Clinical Observations on the Intrathecal Use of Mepivacaine

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NUMEROUS studies have described the toxicity, pharmacologic action and clinical use of the local anesthetic, mepivacaine, first described by Swedish investigators in 1956, and have indicated it to be a safe and potent agent for infiltration and conduction anesthesia. It is a stable drug distinguished by rapid onset and prompt effectiveness, relatively long duration of action and intense effect. Desirable properties include pronounced penetration and diffusion power, characteristics similar to those of lidocaine, to which it is related structurally. Lidocaine, on the other hand, is reported to be unsuitable for use in spinal anesthesia because its superior diffusibility makes prediction of sensory levels of analgesia difficult.[1]

There have been no published reports of the clinical use of mepivacaine to produce spinal anesthesia. The purpose of this clinical study was to evaluate the intrathecal use of mepivacaine with special reference to concentration and dosage levels and to efficiency in predicting the desired level of analgesia.

Material and Methods

Three concentrations of mepivacaine were used for intrathecal injections. The solutions consisted of mepivacaine diluted with 10 per cent dextrose, 1 : 1,000 epinephrine, and cerebrospinal fluid to a final concentration of 1 per cent or less, 1.6 per cent, and 3 per cent. In a preliminary group of patients, a mixture with a final concentration of 1 per cent or less mepivacaine was used. This was judged to be an ineffective concentration of the drug as the resulting blocks were of insufficient intensity, being characterized by the presence of hypesthesia only and no muscle relaxation. This group, which consisted of 30 administrations, is not included in the following discussion.

In 56 patients, a mixture containing a final concentration of 1.6 per cent mepivacaine was used. In another group of 47 patients, a solution containing 2.5 to 3 per cent mepivacaine was given. The patients were unselected other than those for whom spinal analgesia was judged to be the method of choice for the proposed operative procedures, which involved mainly the pelvis, perineum and lower extremities (table 1). Of the 103 patients in these groups, 65 were males and 38 females, their ages ranged from 16 to 87 years. Two thirds of the patients were 50 years of age or older (table 2).

A 20 or 22 gauge spinal needle with stylet was inserted into the subarachnoid space through the fourth or fifth lumbar interspace while the patient lay on the operating table in the lateral position. A 5 ml. syringe containing the mepivacaine, dextrose, epinephrine solution (according to the dosage schedules contained in tables 3 and 4) was attached to the needle and cerebrospinal fluid was aspirated into the syringe in a predetermined amount sufficient to make the desired concentration. The resulting mixture was injected at a rate of approximately 0.5 ml. per second. The patient immediately was placed in supine position. The operating table was kept horizontal if anesthesia was to be below the tenth thoracic level or was tilted head-down 5 degrees when anesthesia above the eighth thoracic level was required. Blood pressure and pulse rate determinations were made every five minutes. The level of analgesia to pin-prick was recorded after a five-minute interval, and again after a twenty-minute interval. Meanwhile, the tilt of the table was adjusted according to the ascension of the level of analgesia.

Received from the Department of Anesthesiology, City of Memphis Hospitals, University of Tennessee, Memphis, Tennessee, and accepted for publication June 4, 1962.

For saddle block analgesia, the patient was placed in a sitting position with the back slightly flexed. After injection of the anesthetic solution, the patient remained sitting for five minutes to allow fixation of the drug in the sacral region, after which the level of analgesia was determined. The patient was then placed in the position required for the operative procedure.

All spinal anesthetics in this series were administered by members of the house staff, closely supervised by the teaching staff. Procedure charts and dosage tables were established and special report forms were used for gathering the data. An intravenous solution, either 5 per cent dextrose in 0.09 per cent saline or 0.9 per cent saline, was administered to each patient throughout the operation. Pulse rate, systolic and diastolic blood pressures were recorded at five-minute intervals. Intramuscular vasopressors were not employed prophylactically, but intravenous methoxamine hydrochloride was administered when, and if, indicated.

TABLE 1. Types of Operative Procedure

Genitourinary	48
General surgery	30
Gynecology	17
Orthopedics	8

TABLE 2. Age and Sex of Patients

Age	Number of Patients
10–19	2
20–29	11
30–39	10
40–49	10
50–59	11
60–69	28
70–79	25
80–89	6
Male	65
Female	38

Results

Mepivacaine 1.6 Per Cent: In the group of 56 patients to whom mepivacaine 1.6 per cent was given, there were four complete failures, attributed to technical errors involving misplacement of the needle during injection. In an additional seven patients in this group, partial effects were reported, with comments such as "fair analgesia," "poor muscle relaxation," "hypesthesia only." In one of the seven, the level of analgesia probably was too low; it was reported to be at the tenth thoracic level, and the patient complained of bladder distention during transurethral resection of the prostate. In an eighth patient, anesthesia lasted only 45 minutes. These unsatisfactory results were attributed to the use of too dilute a solution of mepivacaine, which produced analgesia of insufficient intensity in a high percentage of patients.

With the exceptions noted, the duration of analgesia was adequate for surgical procedures lasting 90 minutes or less. Three spinal anesthetics were supplemented with general anesthesia (nitrous oxide-oxygen-thiamylal sodium, cyclopropane, nitrous oxide-oxygen-fluroxene) after 105, 115, and 125 minutes respectively. On postoperative check, one patient was found to have had anesthesia for 190 minutes.

The range of dosage was from 24 mg. in 1.5 ml. for saddle block or low spinal analgesia to 64 mg. in 4 ml. for analgesia at the fourth–sixth thoracic level. The control of the level of

TABLE 3. Mepivacaine Spinal Anesthesia. Final Concentration 1.6 Per Cent

Mepivacaine, 4 Per Cent		Dextrose 10 Per Cent (ml.)	Cerebrospinal Fluid (ml.)	Total Volume (ml.)
(ml.)	(mg.)			
0.6	24	0.6	0.3	1.5
0.8	32	0.8	0.4	2.0
1.0	40	1.0	0.5	2.5
1.2	48	1.2	0.6	3.0
1.4	56	1.4	0.7	3.5
1.6	64	1.6	0.8	4.0

TABLE 4. Mepivacaine Spinal Anesthesia. Final Concentration 3 Per Cent

Mepivacaine 5 Per Cent with Dextrose		Cerebrospinal Fluid (ml.)	Total Volume (ml.)
(ml.)	(mg.)		
0.6	30	0.4	1.0
0.8	40	0.6	1.4
1.0	50	0.8	1.8
1.2	60	0.8	2.0
1.4	70	1.0	2.4
1.6	80	1.2	2.8

analgesia was satisfactory. In only three patients did the level of anesthesia ascend more than two to three dermatomes higher than required. A wide zone of hypesthesia (several segments) was noted in a few cases. In the majority of patients, the area of analgesia ascended during the time interval between five minutes and 20 minutes after induction. The spread usually was two to three segments, although in two patients, ascension of five and seven segments was noted.

Mepivacaine 3 Per Cent: Of the 47 patients who were given 3 per cent mepivacaine, two failed to secure anesthesia. All the others obtained an adequate level of analgesia. In one instance, the sensory loss was satisfactory for the operative procedure, but the patient was able to move the lower extremities. The range of dosage was from 30 mg. in 1 ml. for saddle block to 89 mg. in 3 ml. for proposed analgesia at the fourth–sixth thoracic level.

The duration of analgesia was sufficient for operations lasting up to 180 minutes. It was not necessary to give supplemental general anesthesia in any case, with the exception of the two failures. In one of these cases, spinal anesthesia was repeated using tetracaine, while nitrous oxide-oxygen-fluroxene was administered to the other patient. Since epinephrine in amounts of 0.1 to 0.5 mg. (1 : 30,000 to 1 : 20,000) was added to all the local anesthetic solutions used, the effect of the vasoconstrictor on the duration of analgesia was not tested.

Control of the level of analgesia was satisfactory. Two patients developed anesthesia to a higher level than intended. Again, a wide zone of hypesthesia was found in some patients. In three fourths of the patients, the level of analgesia ascended during the interval between five minutes and 20 minutes after induction, usually two to three segments. In four patients, the level ascended 5, 6, 7, and 8 segments each, respectively.

Pronounced reduction of the systolic blood pressure occurred in 19 of the 103 patients. It usually was related to the level of sensory analgesia and undoubtedly was the result of reduced sympathetic tone. Small amounts of methoxamine hydrochloride (2.5 to 5 mg.), intravenously, promptly restored the blood pressure to normal levels in these patients.

There were no residual effects noted following the use of intrathecal mepivacaine in this series of patients, who were examined during their postoperative hospitalization and on return visits to the surgery clinic after discharge from the hospital.

Discussion

Adequate analgesia occurred within three to five minutes after the intrathecal injection of mepivacaine. Partial or complete motor paralysis ensued almost simultaneously. Lack of satisfactory analgesia caused delay of the operation in six patients. Whether these failures were due to technical errors or to lack of effectiveness of the drug is not proved, although the former is suspected. In the group of patients in which the more dilute solution of mepivacaine was used, muscle relaxation was poor and/or sensory loss was incomplete in some cases (seven of 56).

As to the level of sensory analgesia, there was little evidence that the drug behaved differently from other intrathecally-administered local anesthetics. From previous experience with tetracaine, it was found that by employing a similar technique, the sensory level of analgesia could be predicted consistently. No appreciable difference was found with mepivacaine in this regard. The gradual ascension of the sensory level for one or more thoracic segments was observed in the first 20 minutes or less following the intrathecal injection of mepivacaine, but there was little change thereafter, until the analgesia began to wane and recede to lower levels.

These observations suggest that mepivacaine, administered intrathecally, becomes fixed at a sensory level which can be established under conditions similar to those using hyperbaric tetracaine solutions. The reported superior diffusibility of mepivacaine apparently was not as disadvantageous as that found with the intrathecal use of lidocaine.[1] There seemed to be no marked tendency for mepivacaine to spread beyond the desired limits. Early fixation, within 20 minutes, appeared to be a feature of the drug when used intrathecally.

Concentrations of mepivacaine in the range of 1 to 1.6 per cent apparently are not effective in all patients. There was an incidence of incomplete anesthesia of approximately 12 per

cent with a concentration of 1.6 per cent. With concentrations up to 3 per cent, this feature was not observed. The duration of anesthesia with the more concentrated solution was longer, up to 180 minutes, as compared with 90 to 125 minutes with the 1.6 per cent solution. Laboratory reports of spinal anesthesia with mepivacaine in animals [2, 3] indicate that 2 per cent solution injected intrathecally produced no residual effects and no evidence of spinal cord damage was found on microscopic examination. However, when 4 and 8 per cent solutions were used, the incidence of residual effects in the animals was 19 and 50 per cent respectively. The upper limit of safety in man is unknown. No residual effects occurred in this series in which 3 per cent mepivacaine was used.

Since tetracaine is now the standard drug for use in spinal anesthesia, the question of the equipotent doses of tetracaine and mepivacaine has been considered. It appears that 8 to 10 mg. mepivacaine are equivalent to 1 mg. tetracaine for intrathecal use. This opinion is based on the resemblance of behavior, when using similar techniques, of an injected concentration of 3 per cent mepivacaine and 0.3 to 0.4 per cent tetracaine. Likewise, the results with 1.6 per cent mepivacaine are similar to those obtained with 0.2 per cent tetracaine.

Summary

A clinical evaluation of the use of intrathecal mepivacaine has been conducted in 103 patients who had various surgical procedures involving the pelvis, perineum and lower extremities. Some degree of sensory analgesia with partial or complete motor paralysis of similar dermatomes was obtained in 97 of the 103 patients.

In this series of spinal anesthetics produced by hyperbaric mepivacaine, the sensory level obtained was predictable. A concentration up to 3 per cent produced satisfactory anesthesia in all patients to whom it was administered, with the exception of two failures attributed to technical error. A concentration of 1.6 per cent produced partial analgesia in approximately 12 per cent of trials. No residual effects following spinal analgesia with mepivacaine were observed.

This paper was read at the Annual Meeting of the Southern Society of Anesthesiologists, Atlanta, Georgia, April 14, 1962.

Ampules of mepivacaine containing 2, 4 and 20 per cent solutions were supplied by Winthrop Laboratories.

References

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