Buprenorphine Added to the Local Anesthetic for Brachial Plexus Block to Provide Postoperative Analgesia in Outpatients

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Background and Objectives: Over the past 10 years, several studies have suggested that the addition of certain opiates to the local anesthetic used for brachial block may provide effective, long-lasting postoperative analgesia. One of these studies indicated that the agonist-antagonist, buprenorphine, added to bupivacaine provided a longer period of postoperative analgesia than the traditional opiates, but in this study, it is impossible to determine the relative contributions of the local anesthetic and the opiate to the postoperative analgesia because of the extremely long duration of the anesthesia provided by the local anesthetic, bupivacaine. By repeating the study using a local anesthetic of a shorter duration, the present study delineates more clearly the contribution of the buprenorphine to postoperative analgesia when added to a shorter-acting local anesthetic.

Methods: Forty, healthy, consenting adult patients scheduled for upper extremity surgery were enrolled in the study. Premedication was provided by intravenous midazolam 2 mg/70 kg and anesthesia by a subclavian perivascular brachial plexus block. The patients were assigned randomly to 1 of 2 equal groups based on the agents used for the blocks. The patients in group I received 40 mL of a local anesthetic alone, while those in group II received the same local anesthetic plus buprenorphine 0.3 mg. The study was kept double-blind by having 1 anesthesiologist prepare the solutions, a second anesthesiologist perform the blocks, and a third anesthesiologist monitor the anesthesia and analgesia thereafter, up to and including the time of the first request for an analgesic medication. The data were reported as means (± SEM), and differences between groups were determined using repeated measures of analysis of variance (ANOVA) and χ^2, followed by the Fisher exact test for post hoc comparison. A P value of less than .05 was considered to be statistically significant.

Results: The mean duration of postoperative pain relief following the injection of the local anesthetic alone was 5.3 (± 0.15) hours as compared with 17.4 (± 1.26) hours when buprenorphine was added, a difference that was statistically (and clinically) significant ($P < .0001$).

Conclusions: The addition of buprenorphine to the local anesthetic used for brachial plexus block in the present study provided a 3-fold increase in the duration of postoperative analgesia, with complete analgesia persisting 30 hours beyond the duration provided by the local anesthetic alone in 75% of the patients. This practice can be of particular benefit to patients undergoing ambulatory upper extremity surgery by providing prolonged analgesia after discharge from the hospital. *Reg Anesth Pain Med 2001;26:352-356.*

Key Words: Brachial plexus block, Buprenorphine, Postoperative analgesia.

The demonstration that opioid receptors exist in the peripheral nervous system[1,2] offers the possibility of providing postoperative analgesia in the ambulatory surgical patient. Over the past decade, many investigators have studied this approach and have compared the efficacy of various opioids added to the local anesthetic injected near the brachial plexus[3-16]; and it appears from several of these studies that buprenorphine provides the longest duration of analgesia, the most important parameter of postoperative analgesia in outpatients. Viel et al[3] showed that the addition of buprenorphine 3 μg/kg to 40 mL of 0.5% bupivacaine provided almost twice the duration of postoperative analgesia as the addition of morphine 50 μ/kg, i.e., a mean of 35 hours as compared with 18 hours. However, in Viel's study, it is difficult to determine the relative

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contributions of the local anesthetic and the opioid to the postoperative analgesia, because the local anesthetic used was bupivacaine. Thus, the analgesia provided by the bupivacaine (which lasts longer than the anesthesia)[17] may overlap and/or obscure the analgesia provided by the opioid. The authors performed the present study to delineate more clearly the contribution of the buprenorphine by repeating the study of Viel et al, but substituting for bupivacaine a local anesthetic mixture having a shorter duration of action. Thus, the present study was undertaken to ascertain the efficacy of buprenorphine in providing prolonged postoperative analgesia when added to a mixture of 1% mepivacaine and 0.2% tetracaine with epinephrine 1:200,000, which, when used alone, provides an average duration of surgical anesthesia of 5.25 hours,[18] much less than that provided by bupivacaine, but long enough to allow completion of surgical procedures in a hospital with a surgical residency.

Materials and Methods

Following approval of the protocol by the Institutional Review Board, 40 consenting, healthy, adult outpatients who were free of drug abuse problems and scheduled to undergo upper extremity surgery under regional anesthesia were enrolled in the study. Patients were assigned randomly to 1 of 2 groups, based solely on whether buprenorphine was to be added to the local anesthetic agent or not. Because the purpose of the study was to evaluate pain and pain relief in the postoperative period, any patient who required intraoperative supplementation because of inadequate anesthesia or whose preoperative drug screen was positive for opioids was dropped from the study and replaced, so that each group consisted of a full complement of 20 patients. Patients were randomly assigned to 1 of the 2 groups by the Department of Pharmacy: patients in group I received a subclavian perivascular brachial plexus block[19] using 40 mL of the local anesthetic mixture without any adjuvants, while patients in group II received the same block using 39 mL of the local anesthetic mixture and 1 mL of buprenorphine 300 μg (approximately 3 μg/kg). In each case, the local anesthetic solution was prepared by 1 of the investigators; the block was administered by a second investigator; and the onset and regression of the anesthesia and the subsequent analgesia were monitored by a third investigator who was unaware of the anesthetic solution used.

After the application of a noninvasive blood pressure monitor, electrocardiogram (ECG), and pulse oximeter, midazolam 2 mg was administered intravenously for sedation, after which the subclavian perivascular brachial plexus block was performed using a 22-gauge, sheathed needle and a nerve stimulator.[19] Following the production of an appropriate twitch response at 0.5 mA or less, the local anesthetic was injected, after which the onset of sensory and motor block was monitored to be certain that anesthesia was adequate for surgery without the need for any supplementation. Following the completion of surgery, the patients were monitored to assess the quality and duration of postoperative analgesia using the technique described by Viel et al[8] to allow data comparison. Thus, the patients were asked to classify their analgesia as good, tolerable, or unsatisfactory every hour for the first 6 hours, and then again at 24, 36, and 48 hours. "Good" analgesia indicated that the patient had no pain; "tolerable" indicated that the patient had mild pain, but did not need an analgesic medication; and "unsatisfactory" indicated that the patients' pain was such that they needed analgesic medication. For the purpose of this study, the duration of analgesia was measured from the time of the injection of local anesthetic for the brachial plexus block. At the time of each subsequent assessment, patients were observed and/or questioned about any subjective and/or objective side effects (sedation, pruritus, nausea, vomiting, or respiratory depression). Data were calculated and expressed as the mean ($\pm$ SEM), and differences between groups were compared using 2-way analysis of variance (ANOVA) and χ^2, followed by the Fisher exact t test for post hoc comparison. A P value of less than .05 was considered to be statistically significant.

Results

There were no significant differences between the 2 groups with respect to age, sex, weight, physical status, or the duration of the surgical procedure (see Table 1). The anesthesia provided by the block was adequate in all patients in both groups; and as

Table 1. Patient Characteristics and Duration of Surgery (values expressed as mean $\pm$ SEM)

	Group I	Group II
Gender		
Male	14	14
Female	6	6
Age (yr)		
Mean	33.05 $\pm$ 2.44	35.0 $\pm$ 2.93
Range	18-58	18-74
Weight (kg)		
Mean	74.65 $\pm$ 5.51	73.44 $\pm$ 5.30
Range	53.63-97.72	50.00-90.90
Duration of surgery (min)		
Mean	118.15 $\pm$ 12.32	122.00 $\pm$ 11.45
Range	45-240	45-180

Table 2. Type of Surgical Procedures

Type of Surgery	Group I	Group II
I & D of abscess	1	3
Removal of foreign body	3	3
Excision of tumor/mass	2	1
Fixation of finger	3	4
Fixation of fractured radius/ulna	7	5
Reduction of dislocation	1	1
Tendon repair	2	3
Nerve repair	1	0

shown in Table 2, the 2 groups were well matched with respect to the type and number of surgical procedures, suggesting their postoperative pain should have been of similar intensity.

The mean duration of postoperative analgesia in group II (17.4 ± 1.26 hours) was 3 times greater than that in group I (5.3 ± 0.15 hours), a highly significant difference, both statistically ($P < .001$) and clinically. Table 3 compares the quality of analgesia in the early postoperative period (1, 2, 3, 4, 5, and 6 hours) and in the later postoperative period (12, 24, 36, and 48 hours); and it clearly indicates that the patients in group II had significantly less pain during both periods. As shown in Fig 1, at the end of 6 hours, all of the patients in group II were pain free, whereas none of the patients were pain free in group I; and at 12, 24, and 36 hours, 95%, 80%, and 75% of the patients, respectively, in group II were still pain free. Equally significant is the finding in Table 3 that, whereas 100% of the patients in group I had requested and received analgesics by 12 hours, only 5% of the patients in group II needed analgesics at 36 hours postinjection (30 hours beyond the duration provided by the local anesthetic alone). Even at 48 hours, only 45% of the patients in group II needed analgesic medications.

It is also important to note that none of the patients in either group reported opioid-related side effects, such as nausea, vomiting, pruritus, or showed any evidence of respiratory depression.

Discussion

Buprenorphine is a semisynthetic, highly lipophilic opioid agonist-antagonist, which is 25 to 50 times or more more potent than morphine.[20-23] Thus, an intramuscular injection of 0.3 mg of buprenorphine is equipotent to 10 mg of morphine, but the analgesia produced by buprenorphine lasts significantly longer.[21-23] This prolonged duration appears to be due to the fact that buprenorphine seems to dissociate very slowly from opioid receptors, so that the usual duration of action is about 8 hours following parenteral administration.

In the study by Viel et al,[3] the authors compared the effect of buprenorphine with that of morphine added to 0.5% bupivacaine on the duration of analgesia following supraclavicular brachial plexus block. They found that the duration of analgesia produced by the addition of buprenorphine to bupivacaine was twice that produced by the addition of morphine. However, because there was no additive-free group, since bupivacaine is known to produce very prolonged anesthesia by itself, i.e, with no additives, the relative contributions of the buprenorphine and the bupivacaine to the prolonged analgesia was unclear. Thus, the present study was undertaken to determine the relative contribution of the buprenorphine to the duration of the postoperative analgesia, first by using a local anesthetic of shorter duration (but long enough to allow surgery to be completed at a teaching institution) and second, by comparing the addition of buprenorphine with a solution of local anesthetic containing no additive. The results obtained with the local anesthetic we used indicate that the addition of buprenorphine provides a 3-fold increase in the mean duration of analgesia, with complete analgesia persisting 30 hours beyond the duration (6 hours) provided by the local anesthetic alone in 75% of the patients.

Regardless of whether such analgesia is the result of opioid agonists acting directly at the peripheral

Table 3. Evaluation of Pain Relief

	Quality of Pain Relief	Early Postoperative Period						Late Postoperative Period			
		1 Hour	2 Hours	3 Hours	4 Hours	5 Hours	6 Hours	12 Hours	24 Hours	36 Hours	48 Hours
Group I	Good	20 (100%)	20 (100%)	19 (95%)	12 (60%)	5 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Tolerable	—	—	1 (5%)	7 (35%)	10 (50%)	5 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Unsatisfactory	—	—	—	1 (5%)	5 (25%)	15 (75%)	20 (100%)	20 (100%)	20 (100%)	20 (100%)
Group II	Good	20 (100%)	20 (100%)	20 (100%)	20 (100%)*	20 (100%)†	20 (100%)†	19 (95%)†	16 (80%)†	15 (75%)†	2 (10%)
	Tolerable	—	—	—	—	—	—	1 (5%)	3 (15%)	4 (20%)	9 (45%)
	Unsatisfactory	—	—	—	—	—	—	0 (0%)	1 (5%)	1 (5%)	9 (45%)

NOTE. Definition of terms used to evaluate quality of pain relief: good, patient has no pain; tolerable, pain is returning, but no medication is necessary; unsatisfactory; pain is significant enough that pain medication is necessary.

*$P < .01$.

†$P < .0001$.

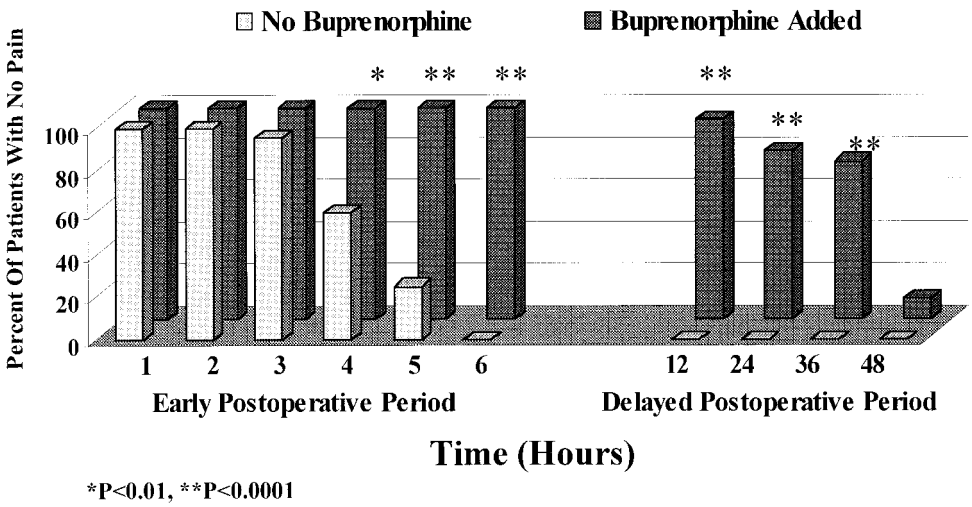

Fig 1. Graphic representation of the data comparing the differences in the duration of complete analgesia provided by local anesthetic mixture alone (group I) and local anesthetic mixture with buprenorphine (group II).

receptors or opioid agonists acting centrally after axonal transport from the periphery, clinical reports have continued to provide evidence of a peripheral perineural mechanism. Gobeaux and Landais[8] demonstrated that the addition of either fentanyl or meperidine significantly reduced the dose of lidocaine needed for brachial plexus block and hypothesized that the effect of the fentanyl and meperidine was due to blockade of peripheral opiate receptors. Even more impressive was the demonstration by Mays et al[24] that they could produce local analgesia without anesthesia by making peripheral perineural injections of morphine alone for chronic intractable pain, a finding that reinforced the notion that morphine exerts a peripheral antinociceptive action distinct from a systemic or central effect.

Whatever the site of action is, our study clearly indicates that buprenorphine added to the local anesthetic injected in performing a subclavian perivascular block does provide prolonged postoperative analgesia and markedly reduces the need for pain medication in both the early and late postoperative periods, at least up to 48 hours. Furthermore, the addition of buprenorphine to the local anesthetic mixture used in our study, although it did not prolong the surgical anesthesia, did provide 3 times the duration of analgesia provided by the local anesthetics alone. And finally, in view of the absence of adverse side effects in this small group of patients, the addition of buprenorphine to subclavian perivascular brachial blocks in patients undergoing same day surgery may be a way to provide postoperative analgesia for outpatients.

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