The addition of clonidine to bupivacaine in combined femoral-sciatic nerve block for anterior cruciate ligament reconstruction

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Clonidine has been shown to prolong sensory analgesia when given as an adjunct to peripheral nerve blocks but has not been evaluated when given in conjunction with a femoral-sciatic nerve block. The purpose of this investigation was to determine whether the addition of clonidine to a femoral-sciatic nerve block would prolong the duration of sensory analgesia in groups of patients undergoing anterior cruciate ligament (ACL) reconstruction.

This prospective, randomized, double-blind investigation was performed on 64 subjects undergoing ACL reconstruction. Patients were assigned randomly to receive a femoral-sciatic nerve block using 30 mL of 0.5% bupivacaine with 1:200,000 epinephrine (control group) or 30 mL of 0.5% bupivacaine with 1:200,000 epinephrine and 1 µg/kg of clonidine (experimental group). Variables measured included demographics, timed pain intensity measurements, postoperative analgesic consumption, duration of analgesia, and patient satisfaction.

No significant differences were noted between groups for pain intensity scores, duration of sensory analgesia, postoperative analgesic requirements, or overall patient satisfaction. Both groups reported minimal amounts of postoperative pain and high analgesic satisfaction scores.

Based on our results, we do not recommend the addition of clonidine to a femoral-sciatic nerve block when given to facilitate postoperative analgesia in patients undergoing ACL reconstruction.

Key words: **Anterior cruciate ligament reconstruction, femoral-sciatic nerve block, postoperative pain management, regional anesthesia.**

Anterior cruciate ligament (ACL) reconstruction is associated with significant postoperative pain that can last as long as 48 hours, often resulting in immobility and a decrease in effective early mobilization.[1,2] Furthermore, this postoperative immobility can result in the development of adhesions, weakened ligament insertion, and muscle atrophy.[3] Therefore, it is important that effective postoperative pain management techniques be used to decrease the incidence of these preventable postoperative complications. Traditionally, oral and parental opioids and nonsteroidal anti-inflammatory agents are used to control the pain following ACL reconstruction. While these pharmacological agents have been shown to adequately control the pain, large doses often are required, which can result in a multitude of undesirable side effects.[4,5]

In an attempt to provide effective postoperative analgesia while minimizing untoward effects, anesthesia providers are continually exploring alternative methods. Of these alternative methods, one technique that has been shown to be highly effective in controlling postoperative pain in patients undergoing ACL reconstruction is the lower extremity peripheral nerve block.[6,7] Lower extremity peripheral nerve blocks in patients undergoing ACL reconstruction have been shown to significantly decrease postoperative analgesic requirements, improve postoperative knee rehabilitation, and decrease the length of time required in the hospital.[6,7] Because of these advantages many practitioners advocate placing a lower extremity peripheral nerve block in all patients undergoing ACL reconstruction. The most common nerves blocks performed to facilitate this analgesia are the femoral nerve block and the combined femoral-sciatic nerve block. However, it has been noted that after initial block resolution, patients must rely on oral analgesics that are associated with undesirable side effects. Therefore, many clinical investigations have been performed to determine ways to increase the duration of analgesia from peripheral nerve blocks. These investigations have analyzed the use of combinations of local

anesthetics or supplemental medications to prolong anesthetic duration with traditional and nontraditional medications.[8-12] One of the nontraditional medications that has shown some promise is the α_2-adrenergic agonist clonidine.

Clonidine has been shown to have an analgesic neuraxial effect and is well described in the literature, but its use is limited by side effects that include an impact on hemodynamic variables.[13] Studies also have shown that clonidine can be administered as an adjunct to local anesthetics in the performance of a peripheral nerve block without having a detrimental effect on hemodynamics.[8-12] However, it has been noted that there are limited studies on what effect clonidine will have when added to a femoral-sciatic nerve block, and, to our knowledge, no study has been performed to date evaluating the effect when given in conjunction with a femoral-sciatic nerve block in patients undergoing ACL reconstruction. Therefore, the purpose of this investigation was to examine whether the addition of 1 µg/kg of clonidine would prolong the duration of analgesia and improve patient outcomes when administered with bupivacaine in a femoral-sciatic block for ACL reconstruction.

Materials and methods

This double-blind prospective investigation was conducted at the Naval Medical Center San Diego (San Diego, Calif), from August 2001 to April 2002. Following approval from the institutional review board and an exemption from the US Food and Drug Administration (IND #63077) to conduct this investigation of a new drug, a total of 64 patients assessed as ASA class I or II were approached and enrolled in the study. After initial consent was obtained, subjects were assigned randomly to a control or experimental group by using a computer-generated random numbers table. Following randomization, an anesthesia provider (J.F.B. and J.P.M.) prepared local anesthetic admixtures and placed them into syringes labeled with subject number and date and delivered these syringes to one of the investigators in the study. The anesthesia provider preparing the solutions maintained custody of the randomization list and was not involved in data collection or block performance, thereby ensuring that investigators and subjects remained blinded as to group assignments until conclusion of the study. Subjects assigned to the control group received medications from syringes containing 30 mL of 0.5% bupivacaine with 1:200,000 epinephrine, while those in the experimental group received medications from syringes containing 30 mL of 0.5% bupivacaine with 1:200,000 epinephrine and 1 µg/kg of clonidine. All subjects then had a femoral-sciatic nerve block performed with the respective syringes by one of the investigators (D.J.C. and H.M.C.)

The femoral-sciatic nerve block was performed in the preoperative block area located immediately adjacent to the operative suites. All subjects were placed in the Sims position on a standard operative gurney, and standard monitors were used, including a noninvasive blood pressure device, a continuous electrocardiogram, and a pulse oximeter. The operative leg was positioned superiorly and flexed at the knee, and a line was drawn from the posterior superior iliac spine to the greater trochanter of the femur. A second line was drawn from the sacral hiatus to the greater trochanter, and a third line was drawn perpendicular to and bisecting the first line. The intersection of the second and third lines was the point of needle entry for placement of the sciatic nerve block. The identified area was prepped with povidone iodine (Betadine) solution and infiltrated with 2 to 3 mL of 1% lidocaine solution subcutaneously. A 22-gauge, 10-cm, insulated, B-bevel needle, aimed perpendicular to the skin, was advanced until posterior tibial nerve distribution was elicited with the aid of a peripheral nerve stimulator. A stimulation frequency of 2 Hz and an intensity level of 1.0 mA were used until a plantar flexion motor response was elicited. The intensity level was decreased to less than 0.5 mA while maintaining the identified motor response. Fifteen milliliters of the local anesthetic solution was injected in 5-mL increments with intermittent syringe aspiration.

After placement of the sciatic nerve block, subjects were placed in a supine position for placement of the femoral nerve block. The site of injection was 1 cm lateral to the femoral artery and 1 cm inferior to the inguinal ligament. The identified area was prepped with povidone iodine solution and infiltrated with 2 to 3 mL of 1% lidocaine solution subcutaneously. A 22-gauge, 4-cm, insulated, B-bevel needle was advanced perpendicular to the skin just lateral to the artery until femoral nerve distribution was elicited with the aid of a peripheral nerve stimulator. With a stimulation frequency of 2 Hz, the intensity level was set at 1.0 mA until quadriceps extension was elicited, then decreased to less than 0.5 mA. Fifteen milliliters of the local anesthetic solution was injected in 5-mL increments with intermittent syringe aspiration.

Before transport to the operative suite, all blocks were assessed using pinprick to determine sensory levels and a modified Bromage scale to determine the degree of motor blockade. Blocks were considered successful if no sensation was noted along the femoral and sciatic dermatomes and a lack of motor strength

was noted when tested. If it was noted that complete sensory or motor blockade was not present 30 minutes following block placement, the block was determined to be a failure. All data were obtained and recorded on a data collection sheet. Vital signs, including blood pressure, heart rate, and oxygen saturation level, were noted and recorded at 5-minute intervals in the preoperative and operative settings and recorded on the data collection sheet.

Following block placement, all subjects were taken to the operating room suite where standard monitors were reapplied. General anesthesia was administered according to the following induction protocol: fentanyl, 2 to 3 µg/kg intravenously; 2% lidocaine, 1 mg/kg intravenously; and propofol, 2.0 mg/kg intravenously. Rocuronium, 0.6 to 1.2 mg/kg intravenously, was used to facilitate tracheal intubation. Anesthesia was maintained with isoflurane, 0.6% to 1.2%, in combination with 50% nitrous oxide and 50% oxygen. Upon completion of the surgical procedure, subjects were transferred to the postanesthesia care unit. Postoperative pain, if it occurred, was treated with intravenous fentanyl or intravenous morphine as needed per subject request while subjects remained in the hospital.

A 0-to-100 numeric rating scale (NRS) was used to measure pain. Subjects were asked to rate their pain on the scale; a score of "0" indicated "no pain" and a score of "100" indicated the "worst pain imaginable." Subjects were asked to rate their pain preoperatively and at 5, 7, 9, 11, 13, 15, 17, and 19 hours after placement of the block.

The *duration of analgesia* was defined as the time from placement of the femoral-sciatic block to the first request for analgesic medication. Data about the first request for analgesics were obtained from the hospital record if the request was made while the subject remained in the hospital or, if the patient had been discharged from the hospital, in a telephone interview approximately 24 hours postoperatively.

Opioid consumption was measured for the first 24 hours following block placement. Data about analgesic requirements were obtained from the postanesthesia care unit and same-day surgical unit records while subjects remained in the hospital. In addition, subjects were asked to maintain a record of analgesic requirements following discharge from the hospital. These data were obtained in the follow-up telephone interview approximately 24 hours postoperatively. Total opioid consumption for the first 24 hours was calculated and converted to morphine equivalents.[14]

Patient satisfaction, as a measure of overall satisfaction with the quality of anesthesia and analgesia provided, was measured by asking subjects to rate their satisfaction level based on a 1-to-5 Likert satisfaction scale that used the following grading criteria: 1, completely dissatisfied; 2, dissatisfied; 3, somewhat satisfied; 4, satisfied; and 5, completely satisfied. This survey was conducted during a follow-up phone call approximately 24 hours after placement of the block.

Descriptive statistics were used to analyze demographic variables. Mean NRS scores between groups recorded preoperatively and at 5, 7, 9, 11, 13, 15, 17, and 19 hours following block placement were compared by using *t* test analysis, as were the mean times of duration of analgesia between groups and the mean amounts of analgesic requirements between groups in 24 hours measured in morphine equivalents. Median patient satisfaction scores measured with a 1-to-5 Likert scale between groups were compared by using the Mann-Whitney *U* test. A *P* value of less than .05 was considered significant. Before the investigation, a power analysis determined that a sample size of 27 subjects per group would be sufficient to detect a difference in postoperative sensory analgesia of 180 minutes when a power of 0.8 and an α of .05 were used. After factoring in an attrition rate of 15%, the final sample size was set at 64 subjects, or 32 subjects per group.

Results

We enrolled 64 subjects in this double-blind investigation. Five subjects in the control group and 4 in the experimental group experienced failed blocks, and their data were not included in the analysis. Statistical analysis was performed on data for the remaining 55 subjects, 27 in the control group and 28 in the experimental group. No significant differences were noted between groups in the demographic variables of age, height, weight, sex, or ASA classification (Table).

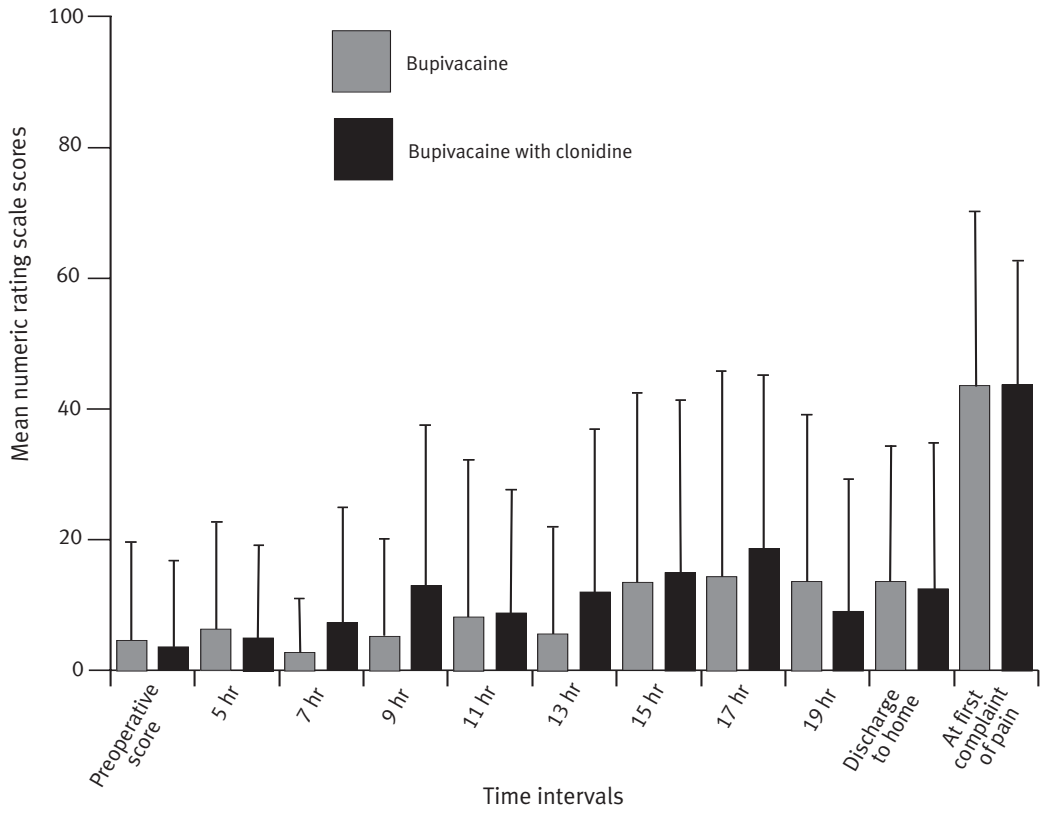
There were no significant differences between

Table. Demographic data for the study groups*

	Bupivacaine (n = 27)	Bupivacaine with clonidine (n = 28)
Age (y)	25.2 ± 4.1	28.5 ± 6.1
Height (cm)	176.9 ± 9.1	176.1 ± 9.0
Weight (kg)	83.1 ± 12.7	86.4 ± 12.1
Sex		
Male	26	27
Female	1	1

*** Data are given as mean ± SD, except for sex, which is given as number of subjects.**

Figure 1. Comparison of mean pain intensity scores between groups



Based on a 0-100 numeric rating scale: 0, no pain; 100, worst pain imaginable. No statistically significant difference was observed between the control (bupivacaine) and experimental (bupivacaine with clonidine) group at each separate time interval ($P > .05$). The line extending above each bar represents standard deviation.

PACU = Postanesthesia care unit

groups in mean NRS scores measured preoperatively or on arrival to the postanesthesia care unit. In addition, no significant differences were noted between groups at any of the 2-hour intervals from 5 to 19 hours following block placement (Figure 1).

No statistically significant differences were noted in the mean duration of analgesia between groups. The mean duration of analgesia for the control group (bupivacaine without clonidine) was 755 minutes, in comparison with 714 minutes for the experimental group (bupivacaine with clonidine) ($P = .758$) (Figure 2).

A statistically significant difference was not observed between groups in the total opioid consumption during the first 24 hours postoperatively. The control group (bupivacaine without clonidine) used a mean of 6.98 mg of morphine, compared with 5.1 mg of morphine in the experimental group (bupivacaine with clonidine) ($P = .171$) (Figure 3).

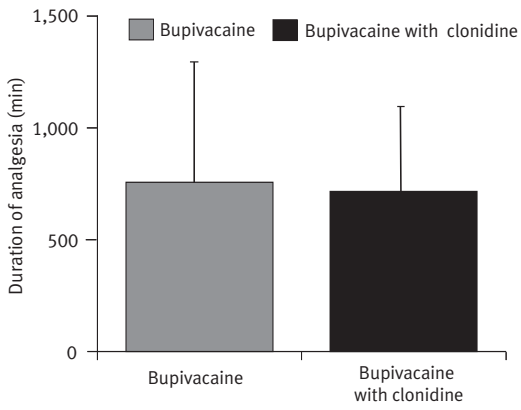
Patient satisfaction scores reported for the 2 groups demonstrated no statistically significant differences. The control group (bupivacaine without clonidine) reported a median satisfaction score of 4, in comparison with 5 for the experimental group (bupivacaine with clonidine) ($P = .063$) (Figure 4).

Vital signs were similar between the groups, and no hemodynamic instability was noted in the preoperative, operative, or postoperative settings. No difference in the incidence of nausea, vomiting, or somnolence was noted between the groups.

Discussion

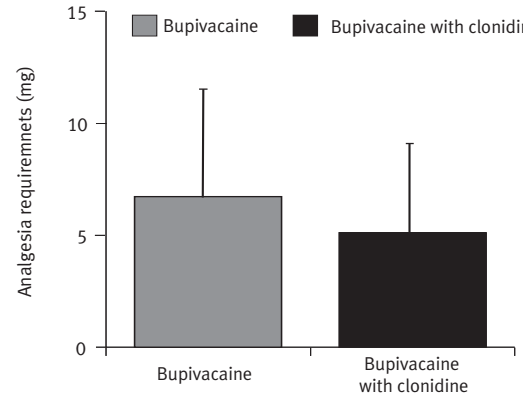
The addition of 1 µg/kg of clonidine to a mixture of 0.5% bupivacaine with 1:200,000 epinephrine in a combined femoral-sciatic nerve block for patients undergoing ACL reconstruction did not significantly decrease NRS scores in this investigation. One possible explanation for this finding was that reported NRS scores were surprisingly low at all post–block placement intervals. It is difficult to detect a difference in pain intensity between groups when subjects in both groups reported little or no pain. A possible flaw in the design of this investigation was that NRS scores

Figure 2. Comparison of the mean duration of analgesia between groups



Measured from the time of block placement to the first request for rescue analgesic medication. No statistically significant difference was observed between the control (bupivacaine) and experimental (bupivacaine with clonidine) groups ($P > .05$). The line extending above each bar represents standard deviation.

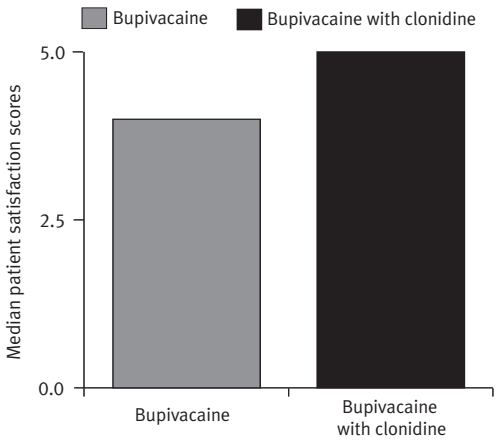
Figure 3. Comparison of the mean postoperative analgesic requirements between groups in 24 hours



Total analgesic medication consumption was recorded and converted to morphine equivalents. No statistically significant difference was observed between the control (bupivacaine) and experimental (bupivacaine with clonidine) groups ($P > .05$). The line extending above each bar represents standard deviation.

were performed only until 19 hours following block placement. Before the initiation of this investigation, many anesthesia providers at Naval Medical Center San Diego estimated the duration of analgesia from a femoral-sciatic nerve block with bupivacaine for an ACL reconstruction to be approximately 12 to 18 hours. We did not anticipate the duration of analgesia

Figure 4. Comparison of median patient satisfaction scores between groups



Overall patient satisfaction was measured by using a 1-5 Likert scale: 1, completely dissatisfied; 2, dissatisfied; 3, somewhat satisfied; 4, satisfied; 5, completely satisfied. No statistically significant difference was observed between the control (bupivacaine) and experimental (bupivacaine with clonidine) groups ($P > .05$).

to be greater than 19 hours. Interestingly, during follow-up appointments in the orthopedic clinic a number of subjects reported little or no pain more than 24 hours after block placement. However, the number of subjects of this anecdotal finding was not recorded. A statistically significant difference between groups may have been detected if NRS scores were measured at intervals past 19 hours, as the blocks began to wear off. In 1 study, a statistically significant decrease in postoperative pain scores was demonstrated when clonidine was added to a brachial plexus nerve block.[10] Subjects receiving 30, 90, or 300 µg of clonidine in a brachial plexus block for carpal tunnel release reported decreased visual analogue scale scores compared with subjects in the control group.[10] However, this decrease occurred only 200 minutes following block placement.

Our investigation also demonstrated that clonidine did not significantly increase the duration of analgesia for subjects undergoing ACL repair. This finding, while not in accordance with the findings of previous investigations, may suggest that postoperative pain associated with ACL reconstruction exceeds that of other surgical procedures in which clonidine has been used.[8-12] Increasing the dose to 1.5 to 2 µg/kg of clonidine may prove to be more efficacious for patients undergoing ACL reconstruction. This observation is supported by a study conducted by Goldfarb et al[11] that enrolled 30 subjects undergoing femoral osteo-

synthesis. All subjects received a femoral and lateral femoral cutaneous nerve block with 1 of 3 solutions. The control group received the block with 30 mL of 0.35% bupivacaine and 250 µg of epinephrine, which resulted in a mean duration of analgesia of 349 minutes. The 2 study groups received the block with 30 mL of 0.35% bupivacaine and 150 µg of clonidine or 30 mL of 0.35% bupivacaine, 250 µg of epinephrine, and 150 µg of clonidine, which resulted in a mean duration of analgesia of 911 minutes and 1,113 minutes, respectively ($P < .01$).[11]

No statistically significant difference was observed between groups in the total amount of opioid consumption during the first 24 hours postoperatively. The amount of opioids consumed during the first 24 hours was minimal for both groups. Considering the amount of pain most patients experience after undergoing ACL reconstruction, the mean amount of morphine equivalents used during the first 24 hours postoperatively was considerably low, less than 8 mg of morphine for both groups. This finding provides further evidence that a femoral-sciatic block is an effective adjunct in providing postoperative analgesia for ACL repair. However, the effect of clonidine on reducing postoperative analgesic requirements when administered peripherally with a local anesthetic remains controversial. A few investigations have found that the addition of clonidine to a local anesthetic for a peripheral nerve block does not reduce the requirement for postoperative analgesic medications.[9,12] One investigation demonstrated results in direct opposition.[15] Clinically, it seems that the most important determinant of successful postoperative pain relief after a femoral-sciatic nerve block is the proximity of the needle to the nerve. Although not examined in this investigation, it seemed that when the clinician performing the block was able to elicit a strong motor response at less than 0.5 mA, subjects reported a longer duration of analgesia than those with a weaker motor response at the same setting.

No statistically significant difference was found in patient satisfaction scores between groups. Subjects reported high satisfaction scores in both groups. This investigation was not powered to detect a difference in patient satisfaction scores using a Likert scale. Despite this limitation, it was interesting to note that satisfaction scores seemed to be approaching a statistically significant difference at the .06 level between groups. This finding suggests that a femoral-sciatic block for ACL repair may add to patient satisfaction. Our patient satisfaction results may have been a misrepresentation of the data secondary to not including subjects who experienced failed blocks in the final analysis.

It seems that a femoral-sciatic nerve block alone provides adequate postoperative analgesia following ACL reconstruction, and the addition of clonidine to the block appears to have no additional benefit.

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