Similar Analgesic Effect After Popliteal Fossa Nerve Blockade with 0.375% and 0.75% Bupivacaine

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Abstract This study tested the hypothesis that increasing the concentration of bupivacaine from 0.375 to 0.75% would increase the duration of postoperative analgesia by 3 h. Seventy patients scheduled for hospital admission after foot or ankle surgery gave consent to enter this prospective randomized trial. Patients were randomly assigned to receive a popliteal fossa block (posterior approach) using 30 cc of either 0.375% or 0.75% bupivacaine, with epinephrine. Patients also received a neuraxial anesthetic and postoperative intravenous patient-controlled analgesia. Patient characteristics, duration of analgesia, pain scores, use of analgesic medications, and side effects of analgesic therapy were determined. Duration of analgesia was similar with both concentrations of bupivacaine (0.375% 14±8 h, 0.75% 13±6 h; mean±SD). Pain scores were the same for both groups on the first postoperative day (3 of 10 at rest, 5 with therapy). Analgesic use and side effects attributable to pain management did not differ between groups. In conclusion, postoperative analgesia was not affected by the concentration of bupivacaine used for the nerve block. There was no

benefit to increasing the concentration of bupivacaine above 0.375% for single-injection popliteal fossa nerve blockade when performed for postoperative analgesia.

Key words analgesia · nerve block · dose–response relationship

Introduction

Popliteal fossa nerve blockade (PFNB) with bupivacaine 0.5% provides relief of postoperative pain for 14 [1] to 20 h [2] after major foot and ankle surgery. However, single-injection nerve blocks may not provide analgesia of sufficient duration to allow a comfortable transition to oral analgesics. Many foot and ankle surgical patients who receive PFNB are initially comfortable, but then awaken with moderate to severe pain during the first night after surgery. This suggests that longer duration of analgesia would be desirable. Sleep disturbance on the night after surgery would presumably be minimized by a nerve block that provided analgesia overnight. Bupivacaine, 0.25 to 0.75%, is commonly used for nerve blocks. There is a perception that increasing the concentration of bupivacaine may prolong the period of analgesia from a nerve block. Published studies are contradictory; increasing the concentration of local anesthetic for peripheral nerve blockade may [3] or may not [4] provide a longer duration of analgesia. Reported side effects of PFNB are few [1, 2]. However, local anesthetic toxicity may be dose-dependant, so concentrated local anesthetic should be used only if a benefit can be demonstrated.

When a thigh tourniquet is used during foot, ankle, or calf surgery, the primary anesthetic at the authors' institution is usually a spinal or combined spinal–epidural anesthetic. PFNB is frequently performed for postoperative analgesia.

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Choices of local anesthetic for peripheral nerve blockade when performed for postoperative analgesia include bupivacaine, levobupivacaine, and ropivacaine. The duration of analgesia after peripheral nerve blockade with bupivacaine is the same as [5] or longer than [6] the analgesic duration provided by ropivacaine. Bupivacaine is less expensive than ropivacaine or levobupivacaine.

This prospective randomized study tested the hypothesis that increasing the concentration of bupivacaine for PFNB from 0.375 to 0.75% would increase the duration of postoperative analgesia by 3 h. Prolonging the duration of analgesia by 3 h was judged to be the minimal increase that would be clinically important.

Materials and methods

After approval by the Hospital for Special Surgery Institutional Review Board, written informed consent was obtained from 70 patients scheduled for hospital admission after foot or ankle surgery. Patients were excluded from the study if the planned surgery would cause pain outside the distribution of the sciatic nerve (high and extensive medial ankle surgery or iliac crest bone graft), if patients suffered from chronic pain, if patients were unable to describe postoperative pain to the investigators (language barrier, psychiatric disorder, or dementia), if there was a contraindication to performance of PFNB, or if there was a contraindication to use of 225 mg bupivacaine for PFNB (e.g., weight less than 40 kg or extensive hepatic disease). All patients in the study were operated on by a single attending surgeon. Operations were classified into two types: acute traumatic (e.g., open reduction, fixation of fracture or Achilles tendon repair) or chronic reconstructive (e.g., joint arthrodesis or fusion).

PFNB was performed with 30 cc of either 0.375 or 0.75% bupivacaine, both with 5 µg/ml epinephrine. Patients were randomized via computer-generated random assignment. Assignment was concealed in closed envelopes until after

Table 1. Patient characteristics

	0.375% (n=34)	0.75% (n=36)
Age (mean±SD, year)	50±14	44±13
Gender (fraction of women)	18/34 (53%)	20/36 (56%)
ASA status (median)	2	2
Body mass index (mean±SD)	28±5	28±6
Tourniquet time (mean±SD, min)	130±29	120±31
Procedure	10 acute traumatic; 24 chronic reconstructive	13 acute traumatic; 23 chronic reconstructive

No significant differences were noted.

ASA = American Society of Anesthesiologist physical status

Table 2. Analgesic outcomes

	0.375%	0.75%
Duration of analgesia (mean±SD, h)	14±8	13±6
NRS Scores, POD 1		
Rest	3±2	3±2
PT	5±3	5±2
NRS Scores, POD 2		
Rest	2±2	2±1
PT	3±2	3±2
Morphine use (mg)		
0–24 h	22	29
Median (25th percentile, 75th percentile)	(12, 38)	(17, 42)
Oral analgesic use (tablets)		
0–24 h	2	0
Median (25th percentile, 75th percentile)	(1, 6)	(0, 7)
Morphine use (mg)		
24–48 h	2	0
Median (25th percentile, 75th percentile)	(0, 7)	(0, 7)
Oral Analgesic Use (tablets)		
24–48 h	6	6
Median (25th percentile, 75th percentile)	(4, 12)	(1, 8)

Duration and NRS data are depicted as mean±SD. No significant differences were noted.

NRS = Numerical rating scale (for pain), POD = postoperative day, PT = physical therapy

recruitment. The envelopes were prepared by a research assistant not involved with patient recruitment or data analysis. PFNB (posterior approach) [7] was performed using a Braun (Bethlehem, PA, USA) 2" Stimuplex needle and a Braun Stimuplex Dig RC nerve stimulator, starting at 1.5 mA and decreasing to ≤0.5 mA (2 Hz). Details of the block performance were recorded (minimum current obtained and type of muscle twitch observed). Side effects that occurred during PFNB were recorded (paresthesia, aspiration of blood, seizures, tachycardia, or other cardiac effects). PFNB was performed in the operating room before performing the neuraxial block. Sedation was given before PFNB, as determined by the attending anesthesiologist. The anesthesiologist performing PFNB was not blinded to group assignment. The patient, the pain management team, and the data analyst were blinded to group assignment.

The primary anesthetic was a spinal or combined spinal–epidural, which allowed the use of a thigh tourniquet during surgery. Saphenous nerve blockade was performed at the level of the proximal tibia with 7 cc 0.5% bupivacaine when indicated by the surgical site. Postoperative intravenous morphine patient-controlled analgesia was used. Patients who reported allergy or intolerance to morphine were given intravenous hydromorphone. Patients were offered oral analgesics concurrent with the intravenous patient-controlled analgesia (acetaminophen with hydrocodone or oxycodone). The primary endpoint of the study was time from performance of PFNB to onset of pain in the distribution of the sciatic nerve, which was determined by patient interview. Secondary endpoints of the study included total analgesic use, NRS scores (numerical rating scale of pain intensity, from 0 to 10), and incidence of side effects attributed to pain control (nausea, sedation, or confusion).

Table 3. Side effects

	0.375%	0.75%
Nausea	20 (59%)	19 (53%)
Emesis	14 (41%)	13 (36%)
Sedation or confusion	0	0
Dysesthesia	3 (8.8%)	0
Neuropraxia	0	0
Site tenderness	0	2 (6%)

No significant differences were noted.

Block duration was defined as time from administration of the nerve block to return of pain, as reported by the patient. Dysesthesia was defined as any abnormal sensation in the distribution of the sciatic nerve, most commonly described as tingling or “pins and needles” sensation. Neuropraxia was defined as an objective abnormality of the neurologic examination in the distribution of the sciatic nerve on the operative side.

A power analysis was performed using preliminary data on 15 patients who received PFNB with 30 cc 0.5% bupivacaine before the study. The mean time from end of surgery to onset of pain was 10.9 h, with a standard deviation of 4.1 h. A *t* test power calculation was performed with the “Sigma-Stat” program (Jandel Scientific, version 2.0, San Rafael, CA, USA). We assumed a standard deviation of 4.1, alpha of 0.05, and a difference in means of 3 h between the two groups (this was thought to be the minimal time difference that would be of clinical importance). Group size of 35 patients provided a power of 0.855.

Post hoc analyses were performed to investigate possible confounding variables. The muscular responses to nerve stimulation were divided into dorsiflexion, eversion, plantar flexion, or inversion, and compared by ANOVA. In the event that compound muscular responses were observed, the predominant response was recorded. Current was evaluated by dividing patients into four groups of similar size, with analysis by ANOVA. Attending anesthesiologists were compared by ANOVA.

Results

Patient demographics were similar in the two groups (Table 1). A dose of 30 cc 0.375% bupivacaine was administered to 34 patients. A dose of 30 cc 0.75% bupivacaine was administered to 36 patients. A suitable muscular response was obtained in all patients. The current was reduced to ≤ 0.5 mA in 69/70 patients. The average time needed to perform PFNB was 6 min (25th percentile, 5 min; 50th percentile 5 min; and 75th percentile, 8 min). Blood was aspirated during PFNB in three patients (one in 0.375%, two in the 0.75% group). Tachycardia occurred during PFNB in one patient (in the 0.75% group). No patients developed other cardiac effects. No paresthesias or seizures were noted during PFNB. Most patients received subarachnoid bupivacaine (mean dose 17 mg) (27/34 in the 0.375% group and 28/36 in the 0.75% group). The

remainder received subarachnoid mepivacaine (mean dose 57 mg). Most patients received combined spinal–epidural anesthetics (55 patients). Spinal anesthesia alone was given to seven patients in the 0.375% group, and to eight patients in the 0.75% group. Additional local anesthetic was given via the epidural catheter in 21 patients; it consisted of 2% lidocaine (19 patients) or 0.75% bupivacaine (2 patients). After resolution of the neuraxial block, all patients reported decreased sensation in the operative foot, indicating successful PFNB.

Sedation before PFNB included midazolam (mean 5 mg, 69 patients), fentanyl (mean 62 μ g, 29 patients), propofol (mean 51 mg, 7 patients), and diazepam (5 or 10 mg, 2 patients). Saphenous nerve blocks were performed in 13/34 (0.375%) and 15/36 (0.75%). Patient-controlled analgesia was provided with intravenous morphine (61 patients) or hydromorphone (8 patients). One patient declined intravenous opioids. Patients were offered oral analgesia consisting of acetaminophen/oxycodone (48 patients), acetaminophen/hydrocodone (18 patients), acetaminophen/propoxyphene (1 patient), or hydromorphone (1 patient). Two patients declined oral analgesics.

Analgesic outcomes did not vary between the two groups (Table 2). Duration of analgesia was similar between the two groups. NRS pain scores were similar between the groups. Analgesic use did not differ between groups. Side effects attributable to the pain management occurred at similar rates between the groups (Table 3). The three cases of dysesthesia resolved within 3 days.

Factors that might contribute to block success were evaluated. The muscular responses to nerve stimulation were divided into dorsiflexion ($n=34$), eversion ($n=16$), plantar flexion ($n=12$), or inversion ($n=7$). The current was evaluated by dividing patients into four groups of similar sizes (300–360 μ A, $n=12$; 370–410 μ A, $n=19$; 420–460 μ A, $n=21$; and ≥ 470 μ A, $n=18$), with analysis by ANOVA. The current obtained before injection, the type of muscular response achieved, and which attending anesthesiologist performed or supervised the anesthetic did not significantly alter the duration of analgesia.

Discussion

Doubling the concentration of bupivacaine from 0.375 to 0.75% for PFNB did not prolong the analgesia provided by the nerve block. One interpretation of this finding would be that once a maximally effective dose is given, further increases in local anesthetic concentration do not prolong the analgesic effect [8]. Alternatively, this finding might represent a type II statistical error. Based on the power analysis the probability of a type II error is less than 15%. Other methods to consider for prolongation of block duration include placement of a perineural catheter [9] or use of additives such as clonidine [10]. Patients reported relatively low pain scores, but opioid use was sufficient to cause high rates of nausea and vomiting. In retrospect, prophylactic antiemetics may have been beneficial.

Duration of pain relief was chosen as the primary outcome because we felt it was of greater importance to patients than duration of sensory or motor blockade. In addition, we thought it was undesirable to subject patients to repeated neurologic examination during the night after surgery. Analgesic duration was determined by patient interview. The interviewer attempted to distinguish pain in the sciatic nerve distribution from pain in the saphenous nerve distribution, but not all patients were able to clearly localize their pain. Saphenous nerve blocks were performed for patients whose surgery involved extensive work on the medial aspect of the ankle, but the duration of saphenous nerve blockade may differ from the duration of PFNB. This may have contributed to the large standard deviation noted for duration of analgesic effect. However, other investigators have also reported wide ranges of analgesic duration after peripheral nerve blockade: 16 h, range 8–24 [11], 19 ± 3.4 h [12], 16 h, range 7–31 [13].

Previous studies have shown that when performing a posterior approach PFNB, inversion or dorsiflexion responses to nerve stimulation yielded the highest number of nerves blocked, and inversion predicted the fastest onset [14]. There was no link in this study between block duration and the muscle response to nerve stimulation. Speed of onset was not measured, as PFNB was performed immediately before the neuraxial anesthetic.

This study relied on patient report of onset of pain. Peripheral nerve blocks with bupivacaine wear off gradually, so the onset of pain depends on patient characteristics and the nature of the surgery. A more objective determination of block offset, such as sensitivity to pinprick, might be more reproducible across patients. This was not judged practical, as it was undesirable to awaken patients during the night to assess their nerve block. In addition, a diverse group of surgeries were analyzed, some of which caused more pain than others. Unfortunately, unlike hip or knee surgery, there is no single ankle operation performed with high frequency at the authors' institution.

This study examined the hypothesis that 0.75% bupivacaine would increase the duration of postoperative analgesia. However, increasing the concentration of bupivacaine from 0.375 to 0.75% for single-injection PFNB provided no additional benefit. Although we observed no evidence of toxicity, we have no reason to recommend exceeding 0.375% bupivacaine for PFNB performed for postoperative analgesia.

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