A Rapid-onset, Long-acting Regional Anesthetic Technique

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The acceptance of regional anesthesia has been limited by two major factors inherent in the local anesthetic agents available for use, namely, slow onset time and short duration of action. Bupivacaine has been used to increase the duration of action of regional anesthetics, but the time from injection of the drug to the establishment of surgical anesthesia may be unacceptably long.[1,2,3]

In a recent study by Moore,[4] compounding local anesthetics was shown to be safe in man. The technique permits one to take advantage of the desirable properties of each drug without producing toxicity.

Chloroprocaine is a local anesthetic of the ester family that has a rapid onset of action, a high safety index, and is readily available in the United States.[5] Combining chloroprocaine and bupivacaine should provide fast onset of surgical anesthesia and a long duration of analgesia. Despite substantial enthusiasm for use of both bupivacaine and compounded local anesthetics, no previous study has utilized a prospective randomized design to compare bupivacaine with a compounded mixture of bupivacaine and chloroprocaine. We undertook such a comparison using the axillary approach to the brachial plexus.

METHODS

Axillary blocks were performed on 25 healthy patients (ASA status I and II) undergoing operations on upper extremities. The patients ranged in age from 17 to 72 years. Each was visited preoperatively, at which time the procedure was explained and informed consent was obtained. No premedication was given. In a double-blind fashion, each patient was randomly assigned to one of two groups. The anesthetic agent for Group I was bupivacaine 0.5 per cent, 30 ml (150 mg), and that for Group II, bupivacaine, 0.5 per cent, 20 ml (100 mg) mixed with chloroprocaine, 3 per cent, 10 ml (300 mg). In every case the dose was less than the usual toxic amount of bupivacaine (175 mg) or chloroprocaine (1,000 mg). Epinephrine was not added.

A standard axillary block approach was used in all cases. A single paresthesia was sought with a 23-gauge needle, preferably over the dermatomes where the operation was to be, and the entire dose was injected at that point. A tourniquet was applied to the upper arm below the axilla to prevent the anesthetic solution spreading distally.

Sensory anesthesia was evaluated in the areas supplied by the major nerves of the forearm and hand, the median, ulnar, radial, musculocutaneous, and medial antebrachial cutaneous nerves. A standard pinprick with an 18-gauge needle depressed to ⅛-inch depth was used as the stimulus. The times from injection of anesthetic to onset of anesthesia and to maximum surgical anesthesia (total latency time) in each nerve was recorded on a sensory-nerve diagram of the forearm and hand. Also recorded were: 1) location of the paresthesia; 2) duration of the anesthesia taken from injection of local anesthetic until first return of pinprick sensation in any area of the hand or forearm; 3) time to full return of normal sensation; 4) the duration of pain relief from surgical trauma; 5) need for postoperative analgesics; 6) time to onset of complete motor blockade, in those cases in which it occurred; 7) time to return of motor function.

RESULTS

There were nine patients in Group I and 16 in Group II. The two groups were com-

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TABLE 1. Time Courses of Anesthesia*

	Group I		Group II		Significance
	Mean	SE	Mean	SE	
Time from injection to:					
Sensory onset (min)	6	± 1	4	± 1	$P < .05$
Maximal surgical anesthesia (min)	47	± 7	23	± 3	$P < .001$
Sensory regression (hours)	4	± 1	4	± 1	NS
Complete sensory return (hours)	19	± 1	19	± 1	NS
Onset of motor blockade (min)	8	± 1	6	± 1	NS
Complete motor blockade (min)	41	± 11	22	± 4	NS
Complete motor return (hours)	7	± 1	5	± 1	NS

* Times of onset and duration of block are shown. All values are rounded off to the nearest minute or hour. Group I consisted of nine patients who received 30 ml of 0.5 per cent bupivacaine. Group II consisted of 16 patients who received 20 ml of 0.5 per cent bupivacaine and 10 ml of 3 per cent chloroprocaine. Significance of differences between means was determined by Students t test.

parable with respect to age, weight, height, sex, physical status, and operative site. The anesthesia was successful in all patients.

The time courses of anesthesia are shown in table 1. The time to onset of the first sensory changes was significantly shorter in Group II ($P < .05$). However, the most striking difference was in the total latency times to surgical anesthesia in all nerves ($P < .001$). Bupivacaine alone took twice as long as the compounded local anesthetic and was less predictable. The mean latency time for bupivacaine was 47 minutes ±7, compared with 23 minutes ±3 for the mixture.

The time to onset and latency time were shortest in the nerve in which the paresthesia was obtained. The compounded drug spread to the other nerves faster than bupivacaine alone. Also, the block was most "solid" in the area of the paresthesia.

The duration of the block was not significantly affected by compounding the two drugs. The times to regression and to complete return of normal sensation were nearly identical in the two groups. This is probably due to the predominant long action of bupivacaine even when used with other local anesthetics.

Complete motor blockade occurred more frequently and quickly in Group II. Four of nine patients (44 per cent) in Group I had complete motor blockade, while 12 of 16 patients (75 per cent) in Group II had complete motor blockade.

One patient had a block on two different occasions. The first time she had the compounded drug, and the second time she had bupivacaine alone. Both the time to onset and total latency time were shorter with the combination than with bupivacaine alone. The durations of the anesthesias were similar.

Postoperatively, none of the patients needed a narcotic analgesic even after apparent return of normal sensation to the extremity. However, a few required mild oral analgesics. Patients who have nerve blocks with bupivacaine appear to have a prolonged period of analgesia that lasts long after normal sensory function returns.

There was no sign of systemic toxic reaction, local tissue toxicity, neuritis, or other neurologic complications resulting from the study.

DISCUSSION

The axillary approach to brachial plexus block was studied since this is one of the most commonly used regional nerve blocks. The two major reasons for this study were to evaluate the latency period to surgical anesthesia using bupivacaine and to determine whether mixing chloroprocaine with bupivacaine would produce a shorter onset time with an equally long duration of anesthesia, but without producing toxicity.

The results of the study demonstrate that the combination of bupivacaine, 0.5 per cent, 20 ml, and chloroprocaine, 3 per cent, 10 ml, does provide a more useful anesthetic for axillary block than bupivacaine, 0.5 per cent, 30 ml. The time from onset of block to surgical anesthesia was considerably shortened without affecting the prolonged action of bupivacaine. With an onset time of 4

minutes and complete surgical anesthesia in all nerves by 20 minutes, the latency period appears similar to that seen when lidocaine is used.

The compounding of these local anesthetics takes advantage of the best properties of the two drugs. In this situation, chloroprocaine offers rapid onset, good spread and penetration, and low toxicity; bupivacaine offers prolonged duration of surgical anesthesia and good postoperative analgesia. In the past, chloroprocaine or lidocaine has been used for rapid establishment of surgical anesthesia, and tetracaine for its prolonged duration of action.[4] However, tetracaine has a shorter duration of action than bupivacaine, and hence does not provide any appreciable postoperative analgesia. Recently, it has been shown that the addition of carbon dioxide to lidocaine substantially decreases the time to onset of the block.[6] Bromage and Gertel have demonstrated an improved supraclavicular brachial plexus block using bupivacaine mixed with carbonated lidocaine.[7] However, carbonated lidocaine shortened the duration of the block by 100 minutes and is not clinically available at present in the United States.

It has been stated that mixtures of local anesthetics may be dangerous since their toxicities would be additive or even synergistic. The evidence for these statements has come mainly from animal toxicity studies. These studies involved rapidly administered, large, intravenous doses of local anesthetic which produced much higher blood levels of local anesthetic than those present in patients, and which caused death in the animals.[8,9] Also, it has been shown that small animals metabolize esters much more slowly than man.[10] Recently, Moore published a series of 10,538 cases in which compounded local anesthesia was used without any increased toxicity.[4] It appears that a generalized toxic reaction is very unlikely to result from compounding an ester and an amide local anesthetic, since their peak blood levels occur at different times. The peak blood level of the ester occurs very rapidly, while the blood level of the amide rises much more slowly.

Concentrations in venous blood, measured after 100–150 mg bupivacaine in various types of blocks, have been less than 1 μg/ml, which is a safe level.[11,12] We omitted epinephrine from our anesthetic solution to accentuate any toxicity that might have occurred as a result of rapid absorption. Even without epinephrine, we saw no sign of systemic toxic reactions.

In summary, this study demonstrates that a solution consisting of bupivacaine, 0.5 per cent, 20 ml, and chloroprocaine, 3 per cent, 10 ml, produces an axillary block that has a rapid onset, prolonged duration, and no increase of toxicity. Postoperative analgesia is both prolonged and excellent.

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