3 extra-abdominal procedures were performed using a dilution of 1:2000. With this concentration, the average dose was increased to 6 mg., but the extent of anesthesia and relaxation was not materially affected. Relaxation was satisfactory for a period of ninety minutes or occasionally longer. In this small series, mild circulatory reactions occurred in 8 instances (10.2 per cent) and a severe depression in one case (0.9 per cent).

The volumes of anesthetic solution used were much larger than those ordinarily employed for spinal anesthesia. The maximum volume administered by the single injection technic was 40 cc. When the continuous method was used this volume was exceeded on many occasions, but the amount injected at one time did not exceed 30 cc. With the larger volumes, especially when they were injected rapidly, headache or momentary unconsciousness due to the sudden increase in intracranial pressure occasionally occurred. Although such reactions occurred rarely and persisted for only a few minutes, it was believed that the use of such large volumes of the anesthetic solution was undesirable. Ordinarily these reactions did not occur when the volume of the solution was limited to 20 cc., and the injection was not rapid.

It was observed that motor block of the abdominal muscles was often obtained without complete sensory anesthesia. Since a hyperbaric solution was used and the patient placed in the dorsal position, this lack of sensory anesthesia was presumably not due to a lack of contact of the anesthetic solution with the sensory nerves in the subarachnoid space. It is of interest to note that although large volumes of the drug were used, the anesthetic effect tended to be segmental in type.

It is stated by Jones (1) that the duration of anesthesia with nupercaine is dependent upon the concentration of the drug. In this series, the relaxation obtained lasted from sixty to ninety minutes with all dilutions. While the duration of relaxation tended to be slightly longer with the higher concentrations of nupercaine, it must be noted that the size of the dose was increased when the less dilute solutions were used (table 2). Thus it appears that the duration of the spinal block is not

materially affected by the dilution of nupercaine. Likewise the degree of relaxation obtained from a given dose of drug did not seem to be influenced by the various dilutions used.

TABLE 1

TYPE OF OPERATION

Dilution	Upper Abdominal		Lower Abdominal		Extra-Abdominal		Total
	No. Cases	Percentage	No. Cases	Percentage	No. Cases	Percentage	
1:10,000	3	8.8	31	91.2	0	0	34
1:6000	46	14.7	257	82.1	10	3.2	313
1:5000	6	13.0	38	82.6	2	4.4	46
1:4000	25	14.1	147	83.1	5	2.8	177
1:3000	64	13.7	361	77.5	41	8.8	466
1:2000	7	8.0	78	88.6	3	3.4	88
Total	151	13.4	912	81.2	61	5.4	1124

TABLE 2

DOSAGE OF NUPERCAINE

Dilution	Max. Dose	Min. Dose	Average Dose
1:10,000	3 mg.	1 mg.	2 mg.
1:6000	4	1	3.3
1:5000	8	2	4
1:4000	8	1	4
1:3000	10	1	5
1:2000	10	0.75	6

There were no neurological sequelae except the usual number of post-lumbar puncture headaches. Serious respiratory depression was not encountered at any time. When circulatory depression occurred, response to vasopressor drugs and oxygen was readily obtained and no further treatment was necessary.

The incidence and severity of circulatory reactions occurring in this series are summarized in table 3. The types of operations in which the various solutions were used were similar, and the proportion of each type of case was approximately the same for all dilutions (table 1). The incidence of all circulatory reactions varied from 8.7 to 20.4 per cent, with an average of 18.2 per cent. This variation is not beyond the limits which may be ascribed to chance.* Likewise, the relative incidence of mild and severe reactions did not differ significantly among the various dilutions of the drug. Thus, in this study, there is no evidence that the dilution of nupercaine has any effect upon either the incidence or the severity of circulatory reactions. A comparison

* These differences were compared by using the test for significance of differences in proportions. No difference gave a critical ratio greater than 1.7, giving a probability of 0.9.

with previous experience using larger doses of nupercaine indicates that smaller doses of the drug do cause fewer and less serious circulatory reactions. Thus it appears likely that the size of the dose, rather than the dilution, is the primary factor to be considered in attempting to minimize circulatory disturbances under nupercaine spinal anesthesia.

TABLE 3

BLOOD PRESSURE REACTIONS

Dilution	Total Cases	No Reaction		Mild Reaction		Severe Reaction	
		No. Cases	Percentage	No. Cases	Percentage	No Cases.	Percentage
1:10,000	34	31	91.3	2	5.8	1	2.9
1:6000	313	248	79.3	55	17.5	10	3.2
1:5000	46	39	84.9	6	13.0	1	2.1
1:4000	177	146	82.7	25	14.0	6	3.3
1:3000	466	376	81.8	68	14.5	22	4.7
1:2000	88	79	88.9	8	10.2	1	0.9
Total	1124	919	81.8	164	14.5	41	3.7

SUMMARY

An investigation of the higher dilutions of nupercaine for spinal anesthesia indicated that the concentration of the drug did not appreciably alter the degree or duration of sensory anesthesia or motor block. Likewise, the incidence and severity of circulatory reactions was not decreased by the use of dilute solutions of nupercaine.

It appears from this study that the toxicity of nupercaine in spinal anesthesia is dependent primarily upon the amount rather than the dilution of the drug. It is concluded that there is little or no advantage in using concentrations of nupercaine less than those ordinarily recommended for spinal anesthesia.

REFERENCES

1. Jones, W. Howard: A New regional and Spinal Analgesic, with Special Reference to High Thoracic Nerve Root Block and a New Technique, Proc. Roy. Soc. Med. **32**: 919–928 (May 30) 1930.
2. Dodd, Harold, and Hunter, J. T.: Cyclopropane "Sleep" with Percaine Spinal Anesthesia, Lancet **1**: 685–688 (March 25) 1939.
3. Fairlie, H. P.: Percaine Sub-Arachnoid Block, Brit. J. Anaesth. **9**: 162–168 (July) 1932.
4. Wilson, W. E.: Concerning Spinal Analgesia, Brit. J. Anaesth. **15**: 135–141 (July) 1937.