Efficacy of Continuous Intra-articular Bupivacaine Infusion for Postoperative Analgesia After Anterior Cruciate Ligament Reconstruction

A Double-Blinded, Placebo-Controlled, Prospective, and Randomized Study

Richard D. Parker,*† MD, Kathleen Streem,† BSN, Leah Schmitz,† PA-C, Marguerite Group,‡ MD, and Paul A. Martineau,† MD, FRCSC
From the †Department of Orthopedic Surgery, Section of Sports Medicine, Cleveland Clinic Foundation, Cleveland, Ohio, and the ‡Department of Anesthesiology, Cleveland Clinic Foundation, Cleveland, Ohio

Background: The increasing trend toward outpatient surgery has stimulated the development of techniques focused on decreasing perioperative and postoperative pain. Pain control infusion pumps are gaining in popularity in orthopaedic procedures to control postoperative pain.

Hypothesis: Continuous infusion of bupivacaine via a catheter placed intra-articular into the knee after anterior cruciate ligament reconstruction using ipsilateral autograft quadrupled semitendinosus will decrease postoperative pain scores and narcotic and NSAID consumption.

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: Three randomized study groups of 21 subjects were evaluated: group I, 0.25% bupivacaine infused intra-articular at 4 mL/hour for 72 hours (study); Group II, 0.9% saline infused intra-articular at 4 mL/hr for 72 hours (placebo); Group III, no intra-articular infusion catheter (control). Each subject received general anesthesia and preemptive intra-articular anesthesia. Visual analog scale pain scores and analgesic use were compiled for the 96-hour study period.

Results: With the exception of significantly higher total narcotic usage in the control group compared with the study group only for the time period of 48 to 72 hours, there were no other statistically significant differences between each of the study groups with respect to pain and narcotic and NSAID use for the entire study period.

Conclusion: The continuous infusion of intra-articular bupivacaine via pain control infusion pumps after anterior cruciate ligament reconstruction using ipsilateral autograft quadrupled semitendinosus cannot be supported when postoperative visual analog scale pain scores and analgesic use are the rationale for justification.

Keywords: postoperative pain; intra-articular local anesthetic; pain control infusion pump; arthroscopic ACL reconstruction

The increasing trend toward outpatient surgery has stimulated the development of a variety of techniques focused on decreasing postoperative pain. The perception of pain is a complex process involving peripheral and central sensitization to nociceptive stimuli.

Catheters to deliver local anesthetic or narcotic agents to surgical sites have been used extensively in nonorthopaedic applications. Pain control infusion pumps (PCIP), which are spring-loaded or bladder-controlled devices delivering constant rates of local anesthetic to the operative site through a catheter, are gaining in popularity in orthopaedic procedures to control postoperative pain.[18] These pumps

*Address correspondence to Richard D. Parker, MD, Cleveland Clinic Sports Health, Cleveland Clinic Foundation, 9500 Euclid Ave, A-41, Cleveland, Ohio 44195 (e-mail: parkerr@ccf.org).

No potential conflict of interest declared.

The American Journal of Sports Medicine, Vol. 35, No. 4
DOI: 10.1177/0363546506296313

infuse at a constant flow rate controlled by the diameter of the catheter and flow restrictors; thus, they potentially provide a safe method of relieving postoperative pain. Although the pharmacokinetics of intra-articular injection of agents such as bupivacaine have been well studied, the use of PCIPs to deliver intra-articular local anesthetic within the knee has not.[13,22,23]

Arthroscopic surgery allows intra-articular orthopaedic procedures to be performed with minimal trauma. The combination of these minimally invasive surgical techniques with preoperative teaching, anesthetic technique, and postoperative cryotherapy has made it possible for most arthroscopic procedures, such as anterior cruciate ligament reconstruction (ACLR), to be performed on an outpatient basis. Several authors have reported on the successful intra-articular use of local anesthetics and analgesics to enhance pain control for these procedures.[1,2,6-10,15,17,21]

The senior author previously found preemptive anesthesia with bupivacaine and morphine to be an effective method of decreasing early postoperative pain after knee arthroscopy and particularly ACLR.[3-5,20] In an effort to find methods to further decrease postoperative pain, we sought to determine the efficacy of continuous infusion of bupivacaine 0.25% with a PCIP via a catheter placed into the knee joint after ACLR for use as an adjunct in postoperative pain management.

MATERIALS AND METHODS

Study Design

This study was a prospective, randomized, double-blinded, placebo-controlled trial. Institutional Review Board approval was obtained before the study. Written informed consent was obtained from each of the study participants before undergoing the intervention.

Study Groups

Sixty-three patients older than age 18 who were to undergo primary isolated intra-articular ACLR using ipsilateral quadrupled semitendinosus graft consented to the study protocol and were enrolled. Patients requiring concomitant partial meniscectomy, all-inside meniscal repair, or chondroplasty were included in the study. However, patients requiring microfracture or inside-out meniscal repair, as well as those with contraindications to general anesthetic, were excluded. Patients were responsible for documenting total amount of oral postoperative analgesics and visual analog scale (VAS) scores and required to complete a pain record sheet for the preoperative and 96-hour postoperative period to be included in the study.

The subjects were randomized to 3 groups of 21 subjects. Randomization was performed by means of sealed opaque envelopes drawn at the end of the case. The senior surgeon was then informed whether an intra-articular catheter was to be inserted before breaking sterile technique. The surgeon and support staff were blinded as to the study solution. Group I (study group) patients were to receive an intra-articular infusion catheter delivering 0.25% bupivacaine at a rate of 4 mL/hr for 72 hours. Group II (placebo group) patients were to receive an intra-articular infusion catheter delivering 0.9% normal saline (NS) at a rate of 4 mL/hr for 72 hours. Group III (control) subjects had consented to the study but were randomized to receive no intra-articular catheter.

Anesthesia Protocol

On arrival in the operating room, general anesthesia was performed in a standardized manner. Anesthesia was induced with propofol (0.2 mL/kg) and maintained with propofol (0.4 mL/kg/hr) and nitrous oxide/oxygen. A standard dose of 5 mcg/kg of fentanyl was given before incision. Intubation was facilitated with tubocurarine chloride and succinylcholine. The total amount of anesthetic agents used during the operation as well as the start/stop infusion times were recorded.

After the examination under anesthesia, with use of aseptic technique, all patients had the operative knee joint injected by the senior author with preemptive anesthetic consisting of 60 mL of 0.25% bupivacaine, 2 mg of preservative-free morphine, and 1:400 000 epinephrine as previously published.[3] In addition, at the conclusion of surgery, all patients received 1 intra-muscular ketorolac (30 mg) injection, cryotherapy, compressive dressing, and brace immobilizer.

Operative Protocol

All patients underwent quadruple bundle autograft ipsilateral semitendinosus hamstring intra-articular endoscopic ACLR performed by the senior surgeon. Chondroplasty was performed as necessary. Irreparable meniscal tears were treated with partial meniscectomy. Repairable tears treated with all-inside repairs were included in the study. Incision line and portal sites were injected with 20 mL of 1.0% lidocaine and 1:100 000 epinephrine before the beginning of the operation. If the patient was randomized to receive an intra-articular catheter (study group I or II), the surgeon was notified at the end of the case. The catheter of the PCIP (PainBuster Post-Op Pain Relief System, I-Flow Corporation, Lake Forest, Calif) was placed arthroscopically through the superior lateral pouch by the senior surgeon and positioned intra-articularly at the level of the graft-tibial tunnel interface in the intercondylar notch while maintaining sterile technique (Figure 1). The catheter was then connected to the PCIP containing the study solutions. The study solutions were prepared by the nursing staff, and the contents were blinded from the entire investigating team. Postoperatively, all patients underwent routine care.

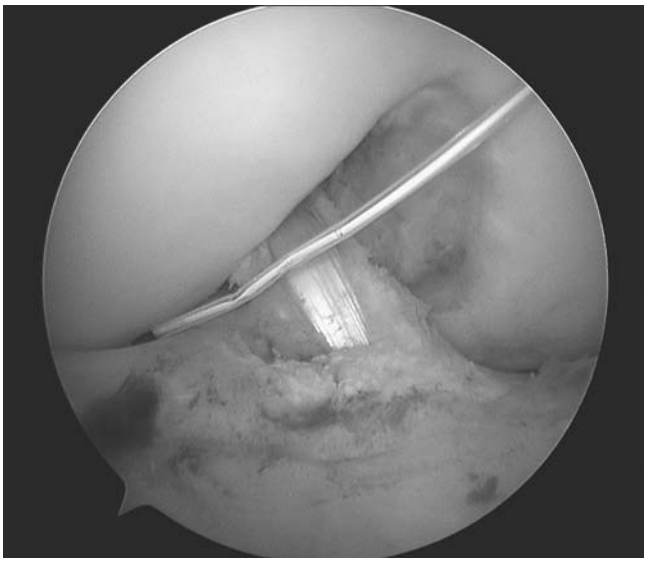

Figure 1. Arthroscopic image of the catheter in place in the intercondylar notch and the tibial tunnel of the ACL reconstruction.

Pain Assessment

Pain was assessed using a 10-point visual analog scale (VAS).[19] A score of 0 describes no pain, whereas a score of 10 describes the worst imaginable pain. Postoperatively, the subjects' narcotic use, NSAID use, and VAS pain scores were noted immediately on arrival to the post-anesthesia care unit (PACU), hourly for the next 6 hours, then every 6 hours for the next 24 hours, and finally every 12 hours until the completion of the 96-hour study period.

Narcotic pain medication, NSAID use, and VAS scores were recorded by the PACU nurses, who were blinded to the solution being injected if the subject had been randomized to a PCIP group. As per the protocol, VAS pain scores of 5 or greater were treated with 50 mcg of fentanyl intravenously at 5-minute intervals until pain scores were less than 5. After transition to second-stage recovery, pain was treated with hydrocodone and acetaminophen tablets (5 mg and 500 mg, respectively) while analgesic use and VAS scores continued to be recorded. Nausea, vomiting, itching, and respiratory depression were also recorded.

Patients were discharged from the hospital the day of surgery in all cases. Each patient was given an exit prescription for hydrocodone and acetaminophen tablets (5 mg/500 mg) to be taken as needed. Post-discharge home narcotic and NSAID use was recorded by the study subjects at the designated intervals up to 96 hours postoperatively. Patients randomized to either of the PCIP groups removed the catheter themselves at 72 hours postoperatively.

Statistical Analysis

Statistical power analysis aiming to identify a statistically significant difference of 2 in the VAS pain score and postoperative analgesic use with a power of 0.90 yielded the need to enroll 63 patients. The VAS pain scores and analgesic use between groups were compared via analysis of variance (ANOVA) (SAS version 9.1, Cary, NC). Pair-wise comparisons were performed with Student t test analysis. Chi-square analysis was used for dichotomous data. $P < .05$ was considered statistically significant.

TABLE 1
Descriptive Statistics of Study Groups[a]

Study Group	Bupivacaine	Placebo	Control
Sex			
Male	9	10	13
Female	12	11	8
Age (range)	19-49	18-46	20-37
Side			
Left	12	11	11
Right	9	10	10
Chronicity			
Subacute	14	15	12
Chronic	7	6	9
Meniscal Repair[b]			
Medial	4	3	4
Lateral		1	3
Partial Meniscectomy			
Medial	6	3	7
Lateral	4	3	6
Chondroplasty			
Medial	5	2	3
Lateral	4	2	2
Patellofemoral	3	5	3

[a]No statistically significant differences between study groups for any of the categories.
[b]All inside repair.

RESULTS

Sixty-three patients were enrolled and successfully completed the study protocol. There were no statistical differences between the study groups in terms of age, sex, chronicity of ACL insufficiency, and preoperative VAS scores or use of analgesics (Table 1). All patients with PCIP were able to safely remove the catheter themselves at 72 hours postoperatively without difficulty, and there were no complications related to the use of the PCIPs.

There were no statistically significant differences between the group with the PCIP infusing bupivacaine (Group I), the group with the PCIP infusing NS (Group II), and the control group (Group III) with respect to average pain, total narcotic use, and total NSAID use for the entire time period of the study (Table 2). A trend toward higher total narcotic use in the control group (group III) compared with groups I and II was identified but this was not statistically significant. When total narcotic use was analyzed by time point, this trend became statistically significant ($P = .015$) when comparing group I and group III only for the time period of 48 to 72 hours, just before removal of the catheter. No other statistically significant differences were

TABLE 2
Mean VAS Scores, Total Narcotic Use, and Total NSAID Use per Study Group

	VAS Scores			Total Narcotic Use[a]			Total NSAID Use[a]		
Study Group, n	Mean	SD	*P* value	Mean	SD	*P* value	Mean	SD	*P* value
Bupivacaine (I), 21	3.36	±1.78		16.12	±10.01		12.38	±11.17	
Placebo (II), 21	3.26	±1.56	0.575	16.79	±9.27	0.065	11.62	±15.48	0.338
Control (III), 21	3.78	±1.78		22.71	±10.22		7.14	±9.59	

[a]Tablets consumed.

TABLE 3
Mean VAS Scores per Study Group by Time Period

	VAS Scores									
	Bupivacaine		Placebo		Control		*P* value			
Time (h)	Mean	SD	Mean	SD	Mean	SD	Overall	Bupivacaine vs Control	Bupivacaine vs Placebo	Placebo vs Control
0	2.95	±2.99	3.05	±2.89	3.17	±2.22	.968	.800	.910	.888
1	3.81	±2.19	3.86	±2.15	3.78	±2.10	.992	.959	.943	.903
2	3.83	±1.85	3.19	±1.97	3.31	±1.74	.493	.364	.266	.836
3	3.45	±1.66	2.93	±1.68	3.60	±1.83	.423	.789	.328	.215
6	3.33	±1.96	2.93	±1.93	3.93	±2.04	.264	.333	.509	.106
12	3.86	±2.97	3.62	±2.48	4.31	±2.65	.704	.590	.777	.412
18	3.62	±2.73	3.67	±3.44	3.76	±2.39	.987	.873	.958	.915
24	3.55	±3.09	3.68	±2.61	4.10	±2.53	.798	.522	.883	.627
36	4.85	±3.27	4.11	±2.47	4.88	±2.61	.641	.967	.421	.399
48	3.83	±2.70	4.13	±2.08	4.81	±2.86	.462	.228	.712	.411
60	3.53	±2.38	4.53	±2.33	4.85	±2.91	.244	.108	.234	.700
72	2.95	±2.16	3.17	±2.09	3.74	±2.57	.529	.277	.773	.442
84	2.87	±2.08	3.03	±2.05	4.03	±2.29	.198	.098	.822	.158
96	2.78	±2.33	2.89	±2.47	3.70	±2.44	.426	.230	.885	.305

TABLE 4
Mean Narcotic Use by Time Period per Study Group

	Narcotic Use[a]									
	Bupivacaine		Placebo		Control		*P* value			
Time Period (h)	Mean	SD	Mean	SD	Mean	SD	Overall	Bupivacaine vs Control	Bupivacaine vs Placebo	Placebo vs Control
0-24	6.38	±3.02	6.81	±3.45	7.43	±2.91	.577	.284	.660	.525
25-48	4.52	±3.14	4.21	±2.02	5.95	±3.46	.144	.124	.740	.069
48-72	2.98	±2.83	4.16	±2.67	5.48	±3.97	.050	.015	.252	.202
73-96	2.24	±3.24	2.66	±2.47	3.86	±3.69	.244	.106	.680	.241

[a]Tablets consumed.

identified for average VAS pain scores, total narcotic use, and total NSAID use at any other time points (Tables 3, 4, and 5).

DISCUSSION

The recent trend toward decreasing hospital stays and performing more outpatient surgery has led to an increased awareness and attention to effectively controlling postoperative pain. In addition to shortening the length of time spent in the hospital and potentially reducing hospital costs, efficient control of postoperative pain may accelerate recovery and rehabilitation, decrease systemic narcotic-related side-effects, and lead to more favorable surgical outcomes. In previous work, the senior author demonstrated that the use of preemptive intra-articular analgesia was an effective

TABLE 5
Mean NSAID Use by Time Period per Study Group

	NSAID Use[a]									
	Bupivacaine		Placebo		Control		*P* value			
Time Period (h)	Mean	SD	Mean	SD	Mean	SD	Overall	Bupivacaine vs Control	Bupivacaine vs Placebo	Placebo vs Control
0-24	2.62	±3.72	1.70	±2.54	2.29	±2.37	.603	.715	.322	.527
25-48	3.52	±3.66	2.00	±2.40	3.10	±5.12	.459	.725	.226	.382
48-72	3.10	±2.90	1.89	±2.64	3.52	±5.05	.369	.710	.312	.172
73-96	3.14	±3.26	2.21	±3.33	2.71	±4.15	.718	.702	.418	.661

[a]Tablets consumed.

method of decreasing postoperative pain in knee arthroscopy and arthroscopic ACLR.[3-5,20] In an effort to continue to improve our methods of decreasing postoperative pain, we sought to determine the efficacy of continuous infusion of bupivacaine 0.25% with a PCIP via a catheter placed intra-articular in the knee joint after ACLR.

Mallon[11] first described the use of extended intra-articular delivery of local anesthetic to the operative site in orthopaedic surgery. The author used a variation of the patient-controlled anesthesia pump (PCA) usually used for intravenous narcotics to deliver a constant infusion rate and boluses of lidocaine into the subacromial space via a catheter inserted after acromioplasty. Although the study was a case series without control group, they found this novel technique to be an effective and safe method to control postoperative pain after subacromial decompression. However, the complexity of the PCA pumps and the requirement of skilled nursing for their use and maintenance have rendered home use of this technique unfeasible.

There has been a renewed interest in the use of extended intra-articular delivery of local anesthetic after orthopaedic procedures since the development of PCIPs. These are simple spring-loaded or bladder-controlled devices that deliver a constant rate of infusion as a function of the diameter of the catheter and flow restrictor valves. A study by Savoie et al[18] looked at the use of a PCIP to provide postoperative pain control in shoulder surgery. The study was a prospective, nonblinded, randomized trial conducted on patients undergoing arthroscopic subacromial decompression. The patients had a catheter inserted into the subacromial space and were randomized to receive either 0.25% bupivacaine or NS. The authors found statistically significant inferior pain scores and higher analgesic use in those patients receiving continuous bupivacaine infusion. Similarly, Yamaguchi et al[24] found the placement of an intra-articular pain catheter within the glenohumeral joint delivering 0.5% bupivacaine to be highly effective at providing postoperative pain control in cases of adhesive capsulitis.

However, to our knowledge, this is the first study presented in the literature that analyzes the use of a PCIP as an adjunct for pain control after knee arthroscopy, particularly in the setting of hamstring ACLR. We did not find any statistically significant differences in VAS pain scores, total narcotic use, or total NSAID use between the study groups. However, it may be that the results of our study were a function of the study conditions. Although previous studies by the senior author have supported the use of 0.25% bupivacaine for intra-articular anesthesia, another group has demonstrated that intra-articular 0.75% ropivacaine may provide better analgesia than 0.5% bupivacaine after arthroscopic knee surgery.[3-5,12,20] In addition, supplementation with intra-articular morphine and ketorolac may also augment the analgesic effects of intra-articular local anesthetic.[14]

Nevertheless, the randomized, double-blinded, placebo-controlled study design reinforces the results. The randomization process provided 3 comparable study groups. In particular, gender distribution was equal, which is important since gender is known to be a significant confounding factor in pain trials.[16] The study was also uniform, with all patients undergoing the same arthroscopic quadruple-bundle autograft ipsilateral semitendinosus ACLR performed by 1 senior surgeon. Furthermore, any patients requiring more than a concomitant partial meniscectomy, all-inside meniscal repair, or chondroplasty were excluded from the study. Therefore, under the standardized and uniform conditions of the study, we cannot recommend the use of a PCIP to supplement postoperative pain control.

CONCLUSION

As increasing outpatient surgery is becoming an important method of controlling hospital costs, developing effective means of controlling postoperative pain is becoming a priority. However, the continuous infusion of intra-articular bupivacaine via a PCIP after arthroscopic ACLR using ipsilateral semitendinosus cannot be supported when postoperative VAS pain scores and analgesic use are the rationale for justification.

ACKNOWLEDGMENT

The authors acknowledge the contribution of Dr. Brian McDermott to this endeavor.

REFERENCES

1. Ates Y, Kinik H, Binnet MS, Ates Y, Canakci N, Kecik Y. Comparison of prilocaine and bupivacaine for post-arthroscopy analgesia: a placebo-controlled, double-blind trial. *Arthroscopy.* 1994;10(1):108-109.
2. Boden BP, Fassler S, Cooper S, Marchetto PA, Moyer RA. Analgesic effect of intra-articular morphine, bupivacaine, and morphine/bupivacaine after arthroscopic knee surgery. *Arthroscopy.* 1994;10(1):104-107.
3. Gatt CJ Jr, Parker RD, Tetzlaff JE, Szabo MZ, Dickerson AB. Preemptive analgesia: its role and efficacy in anterior cruciate ligament reconstruction. *Am J Sports Med.* 1998;26(4):524-529.
4. Goodwin RC, Amjadi F, Parker RD. Short-term analgesic effects of intra-articular injections after knee arthroscopy. *Arthroscopy.* 2005;21(3): 307-312.
5. Goodwin RC, Parker RD. Comparison of the analgesic effects of intra-articular injections administered preoperatively and postoperatively in knee arthroscopy. *J Knee Surg.* 2005;18(1):17-24.
6. Heard SO, Edwards WT, Ferrari D, et al. Analgesic effect of intra-articular bupivacaine or morphine after arthroscopic knee surgery: a randomized, prospective, double-blind study. *Anesth Analg.* 1992;74(6):822-826.
7. Henderson RC, Campion ER, DeMasi RA, Taft TN. Postarthroscopy analgesia with bupivacaine. A prospective, randomized, blinded evaluation. *Am J Sports Med.* 1990;18(6):614-617.
8. Joshi GP, McCarroll SM, Cooney CM, Blunnie WP, O'Brien TM, Lawrence AJ. Intra-articular morphine for pain relief after knee arthroscopy. *J Bone Joint Surg Br.* 1992;74(5):749-751.
9. Joshi GP, McCarroll SM, McSwiney M, O'Rourke P, Hurson BJ. Effects of intra-articular morphine on analgesic requirements after anterior cruciate ligament repair. *Reg Anesth.* 1993;18(4):254-257.
10. Joshi GP, McCarroll SM, O'Brien TM, Lenane P. Intra-articular analgesia following knee arthroscopy. *Anesth Analg.* 1993;76(2):333-336.
11. Mallon WJ, Thomas CW. Patient-controlled lidocaine analgesia for acromioplasty surgery. *J Shoulder Elbow Surg.* 2000;9(2):85-88.
12. Marret E, Gentili M, Bonnet MP, Bonnet F. Intra-articular ropivacaine 0.75% and bupivacaine 0.50% for analgesia after arthroscopic knee surgery: a randomized prospective study. *Arthroscopy.* 2005;21(3): 313-316.
13. Meinig RP, Holtgrewe JL, Wiedel JD, Christie DB, Kestin KJ. Plasma bupivacaine levels following single dose intra-articular instillation for arthroscopy. *Am J Sports Med.* 1988;16(3):295-300.
14. Ng HP, Nordstrom U, Axelsson K, et al. Efficacy of intra-articular bupivacaine, ropivacaine, or a combination of ropivacaine, morphine, and ketorolac on postoperative pain relief after ambulatory arthroscopic knee surgery: a randomized double-blind study. *Reg Anesth Pain Med.* 2006;31(1):26-33.
15. Raja SN, Dickstein RE, Johnson CA. Comparison of postoperative analgesic effects of intra-articular bupivacaine and morphine following arthroscopic knee surgery. *Anesthesiology.* 1992;77(6):1143-1147.
16. Rosseland LA, Stubhaug A. Gender is a confounding factor in pain trials: women report more pain than men after arthroscopic surgery. *Pain.* 2004;112(3):248-253.
17. Ruwe PA, Klein I, Shields CL. The effect of intra-articular injection of morphine and bupivacaine on postarthroscopic pain control. *Am J Sports Med.* 1995;23(1):59-64.
18. Savoie FH, Field LD, Jenkins RN, Mallon WJ, Phelps RA. The pain control infusion pump for postoperative pain control in shoulder surgery. *Arthroscopy.* 2000;16(4):339-342.
19. Scott J, Huskisson EC. Graphic representation of pain. *Pain.* 1976;2(2):175-184.
20. Tetzlaff JE, Dilger JA, Abate J, Parker RD. Preoperative intra-articular morphine and bupivacaine for pain control after outpatient arthroscopic anterior cruciate ligament reconstruction. *Reg Anesth Pain Med.* 1999;24(3):220-224.
21. VanNess SA, Gittins ME. Comparison of intra-articular morphine and bupivacaine following knee arthroscopy. *Orthop Rev.* 1994;23(9):743-747.
22. Wasudev G, Smith BE, Limbird TJ. Blood levels of bupivacaine after arthroscopy of the knee joint. *Arthroscopy.* 1990;6(1):40-42.
23. Weiker GG, Kuivila TE, Pippinger CE. Serum lidocaine and bupivacaine levels in local technique knee arthroscopy. *Am J Sports Med.* 1991;19(5):499-502.
24. Yamaguchi K, Sethi N, Bauer GS. Postoperative pain control following arthroscopic release of adhesive capsulitis: a short-term retrospective review study of the use of an intra-articular pain catheter. *Arthroscopy.* 2002;18(4):359-365.