

Clinical Workshop

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Accumulation of Mepivacaine Hydrochloride during Caudal Block

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Studies in mice and rabbits show that toxic reactions from mepivacaine (carbocaine) injected subcutaneously are often delayed and that the drug has a cumulative effect.¹⁻³ Cumulative-type reactions in three patients given mepivacaine during continuous caudal block have been reported by us.⁴ These cases had the following characteristics: (1) the initial signs and symptoms started four to six hours after the first dose and followed the third dose in one patient, the fourth dose in the second patient, and the fifth dose in the third patient; (2) initially, all three patients exhibited signs of central nervous system stimulation, i.e., agitation, disorientation, excitability, and hysteria; and (3) all patients had tonic and clonic convulsions. Each initial and subsequent dose of mepivacaine was within the recommended volume and concentration range for a single injection of mepivacaine, 300 to 600 mg. None of the reinforcing doses were given until sensory analgesia from the previous dose had dissipated and labor pains had returned. The total amount of mepivacaine received by the first patient was 1,480 mg.; the second patient 1,890 mg.; the third patient 2,025 mg. Apparently, a high blood level resulted from either (1) increase of the mepivacaine or a metabolic byproduct with each subsequent dose; (2) slow hydrolysis, detoxification, etc., or (3) a combination of these.

This paper presents five cases of vaginal obstetrical delivery during continuous caudal block using 1.5 per cent mepivacaine without epinephrine. We sought to determine whether the blood level of mepivacaine increased with reinforcing doses, and to what degree.

METHOD

Technique of Continuous Caudal Block: The plastic tubing technique, as described by Moore, was employed.⁴ The initial dosage of mepivacaine and each reinforcing dose was approximately the same, 300 to 450 mg. A 1.5 per cent solution was used for all doses, except in the fifth case in which 1.0 per cent was injected for the fifth dose. No patient was given an additional dose until the pain of labor recurred.

Blood Sampling: A teflon needle was placed in an antecubital vein and the lumen occluded with an obturator. At least twenty samples per patient were drawn at predetermined intervals. At delivery, maternal and cord blood were sampled simultaneously. Syringes containing 0.2 mg. (2,000 U.S.P. units) of sodium heparin (Panheparin) were used to withdraw 5 ml. of blood, which was placed in numbered vials containing sodium oxalate and vigorously shaken. The vials were stored in the freezing compartment of a refrigerator. Prior to shipping, the vials were frozen in a bath of dry ice and acetone and sent for analysis in a thermal chest to keep the samples frozen.

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TABLE 1. Apgar Ratings as Related to Total Amount of Mepivacaine and Duration of Caudal Block Prior to Delivery

Case Number	Total mg. of Mepivacaine Administered	Duration of Continuous Caudal Block Prior to Delivery	Micrograms of Mepivacaine per Milliliter of Venous Blood		Apgar Score of Newborn	
			Maternal	Cord	1 Minute	5 Minutes
00080	900 mg.	1 hr. 55 min.	3.9	2.5	9	9
00647	1,200 mg.	4 hr. 20 min.	7.5	4.3	9	10
01581	1,200 mg.	5 hr. 3 min.	7.2	3.5	7	9
02532	1,200 mg.	4 hr. 13 min.	8.6	7.9	4*	9
02976	1,480 mg.	8 hr. 15 min.	7.5	6.2	6	9

* This newborn had a 30-second Apgar score of 8. However, aspirated mucus had to be removed subsequently by laryngoscopy.

Analysis of Mepivacaine: The samples were analyzed for mepivacaine by Pratt *et al.*, using gas chromatography.⁵

($P < 0.05$) (figs. 1 and 2). Mepivacaine passed the placental barrier in all cases. In none of the newborns did the Apgar ratings indicate evidence of fetal depression (table 1).

RESULTS

The blood levels rose significantly above the previous level with each subsequent injection

DISCUSSION

None of the patients in this study showed

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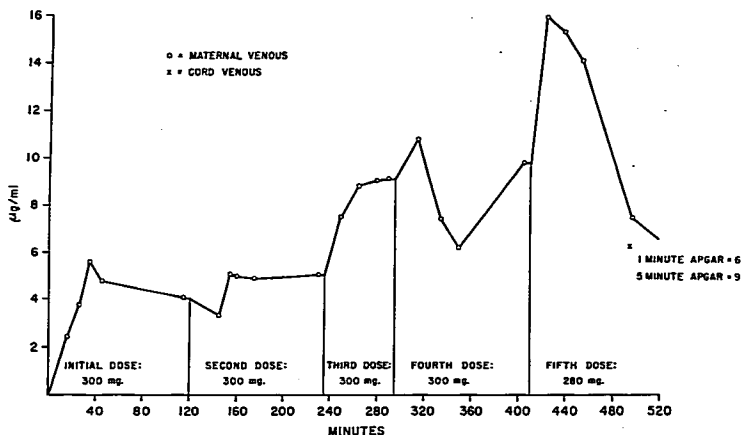


FIG. 1. The graphs of the five patients were similar when the microgram levels of mepivacaine per milliliter of blood were compared with the duration of anesthesia. This patient is an example. She received 1,480 mg. of mepivacaine; the graph demonstrates the increased level of mepivacaine with each reinforcing dose. It might be expected that immediately following a reinforcing dose the blood samples would reflect an increase in mepivacaine, but on occasion the mepivacaine levels were significantly lower (samples 7 and 18). At the present, the reason for this is not clear.

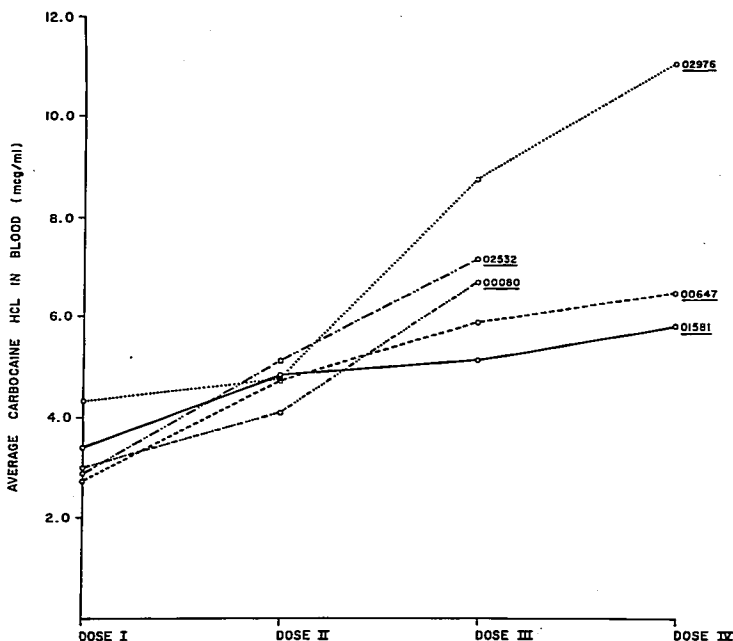


FIG. 2. Composite graph (prepared by statistician) of the five patients studied, showing evidence of increase in mepivacaine level in the blood with each reinforcing dose.

signs of central nervous system stimulation. However, we have employed mepivacaine for continuous caudal block for vaginal delivery in more than 5,000 cases, and 28 patients have shown varying degrees of central nervous stimulation. Five of these 28 patients convulsed: two following inadvertent intravenous injections and the three cited previously from accumulation.⁶

To date, the blood levels at which systemic toxic reactions with mepivacaine are most likely to occur have not been determined. Nonetheless, when mepivacaine is employed in a continuous technique, not only must a single dose be determined, but a total maximum dosage should be selected. From our experience with mepivacaine we have concluded that for a continuous caudal block for

vaginal delivery a cumulative dose of 1,000 mg. suggests a maximum is being approached, and a total dosage of more than 1,500 mg. probably should not be used.

Depression of 12 of 56 babies by dosages of mepivacaine ranging from 360 mg. to 750 mg. has been suggested.⁷ The Apgar scores of the infants in our study would not indicate that mepivacaine alone plays a significant role in fetal depression (table 1). Apgar ratings in five minutes would not be 9 and 10 if drug depression with mepivacaine were significant.

SUMMARY

Gas chromatography was used to study blood levels of mepivacaine in five cases of vaginal delivery in which continuous caudal block was employed as the anesthetic tech-

nique. All five cases showed a statistically significant increase in the blood levels of mepivacaine with each refill dose. Mepivacaine crossed the placental barrier but did not depress the neonate.

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Resistance of Nasotracheal Tubes Used in Infants

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Currently, nasotracheal intubation is preferred to tracheostomy for prolonged maintenance of the airway in the newborn infant.^{1,2} Management of the airway is simpler and there appear to be fewer post-extubation complications.³

An endotracheal tube has a smaller internal diameter than an infant's glottis, and may produce a significantly greater airway resistance than that of the infant's upper airway. Mechanical ventilation can be used to overcome such an increase in resistance, but during spontaneous ventilation the increase in total airway resistance would increase the work of breathing. This situation arises during the period of weaning from a ventilator, when it is desirable to leave the tube in place and avoid frequent reintubation.

The purpose of this investigation was to study the airway resistance of nasotracheal tubes of sizes commonly used for prolonged intubation of infants^{4,5} and to make a comparison with the reported upper airway resistance of the newborn.⁶

METHOD AND MATERIALS

Three sizes of plastic tubes were chosen for study (table 1). They were cut to lengths usually required to maintain the tip of the tube in the trachea, midway between the carina and the glottis. Connectors (Bennett ‡)

‡ Puritan Bennett, subsidiary of Puritan Compressed Gas Corporation, Kansas City, Missouri.

TABLE 1. Dimensions of Tubes Studied

French Scale	Magill No.	Int. Diam. in. mm.	Davol No.	Length in cm.	Connector Size
12	<00	2.5	0	10	2 L
14	00-0	3.0	<1	11	3 S
16	0	3.5	>1	12	4 S

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