A LABORATORY AND CLINICAL EVALUATION OF MEPIVACAINE (CARBOCAINE ®)

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MEPIVACAINE (Carbocaine ®) is a local anaesthetic agent which was described by Ekenstam, Egnér, and Pettersson (1) in 1956. The structural formula of the drug is shown below:

MEPIVACAINE (CARBOCAINE ®)

Mepivacaine is a white, crystalline, odourless powder, melting point 261° C., molecular weight 285.5. The hydrochloride is easily soluble in water, stable in solution, very resistant to acid and alkaline hydrolysis, and can be repeatedly boiled without decomposition.

ACUTE TOXICITY

The acute toxicity of mepivacaine HCl (Carbocaine ®) was compared with that of lidocaine by subcutaneous administration in rats and mice. (Table I, Figure 1.) Isotonic saline was used as the diluent. The volume of injection to body weight for each animal was kept constant at 10 ml./kg. of the various concentrations of both local anaesthetic agents. However, the majority of rats surviving doses of both drugs above the LD₅₀ developed skin sloughs at the site of injection. None of the mice developed lesions.

Male mice between 20 and 30 gm. were used. The rats were females between 200 and 300 gm. The absolute volume of injection was consequently greater in the rats although the drug concentration at the various dosage levels was the same in both species.

NOTE. The subcutaneous LD₅₀ values for mepivacaine and lidocaine are indistinguishable statistically in both the mouse and the rat. However, the log dose : probit response slope is slightly greater with lidocaine in both species

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FIGURE 1

TABLE I
ACUTE TOXICITY OF MEPIVACAINE HCl COMPARED WITH LIDOCAINE HCl
(SUBCUTANEOUS ADMINISTRATION IN MICE AND RATS)

Species	Number of animals	Sex	Mepivacaine HCl		Lidocaine HCl	
			LD ₅₀ ± stn. dev. in mg./kg.	Slope	LD ₅₀ ± stn. dev. in mg./kg.	Slope
Mouse	120	Male	318 ± 21	14.82	301 ± 20	16.04
Rat	200	Female	548 ± 48	7.73	574 ± 49	9.00

(Figure 1). The animals receiving subcutaneous lidocaine were observed to die more quickly than those receiving mepivacaine.

DURATION, SPREAD, AND TISSUE REACTION

The duration, spread of anaesthesia, and tissue reaction with mepivacaine (Carbocaine®) were compared with procaine and lidocaine in five subjects in standard skin wheals on the volar surface of the forearm. Each drug was injected in 1 per cent solution in isotonic saline, and saline alone was used as a control in a

fourth wheal. Each wheal contained 0.1 cc. of solution. Injections were made in random order, and neither the subjects nor the investigator were aware of the identity of the substances injected at each site until the observations had been completed. Anaesthesia was tested with a hypodermic needle at each site at 15 min. intervals until the prick of the needle was appreciated as sharp or painful. Absolute anaesthesia was recorded as (++) , appreciation of touch without pain as (+). These observations are recorded in Table II.

TABLE II
DURATION OF ANAESTHESIA WITH INTRACUTANEOUS WHEELS
(SOLUTION 0.1 cc. OF 1 PER CENT IN SALINE IN EACH CASE)

Subject	Drug	15 min.	30 min.	45 min.	60 min.	75 min.	90 min.
1	Saline	—	—	—	—	—	—
	Procaine 1%	++	—	—	—	—	—
	Lidocaine 1%	++	+	+	—	—	—
	Carbocaine 1%	++	++	++	++	+	—
2	Saline	—	—	—	—	—	—
	Procaine 1%	++	—	—	—	—	—
	Lidocaine 1%	++	+	+	—	—	—
	Carbocaine 1%	++	++	++	++	+	—
3	Saline	—	—	—	—	—	—
	Procaine 1%	++	—	—	—	—	—
	Lidocaine 1%	++	+	—	—	—	—
	Carbocaine 1%	++	+	—	—	—	—
4	Saline	—	—	—	—	—	—
	Procaine 1%	++	—	—	—	—	—
	Lidocaine 1%	++	++	+	—	—	—
	Carbocaine 1%	++	++	++	+	—	—
5	Saline	—	—	—	—	—	—
	Procaine 1%	++	—	—	—	—	—
	Lidocaine 1%	++	++	+	—	—	—
	Carbocaine 1%	++	++	++	+	—	—

The maximum diameter of the area of anaesthesia produced by the standard intracutaneous wheal was also noted in each case, as was the reaction of the tissue as indicated by flare formation or erythema. The results in the five subjects are recorded in Table III.

From these observations it appears that mepivacaine (Carbocaine®) has a significantly longer duration of action than lidocaine, and several times the duration of procaine, in equal concentration. In four subjects of the five tested, the spreading power of mepivacaine exceeded that of procaine or lidocaine. Of the three drugs tested, procaine alone produced any signs of tissue reaction.

CLINICAL USE

Mepivacaine (Carbocaine®) has been employed for regional anaesthesia in 230 patients, as shown in Table IV.

TABLE III
SPREAD OF ANAESTHESIA AND TISSUE REACTION FROM
INTRACUTANEOUS WHEELS

Subject	Drug	Maximum area of anaesthesia	Tissue reaction	
			Immediate	Late
1	Saline	Nil	Nil	Nil
	Procaine 1%	0.6 cm.	Flare 2x wheal	Nil
	Lidocaine 1%	1.0 cm.	Nil	Nil
	Carbocaine 1%	1.8 cm.	Nil	Nil
2	Saline	Nil	Nil	Nil
	Procaine 1%	0.6 cm.	Flare	Nil
	Lidocaine 1%	1.0 cm.	Nil	Nil
	Carbocaine 1%	2.0 cm.	Nil	Nil
3	Saline	Nil	Nil	Nil
	Procaine 1%	0.7 cm.	Flare	Nil
	Lidocaine 1%	1.0 cm.	Nil	Nil
	Carbocaine 1%	1.0 cm.	Nil	Nil
4	Saline	Nil	Nil	Nil
	Procaine 1%	0.7 cm.	Flare	Nil
	Lidocaine 1%	1.2 cm.	Nil	Nil
	Carbocaine 1%	2.3 cm.	Nil	Nil
5	Saline	Nil	Nil	Nil
	Procaine 1%	0.8 cm.	Erythema	Nil
	Lidocaine 1%	1.5 cm.	Nil	Nil
	Carbocaine 1%	2.8 cm.	Nil	Nil

TABLE IV

Epidural block	
Lumbar	180
Caudal	3
Brachial plexus block	5
Paravertebral block (somatic)	6
Obturator block (bilateral)	1
Ankle block (anterior and posterior tibial)	1
Maxillary block	2
Stellate ganglion block	20
Lumbar sympathetic block	12
TOTAL	230

MATERIAL USED

Mepivacaine (Carbocaine[®]) was used in 2 per cent solution in isotonic saline solution for epidural anaesthesia and peripheral somatic nerve blocks, and in 1 per cent solution and $\frac{1}{2}$ per cent solution in saline for sympathetic blocks (stellate ganglion and lumbar sympathetic chain). The 2 per cent solution was re-autoclaved in the hospital before use.

RESULTS

Epidural Anaesthesia

The most common use of regional anaesthesia in the authors' practice is epidural anaesthesia for the obstetrical patient, the induction of anaesthesia

being delayed until the patient is judged to be ready for delivery. Of the 180 epidural anaesthetics by the lumbar route included in this study, 165 were given for vaginal delivery of obstetrical patients and 15 for Caesarean section. Of the patients delivered per vaginam, 16.5 per cent delivered spontaneously, while 83.5 per cent were delivered by forceps. The obstetricians prefer generally to control the head at the outlet by forceps. This accounts for the large proportion of forceps deliveries in this series.

Onset of Analgesia in Epidural Block

The time to onset of analgesia measured from the time of injection of 2 per cent mepivacaine (Carbocaine®) in saline was recorded in 90 patients having epidural anaesthesia for obstetrical procedures. The range was from 3 to 23 min., with 96 per cent occurring between 3 and 15 min., and 74.7 per cent in the first 10 min. We have noted that the transition from no anaesthesia to complete analgesia appears in most instances to be quite sudden.

Duration of Anaesthesia in Epidural Block

The duration of anaesthesia after the establishment of epidural block was determined in 63 obstetrical patients. The end-point used was the appreciation of the sharpness of a hypodermic needle or pain on pinching the skin. The shortest period of analgesia was 55 min. and the longest was 220 min.: 63.5 per cent of patients had a duration between 90 and 135 min. ($1\frac{1}{2}$ hrs. to $2\frac{1}{4}$ hrs.), while 53.9 per cent lasted 120 min. (2 hrs.) or more.

Spread of Anaesthesia in Epidural Block

The volume of solution injected into the epidural space in the obstetrical patients studied in this series varied from 13 cc. to 20 cc. Sites of injection were the interspaces between the third and fourth or the fourth and fifth lumbar vertebrae. The spread of anaesthesia varied from two segments above the site of injection to 13 segments above (second thoracic segment). Only three patients received volumes under 15 cc. In 68.1 per cent of those receiving 15 cc. or more, the upper limit of anaesthesia was between 5 and 8 segments above the point of injection. There did not appear to be any fixed relationship between volume injected and level of anaesthesia through this range. We believe this is due to factors for which we have not been able to account, such as rate and force of injection, the influence of uterine contractions and straining in the patient in labour.

Hypotension in Epidural Block

The occurrence of hypotension during epidural block with mepivacaine (Carbocaine®) 2 per cent was examined in 147 obstetrical patients in which the records were considered adequate for evaluation. Of these, 132 were delivered per vaginam, and 15 were Caesarean sections. Of these, 16 (12.1 per cent) of the patients for vaginal delivery and 9 (60 per cent) of the Caesarean sections

showed a drop of 20 mm. Hg or more in systolic blood pressure before delivery. Four of the patients for vaginal delivery and six of the Caesarean sections received vasopressor drugs to reverse the hypotension. The higher proportion of Caesarean section patients requiring vasopressor drugs is due to the sympathetic paralysis associated with the higher levels of anaesthesia required for this operation.

Sympathetic Blocks

Twenty stellate ganglion blocks and twelve blocks of the lumbar sympathetic chain were done for diagnostic or therapeutic indications. Mepivacaine (Carbocaine®) in 1 per cent solution was used in ten of the stellate blocks and in two of the lumbar sympathetic blocks, 0.5 per cent solution in saline being employed for the remainder. The use of 1 per cent solution in blocks of the lumbar sympathetic chain resulted in prolonged "overflow" blocking of somatic roots, which lasted for more than two hours. The 0.5 per cent solution proved to be equally effective in producing prompt sympathetic blocks, without overflow effect on the somatic roots. No complications occurred in any of these patients.

Other Somatic Nerve Blocks

The number of patients in whom mepivacaine (Carbocaine®) has been used in regional anaesthesia other than epidural block and sympathetic block is as yet too small for analysis. It may be noted, however, that in each case in which it has been employed (see Table IV) it has proved to be a satisfactory agent, having a prolonged action without the addition of vasoconstrictor substances. The solution used has been 2 per cent saline.

SUMMARY AND CONCLUSIONS

The acute toxicities of mepivacaine (Carbocaine®) and lidocaine as determined by the subcutaneous LD₅₀ in rats and mice are indistinguishable statistically although the log dose : probit response slope is slightly greater with lidocaine in both species.

Comparison of 1 per cent solutions of mepivacaine, lidocaine, and procaine in standard skin wheals showed that anaesthesia produced by mepivacaine lasted three to four times as long as that obtained with procaine, and 50 per cent longer than that produced by lidocaine, while the maximum area of anaesthesia was significantly greater with mepivacaine than with the other two drugs.

Experience with mepivacaine as a local anaesthetic agent in 230 patients has demonstrated that it produces satisfactory and prolonged anaesthesia without the necessity of adding vasoconstrictor substances to the solution. Of the 230 patients recorded in this study, 183 received epidural blocks. Onset of anaesthesia is rapid and no toxic manifestations or evidences of tissue irritation have been seen.

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