

ral artery. In each five sheep, mepivacaine, 2 per cent, 300 mg, was infiltrated around the femoral artery. In the remaining animal, the drug was injected directly into the vessel. Simultaneous popliteal and carotid arterial blood samples were drawn 1, 3, 5, 7, 9, 15 and 30 minutes following injection. All samples were analyzed for mepivacaine using a gas-liquid chromatographic technique.³

Popliteal arterial mepivacaine concentrations were three to four times higher than those in the carotid artery (fig. 1). This gradient appeared in one minute and reached its maximum five to ten minutes after injection. That this difference is not due to a direct intravascular injection is shown by the data from such an injection (fig. 2). Placing mepivacaine into the femoral artery produced a different type of decay curve with little difference between popliteal and carotid concentrations after the first minute.

CONCLUSIONS

Mepivacaine rapidly crosses the intact wall of a major artery. This absorption may explain the unusually high concentration of local anesthetic sometimes found in the human fetus following paracervical block for obstetrical analgesia.

REFERENCES

1. Asling, J. H., Shnider, S. M., Margolis, A. J., Wilkinson, G. R., and Way, E. L.: Paracervical block anesthesia in obstetrics. II. Etiology of fetal bradycardia following paracervical block anesthesia, *Amer. J. Obstet. Gynec.* (in press).
2. Kobak, A. J., Sadove, M. S., and Mazerod, W. T.: Anatomic studies on transvaginal regional anesthesia: Roentgenographic visualization of neural pathways, *Obstet. Gynec.* 19: 302, 1962.
3. Asling, J. H., Shnider, S. M., Wilkinson, G. R., and Way, E. L.: Gas chromatographic determination of mepivacaine in capillary blood, *ANESTHESIOLOGY* 31: 458, 1969.

Bupivacaine for Peripheral Nerve Block: A Comparison with Mepivacaine, Lidocaine, and Tetracaine

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Investigators who have compared bupivacaine (Marcaine) with lidocaine (Xylocaine), mepivacaine (Carbocaine), and tetracaine (Pontocaine) for epidural, caudal, and peripheral nerve block have concluded that the duration of action of bupivacaine is two to three times longer than that of lidocaine or mepivacaine and 20 to 30 per cent longer than that of tetracaine.¹⁻⁴ Most of these investigators arrived at this conclusion by comparing one patient with another, not by using the patient as a control. The latter technique was used, however, by Telivuo, who com-

pared bilateral intercostal nerve blocks with bupivacaine and with mepivacaine to relieve postoperative pain following thoracotomy in 58 patients; by Widman, who compared bupivacaine and mepivacaine for digital blocks in 16 volunteers; and by Albert and Lofstrom, who compared bupivacaine, mepivacaine, and tetracaine for ulnar block in 12 volunteers.¹⁻³

This study was designed to compare bupivacaine with lidocaine, mepivacaine, and tetracaine in peripheral nerve block for surgical procedures, using the patient as his own control.

METHOD OF STUDY

Selection of Patients and Premedication

This study was carried out on patients who were to receive regional blocks, whose surgical procedure involved similar areas of anes-

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thetia bilaterally. For premedication morphine or meperidine (Demerol), with or without atropine or scopolamine, was used. Barbiturates were not used.

Concentrations and Volumes of Solution

Bupivacaine in a concentration of 0.25 per cent was compared with 1.0 per cent lidocaine, 1.0 per cent mepivacaine, or 0.25 per cent tetracaine. According to animal studies, these would be comparable concentrations of these agents.¹⁵ Volumes of solutions injected bilaterally were identical. For example, in intercostal nerve block, if 4 ml of 0.25 per cent bupivacaine were injected around each of the lower seven intercostal nerves on the right side of the patient, 4 ml of 1.0 per cent lidocaine were placed around each of the same intercostal nerves on the patient's left side.

Local anesthetic solutions being compared in a specific patient contained like amounts of epinephrine (Adrenalin), 1:200,000 concentration.

Types of Blocks

Intercostal, brachial plexus, and sciatic and femoral nerve blocks were used. Bupivacaine was used on one side; lidocaine, mepivacaine, or tetracaine on the other. Some patients who had intercostal nerve blocks with bupivacaine and lidocaine or mepivacaine were blocked with tetracaine as soon as pain returned on the side in which lidocaine or mepivacaine had been injected. All blocks were done by staff anesthesiologists and residents.

Regression of Anesthesia, and Complete Return of Sensation

The stages of anesthesia were determined by the same technician, using the same Allis forceps. Like dermatome areas were tested for comparison. Testing was done at two-minute or shorter intervals from the time the agent was injected until maximum sensory anesthesia occurred. In the establishment of regression of the block in patients whose blocks had been adequate for the entire surgical procedure, 15-minute intervals were allowed to elapse between tests. When regression started, the intervals were reduced to five minutes or less so that a relatively accurate evaluation of

return of complete sensation could be made. Return of sensation was considered complete when equal responses were elicited from an unblocked area and from the blocked areas. If a surgical procedure was in process and anesthesia on the side blocked with lidocaine or mepivacaine started to regress as evidenced by pain, this was scored as complete return of sensation.

Number of Patients and Dosage of Local Anesthetic Agents

Intercostal nerve block: Seventy-five patients received, for intra-abdominal operations, bilateral intercostal nerve blocks of the lowest seven or eight nerves (table 1). In each patient bupivacaine was injected on one side. On the other, lidocaine was injected in 25 patients, mepivacaine in 25, and tetracaine in 25. Of the 25 patients blocked with lidocaine, 17 were blocked with tetracaine on the lidocaine side in the postanesthetic recovery unit when the effect of lidocaine had disappeared as determined by Allis forceps pinch comparison of blocked and unblocked areas. This was done in 18 of the 25 patients who received mepivacaine. The total quantities used were: 125 to 150 mg bupivacaine and 125 to 150 mg tetracaine; or 125 to 150 mg bupivacaine and 400 to 500 mg lidocaine or mepivacaine.

Sciatic and femoral nerve block: A total of 35 patients received bilateral sciatic and femoral nerve blocks with or without block of the lateral femoral cutaneous nerve and/or obturator nerve for surgical operations on the lower extremities (table 1). One side was blocked with bupivacaine. The other was blocked with: 1) lidocaine (six patients); 2) mepivacaine (five patients); 3) mepivacaine plus tetracaine (four patients); or 4) tetracaine (20 patients).

The total quantities used were: 1) and 2), 150 to 250 mg bupivacaine and 400 to 500 mg lidocaine or mepivacaine; 3) 150 to 250 mg bupivacaine and 400 to 500 mg mepivacaine to which 80 to 100 mg tetracaine had been added; 4) 150 to 250 mg bupivacaine and 150 to 200 mg tetracaine.

Brachial plexus block: Seven patients received bilateral brachial plexus blocks—one side accomplished using the supraclavicular

TABLE 1. Times to Onset and Maximum Anesthesia and Durations of Action of Bupivacaine, Lidocaine, Mepivacaine, and Tetracaine, Using Each Patient as His Own Control

	Number of Patients	Injection to Onset (min) (Mean \pm SD)	Injection to Maximum Anesthesia (min) (Mean \pm SD)	Injection to Regression of Anesthesia (min) (Mean \pm SD)	Injection to Return of Complete Sensation (min) (Mean \pm SD)
Bilateral intercostal nerve block					
Bupivacaine, 0.25 per cent	75	6.2 \pm 2.3	16.2 \pm 3.10	623 \pm 106	731 \pm 124
Lidocaine, 1.0 per cent	25	3.6 \pm 0.7	11.4 \pm 2.0	157 \pm 44	220 \pm 60
Mepivacaine, 1.0 per cent	25	4.7 \pm 0.95	14.4 \pm 3.0	196 \pm 50	256 \pm 74
Tetracaine, 0.25 per cent	60	5.7 \pm 3.1	13.8 \pm 4.8	429 \pm 93	515 \pm 99
Bilateral sciatic and femoral nerve blocks					
Bupivacaine, 0.25 per cent	35	4.3 \pm 1.8	16.4 \pm 5.6	758 \pm 208	914 \pm 238
Lidocaine, 1.0 per cent	6*	2.5 (2-5)	11.7 (10-20)	269 (207-315)	359 (245-405)
Mepivacaine, 1.0 per cent	5*	5.0 (3-9)	14.2 (8-21)	321 (270-390)	382 (305-480)
Tetracaine, 0.25 per cent	20	2.5 \pm 0.76	10.6 \pm 3.4	507 \pm 156	623 \pm 149
Mepivacaine, 1.0 per cent, + Tetracaine, 0.2 per cent	4*	5.8 (2-10)	16.2 (10-20)	450 (330-600)	577 (455-730)
Bilateral brachial plexus nerve blocks					
Bupivacaine, 0.25 per cent	7*	5.6 (2-18)	15.4 (10-23)	782 (495-1020)	939 (660-1107)
Lidocaine, 1.0 per cent	2*	2.5 (2-3)	10	240 (220-260)	390 (370-410)
Mepivacaine, 1.0 per cent	1*	11	23	451	571
Tetracaine, 0.25 per cent	4*	2.7 (2-5)	18.0 (7-45)	495 (195-675)	619 (345-795)

* Number of patients too small to permit determination of means and standard deviations. Therefore, an average is given and the figures contained within parentheses represent the shortest and longest times. Intercostal nerve blocks comparing all agents were subjected to Student's *t* test. Sciatic and femoral nerve blocks comparing bupivacaine with tetracaine were also subjected to this test. In all instances the differences between the sets were significant.

approach and the other with the axillary approach (table 1). One side was blocked with bupivacaine. The other side was blocked with 1) lidocaine in two patients, 2) mepivacaine in one, and 3) tetracaine in four. The doses used were: 1) and 2), 125 mg bupivacaine and 500 mg lidocaine or mepivacaine; 3) 125 mg bupivacaine and 125 mg tetracaine.

RESULTS

Onset, Maximum Anesthesia, and Durations

The times from injection to onset and to maximum anesthesia of all four local anesthetic agents varied slightly (table 1). The times from injection to regression and to complete return of sensation indicated that the duration of action of bupivacaine was two to three times longer than that of lidocaine or mepivacaine and 20 to 30 per cent longer than that of tetracaine (table 1). The durations of

sensory anesthesia with all agents were shortest with intercostal nerve block.

Quality of Anesthesia

All anesthetics produced satisfactory surgical anesthesia for the duration of their effectiveness measured by the Allis clamp. In all blocks, pain returned clinically between the time that regression started and the time that complete sensation returned as determined by clamp testing. With intercostal nerve block for intra-abdominal surgical procedures, post-operative patients occasionally experienced two types of pain prior to regression of anesthesia. If the celiac plexus was not blocked, visceral pain characterized by a dull aching in the abdomen, which was not accentuated by digital pressure on the incision, was noted. The other type was shoulder pain from diaphragmatic irritation mediated by the phrenic

nerve. Both types persisted for 12 to 24 hours, were not severe compared with incisional pain, and, in the presence of effective intercostal nerve block, could be controlled with small doses of narcotics, for example, 25 to 50 mg meperidine.

Complications

There were no systemic toxic reactions to any of the local anesthetic solutions. No instance of pneumothorax occurred, nor were there any neurologic sequelae.

CONCLUSIONS

This study showed, first, that the sensory effects of bupivacaine last two to three times longer than those of lidocaine or mepivacaine. Second, bupivacaine provides sensory anesthesia which lasts 20 to 30 per cent longer than that provided by tetracaine. Third, tetracaine lasts approximately twice as long as lidocaine or mepivacaine. Fourth, the area blocked may determine the duration of anesthesia which can be expected from a local anesthetic agent—for example, with all agents, durations of action were shortest in intercostal nerve blocks. Finally, the duration of sensory anesthesia of a local anesthetic agent varies considerably from patient to patient. For example, with bupivacaine in sciatic and femoral nerve blocks, the shortest time from injection to return of complete sensation was 540 minutes and the longest was 1,680 minutes. In one patient, bupivacaine and lidocaine analgesia following a bilateral intercostal nerve block regressed at approximately the same time; this short duration of the effects of bupivacaine was an exception.

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REFERENCES

1. Telivuo, L.: A new long-acting local anesthetic solution for pain relief after thoracotomy, *Ann. Chir. Gynaec. Fenn.* 52: 513, 1963.
2. Widman, B.: Clinical trial of a new local anaesthetic (LAC-43) with the aid of the pinprick and ninhydrin methods in finger blocks, *Acta Anaesth. Scand.* 8: 219, 1964.
3. Albert, J., and Lofstrom, B.: Bilateral ulnar nerve blocks for the evaluation of local anaesthetic agents, *Acta Anaesth. Scand.* 9: 1, 1965.
4. Ekblom, L., and Widman, B.: A comparison of the properties of LAC-43, prilocaine and mepivacaine in extradural anaesthesia, *Acta Anaesth. Scand. Suppl.* XXI: 33, 1966.
5. Nishimura, N.: Clinical experience of epidural anaesthesia with a new local anesthetic "LAC-43," *Jap. J. Anesth.* 15: 620, 1966.
6. Dhuner, K.-G.: Clinical experience with Marcaine (LAC-43), a new local anaesthetic, *Acta Anaesth. Scand. Suppl.* XXIII: 395, 1966.
7. Hollmen, A.: Experience with LAC-43, a new anaesthetic with prolonged action, in operative and therapeutic epidural and regional anaesthesia, *Ann. Chir. Gynaec. Fenn.* 55: 322, 1966.
8. Stockhausen, H.: Erfahrungen mit einem neuen lokalanästhetikum bei der parazervikalblockade, *Deutsch. Med. Wschr.* 48: 2220, 1967.
9. Watt, M. J., Ross, D. M., and Atkinson, R. S.: A clinical trial of bupivacaine, *Anaesthesia* 23: 2, 1968.
10. Steel, G. C., and Massey Dawkins, C. J.: Extradural lumbar block with bupivacaine (Marcaine: LAC-43), *Anaesthesia* 23: 14, 1968.
11. Duthie, A. M., Wyman, J. B., and Lewis, G. A.: Bupivacaine in labor, *Anaesthesia* 23: 20, 1968.
12. Nolte, H., and Puente-Egido, J. J.: Das neue lokalanästhetikum bupivacain (Carbostesin) in der klinischen anwendung, *Der Anaesthetist* 18: 264, 1969.
13. Bromage, P. R.: A comparison of bupivacaine and tetracaine in epidural block for surgery, *Canad. Anaesth. Soc. J.* 16: 37, 1969.
14. Bromage, P. R.: An evaluation of bupivacaine in epidural analgesia for obstetrics, *Canad. Anaesth. Soc. J.* 16: 46, 1969.
15. Henn, F., and Brattsand, R.: Some pharmacological and toxicological properties of a new long-acting local analgesic, LAC-43 (Marcaine), in comparison with mepivacaine and tetracaine, *Acta Anaesth. Scand. Suppl.* XXI: 9, 1966.