Preemptive intraarticular tramadol for pain control after arthroscopic knee surgery

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ÖZET

Artroskopik diz cerrahisi sonrası ağrı kontrolünde preemptif intraartiküler tramadol

Bu çalışmada artroskopik diz cerrahisinde intraartiküler (ia) tramadol ve bupivakainin analjezik etkileri ve preemptif ia tramadolün etkinliği araştırıldı. Fakülte etik kurul onayı alındıktan sonra, 60 olgu randomize olarak 20'şer kişilik 3 gruba ayrıldı: Grup I'de operasyonun sonunda ia 20 ml % 0.25 bupivakain; Grup II'de operasyonun sonunda ia 20 ml %0.25 bupivakain ve 100 mg tramadol hidroklorür ve Grup III'te operasyondan 30 dk önce ia 20 ml izotonik NaCl solusyonu içinde 100 mg tramadol hidroklorür ve operasyonun sonunda ia 20 ml %0.25 bupivakain uygulandı. İlk analjezik ihtiyacı, postoperatif dönemde toplam kullanılan analjezik miktarı, postoperatif istirahat ve hareket halindeki VAS değerleri, Grup II ve III'te, Grup I'e göre anlamlı şekilde düşük, hasta memnuniyeti de anlamlı şekilde yüksek bulundu. Preemptif tramadol grubu postoperatif tramadol grubu ile karşılaştırıldığında, toplam kullanılan analjezik miktarı ve ek analjezik kullanan olguların sayısı anlamlı derecede düşük bulundu. Sonuç olarak, preemptif ia tramadol uygulamasının artroskopik diz cerrahilerinden sonra etkin ve güvenli bir analjezi sağladığı saptandı ve postoperatif uygulamaya göre tercih edilebileceği kanısına varıldı.

Anahtar kelimeler: İntraartiküler tramadol, preemptif analjezi, postoperatif analjezi

SUMMARY

The purpose of this study was to determine the effectiveness of intraarticular (ia) bupivacaine and tramadol injection and preemptive intraarticular tramadol in providing pain control after arthroscopic knee surgery. Following local research ethics committee approval, 60 patients were assigned in a randomized manner into three groups: Group I received ia 20 ml of 0.25% bupivacaine at the end of the operation, Group II received ia 20 ml of 0.25% bupivacaine and 100 mg of tramadol at the end of the operation and Group III received ia 100 mg of tramadol diluted in 20 ml of saline solution 30 minutes before skin inscision and 20 ml of 0.25% bupivacaine at the end of the operation as well. Analgesic duration, total analgesic consumption and postoperative VAS pain scores recorded at rest and with movement were significantly lower and patient satisfaction was significantly higher in Group II and III, compared to Group I. Total analgesic consumption and the number of patients requiring supplementary analgesics were significantly lower in the preemptive tramadol group compared to the postoperative tramadol group. In conclusion, preemptive ia tramadol provided effective and reliable pain control after artroscopic knee surgeries and may be preferred to postoperative administration.

Key words: Intraarticular tramadol, preemptive analgesia, postoperative analgesia

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Introduction

Arthroscopy of the knee under general anesthesia is routinely performed on an outpatient basis. As this common procedure may cause pain and discomfort to delay rehabilitation and discharge, aggressive pain management in the early postoperative period is essential.

One of the analgesic techniques for pain management of arthroscopic knee surgeries is the intraarticular (ia) route. Intraarticular instillation of local anesthetics during arthroscopic procedures has been used by many orthopedic surgeons. After demonstration of peripheral local opioid receptors (Levine and Taiwo 1989, Lawrence et al. 1992, Stein et al. 1993), opioids have been extensively utilized intraarticularly, as well (Stein et al. 1991). However, there are only a few studies investigating ia tramadol, a selective μ receptor agonist and norepinephrine and serotonin reuptake inhibitor, for postoperative pain management (Likar et al. 1995, Kürsad et al. 1998, Akıncı et al. 2003, Alagöl et al. 2003).

Preemptive analgesia, utilizing analgesics before the painful stimuli, prevents the establishment of hypersensitivity and amplification of postoperative pain (Woolf and Chong 1993). There are limited number of studies investigating preemptive intraarticular administrations (Gyrn et al. 1992, Denti et al. 1997, Tetzlaff et al. 1999, Reuben et al. 2001, Fagan et al. 2003). The analgesic effects of preemptive ia tramadol has not been studied yet.

The aim of this study was to assess the effectiveness of ia bupivacaine and tramadol injection and whether ia tramadol administered preemptively, reduced postoperative pain scores both at rest and at movement, the need for and use of supplementary analgesics and the time to first request of analgesics.

Material and Method

Following local research ethics committee approval, informed written consent was obtained from 60 patients of American Society of Anesthesiologists (ASA) class 1 or 2, scheduled to undergo elective arthroscopic surgery of the knee. Patients of 18 -70 years of age and with bodyweight between 50 and 90 kg were included in the study. Exclusion criteria were severe systemic disease, allergy to study drugs, long term treatment with analgesics, consumption of analgesics or non-steroid antiinflammatory drugs (NSAIDs) within 24 h of surgery, seizure disorder, anterior cruciate ligament reconstruction, surgical debridment or synovectomy, traumatic injury to the knee and refusal by the patient.

All patients were familiarized with a 10 cm visual analogue scale (VAS) preoperatively with 0: no pain and 10: the worse imaginable pain. Preoperative VAS scores were obtained from all patients by asking the average intensity of pain at rest and on active movement of the knee.

Premedication was not administered. Standard monitoring techniques were used, including electrocardiography, blood pressure and pulse oximetry. Patients were assigned in a randomized manner into 3 groups. Group assignments were randomized using a sealed envelope technique. Group I received ia 20 ml of 0.25 % bupivacaine at the end of the operation, Group II received ia 20 ml of 0.25 % bupivacaine and 100 mg of tramadol at the end of the operation and Group III received ia 100 mg of tramadol diluted in 20 ml of saline solution 30 minutes before skin incision and 20 ml of 0.25 % bupivacaine at the end of the operation as well (Table 1). All ia injections were performed by the surgeon. No intraarticular drain was placed.

In all groups, anesthesia was induced intravenously with fentanyl 1μg kg-1 and propofol 2 mg kg-1 and maintained with an infusion of propofol 6-10 mg kg-1 h-1. All patients received air in oxygen by face mask and spontaneous ventilation was maintained throughout the procedure. Increments of 30 mg of propofol was given to keep the blood pressure and heart rate within

Table 1. Intraarticular solutions administered.

	Group I (n=20)	Group II (n=20)	Group III (n=20)
30 min before the operation	--	--	ia 100 mg tramadol in 20 ml saline solution
At the end of the operation	ia 20 ml of 0.25% bupivacaine	ia 100 mg tramadol in 20 ml 0.25% bupivacaine	ia 20 ml 0.25% bupivacaine

Table 2: Demographic variables and the duration of anesthesia and surgery (mean±SD)*.

	Group I (n=20)	Group II (n=20)	Group III (n=20)
Gender (Male/Female)	5/15	7/13	10/10
Age (years)	45.4±15.6 (19-68)	43.0±12.1 (17-57)	40.6±14.3 (17-69)
Weight (kg)	71.7±9.8 (60-88)	74.3±11.4 (48-90)	71.2±10.8 (55-90)
Height (cm)	164.6±10.2 (154-188)	163.6±6.9 (150-176)	167.0±11.0 (149-196)
ASA (I/II)	12/8	16/4	15/5
Knee (left/right)	10/10	9/11	7/13
Tourniquet (-/+)	7/13	12/8	10/10
Duration of anesthesia (min)	32.6±12.6 (16-55)	29.6±11.6 (15-57)	34.5±12.9 (14-60)
Duration of surgery (min)	25.1±12.0 (10-52)	25.3±10.4 (13-47)	28.8±11.8 (12-51)

% 25 of the preoperative values. Systolic, diastolic and mean arterial blood pressure, heart rate, respiratory rate and oxygen saturation were recorded intraoperatively. When surgery was terminated and after the cleaning solution removed, the surgeon injected 20 ml of the appropriate study group solution into the knee joint. At the end of the procedure the duration of anesthesia was recorded.

After the operation, patients were transferred to the recovery room where they stayed for 1 hour and then transferred to their rooms. Follow-up was continuous during this period, and was carried out by nursing staff. VAS pain scores were obtained from all patients at 1,2,4,6,8,12 and 24 hours after the end of the operation at rest and on movement (active flexion of the operated knee) by an anesthesiologist who did not participate in the operation. All pain measurements were performed during the hospital stay. Routine protocole for the postoperative arthroscopy procedures were followed and patients were discharged the day after surgery.

Systolic, diastolic and mean arterial blood pressure, heart rate, respiratory rate and oxygen saturation and the presence of side effects such as nausea, vomiting, sedation, hypotension (systolic arterial pressure<90 mmHg), dizziness, headache, dry mouth, allergic reaction, respiratory depression and urinary retention were recorded postoperatively for each patient at the same time as pain measurements.

In case of inadequate analgesia (VAS>3), patients of all groups received sodium diclophenac, i.m. 75 mg of starting dose as a rescue medication once it was requested and at a maximum dose of 150 mg daily. The time to first analgesic use and 24 hour total analgesic consumption were recorded. Analgesic duration was defined as the time from completion of surgery until the first request for sodium diclophenac.

Patients were asked to indicate the degree of overall satisfaction with postoperative pain management on a 4-point satisfaction scale before discharge: 0=unsatisfactory/poor, 1=somewhat satisfactory/adequate, 2=satisfactory/adequate, 3=very good, 4 = excellent.

Statical analysis was performed using SPSS 10,0 for windows (SPSS Institue, Chicago, IL). P values <0.05 were considered significant. Data are presented as mean values and standard deviation (mean±SD). Demographic data, duration of anesthesia and surgery, the first analgesic time and total analgesic consumption between the groups were analyzed using ANOVA, followed by Bonferroni when significance was obtained. Pain scores and the number of analgesic consumption were analyzed with the Kruskal-Wallis test. Wilcoxon X test was used to compare postoperative VAS values to the preoperative VAS values. Patient satisfaction among groups was analyzed using _2 test. Sex, ASA, tourniquet application, the number of patients requiring suplemental

Table 3: Time to first analgesic requirement (mean±SD) and postoperative analgesic consumption (median±SD).

	Group I (n=20)	Group II (n=20)	Group III (n=20)
Time to first analgesic requirement (min)	142.6±197.7 (10-696)	351.9±297.4[a] (60-960)	444.13±368.4[a] (30-1028)
Analgesic consumption in the first 6 h (mg)	75.0±48.6 (0-150)	33.8±38.5[a] (0-75)	11.3±27.4 [a, b] (0-75)
Analgesic consumption in the first 12 h (mg)	108.8±51.5 (0-150)	52.5±35.3[a] (0-75)	22.5±35.5 [a, b] (0-75)
24 h analgesic consumption (mg)	112.50±51.8 (0-150)	60.0±30.8[a] (0-75)	30.0±37.5 [a, b] (0-75)
Number of patients requiring analgesics (n)	18/20	16/20	8/20 [a, b]

[a]: $p<0.05$ (compared to Group I)
[b]: $p<0.05$ (compared to Group II)

analgesics and the incidence of side effects were analyzed with Fisher' s test and _2 test.

Results

Demographic and surgical data are presented in Table 2. No significant difference was found among the groups with respect to demographic variables (age, gender, weight, height), ASA physical status, tourniquet application, the mean duration of anesthesia and surgery.

Time to first analgesic requirement was significantly longer in Group II and Group III, compared to Group I ($p<0.05$). The total analgesic consumption measured in the number of doses in 6, 12 and 24 hours were significantly lower in Group II and Group III compared to Group I, and significantly lower in Group III compared to Group II ($p<0.05$). The number of patients requiring supplementary analgesics was higher in Group III, compared to Group I and II ($p<0.05$) (Table 3).

The changes in VAS pain scores 1-24 hours after the operation at rest and with movement are shown in Figures 1 and 2, respectively. No differences were found among the groups in the preoperative VAS pain scores recorded at rest or with movement.

There was not a statistically significant difference in VAS pain scores recorded at rest within the group in Group III, but VAS pain scores recorded at rest at 1, 2, 4, 6, 8 and 12 h in Group I and 1, 2, 4 and 6 h in Group II were significantly higher compared to their preoperative control values ($p<0.05$). VAS pain scores at rest in Group II and III at 1, 2, 4, 6, 8, 12 and 24 h after the operation were significantly lower compared to Group I ($p<0.05$), while no significant difference was found between Group II and III (Fig 1).

There was a significant difference in VAS pain scores recorded with movement within the groups. VAS pain scores recorded with movement at 1, 2, 4 and 6 h in Group I, 4 and 6 h in Group II and 8 h in Group III were significantly higher compared to their preoperative control values ($p<0.05$). VAS pain scores recorded with movement at 1, 2, 4 and 12 h in Group II were significantly lower compared to Group I ($p<0.05$) and VAS pain scores recorded with movement at 1, 2, 4, 6 and 24 h in Group III were significantly lower compared to Group I ($p<0.05$), while no significant difference was found between Group II and III (Fig 2).

Side effects are presented in Table 4. Vomiting, allergic reaction, dry mouth, respiratory depression and urinary retention were not observed in any of the groups and there were no differences between the groups with respect to nausea, sedation, dizziness, headache and hypotension.

The degree of overall satisfaction with postoperative pain management is presented in Table 5. The degree of overall satisfaction with postoperative pain management on a 4-point satisfaction scale was better in Group II and III, compared to Group I ($p<0.05$). Significantly more patients in Group II and III stated that the pain management was perfect compared to Group I ($p<0.05$).

Discussion

There are limited number of studies investigating the analgesic effects of intraarticularly adminis-

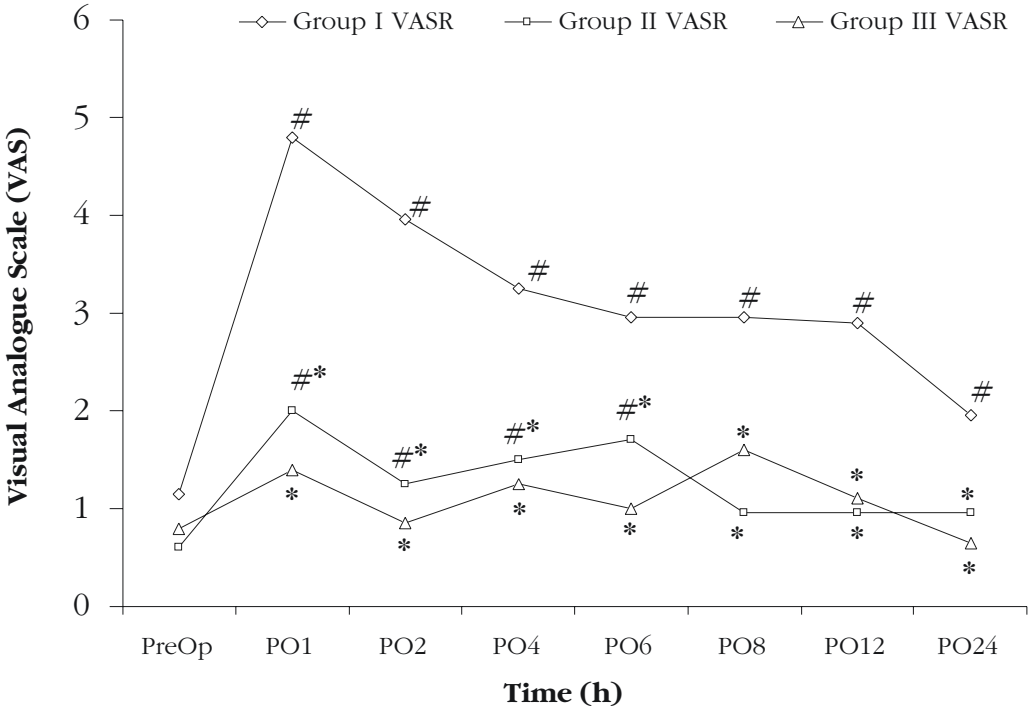

Figure 1: Preoperative and postoperative VAS pain scores at rest (median).

VASR: VAS pain scores at rest, PreOp: Preoperative, PO: Postoperative, #: $p<0.05$ (compared to control value within the group), *: $p<0.05$ (compared to Group I)

tered tramadol in various doses after arthroscopic knee surgery (Likar et al. 1995, Kürsad et al. 1998, Akıncı et al. 2003). Recently, the optimum dose, analgesic effects and side effects of ia tramadol was investigated in a double-blind prospective study and it was reported that 100 mg ia tramadol provided excellent analgesic effect (Alagöl et al. 2003). Consequently, we adapted this amount of tramadol in the present study. Preemptive ia administrations were investigated only in a limit-

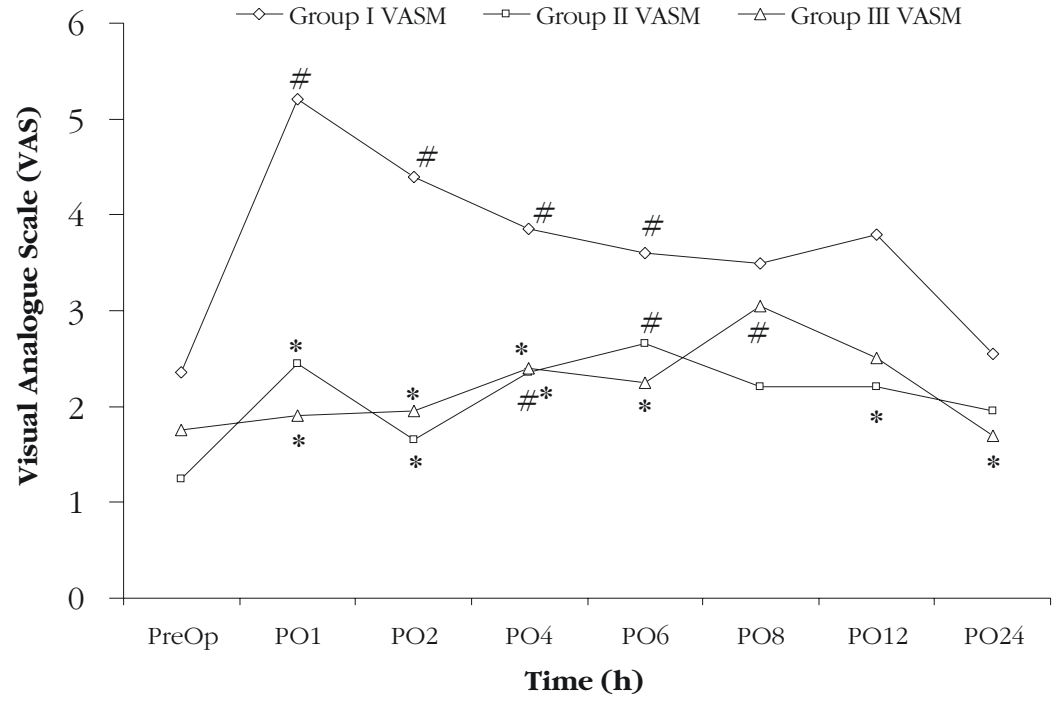

Figure 2: Preoperative and postoperative VAS pain scores on movement (median).

VASM: VAS pain scores on movement, PreOp: Preoperative, PO: Postoperative, #: $p<0.05$ (compared to control value within the group), *: $p<0.05$ (compared to Group I)

Table 4: The incidence of postoperative side effects (%).

	Group I (n=20)	Group II (n=20)	Group III (n=20)
Nausea	0	0	2 (%10)
Vomiting	0	0	0
Dizziness	0	2 (%10)	0
Headache	0	0	2 (%10)
Sedation	0	1 (%5)	0
Allergy	0	0	0
Dry mouth	0	0	0
Hypotension	1 (%5)	0	1 (%5)
Urinary retention	0	0	0
Respiratory depression	0	0	0

ed number of studies (Gyrn et al. 1992, Denti et al. 1997, Tetzlaff et al. 1999, Reuben et al. 2001, Fagan et al. 2003). The analgesic effects of preemptive ia tramadol has not been studied yet.

Studies with preoperative intraarticular morphine, showed a decrease in pain scores in ACL reconstruction and arthroscopic knee surgeries (Reuben et al. 2001, Tetzlaff et al. 1999, Denti et al. 1997). On the other hand, Fagan et al. failed to demonstrate a significant analgesic effect of 15 ml of 5 mg/ml bupivacaine administered both intraarticularly and at the port sites (Fagan et al. 2003). Several factors such as study design, the dose and time of bupivacaine administration and surgical techniques may explain the differences in efficacy between studies.

In the present study, ia tramadol and bupivacaine either applied preoperatively or postoperatively provided better pain control without any significant side effects, compared to ia bupivacaine alone and significant analgesic effects were found with ia tramadol when administered in the preoperative versus postoperative period in patients undergoing arthroscopic knee surgery which was evidenced by reduced total analgesic consumption and number of patients requiring supplementary analgesics.

Bupivacaine has been extensively utilized within ia local anesthetics because of its longer analgesic duration (Reuben and Sklar 2000). It has been demonstrated that its analgesic effect lasted 1-4 h in the early postoperative period after arthroscopic knee surgeries (Kaeding et al. 1990, Smith et al. 1992, Joshi et al. 1993, Boden et al. 1994, Cepeda et al. 1997, Andres et al. 1998). In our study, we administered ia bupivacaine to all study groups to provide analgesia in the early postoperative period. In our study group (Group I) where only ia bupivacaine was administered, the duration of analgesia was comparable with similar studies in the literature (Kaeding et al. 1990, Smith et al. 1992, Joshi et al. 1993, Boden et al. 1994, Cepeda et al. 1997, Andres et al. 1998).

The time to first analgesic request was statistically longer in Group II in which bupivacaine and tramadol were administered at the end of the operation (351.9±297.4 min) compared to Group I where only bupivacaine was administered (142.6±197.7 min). However, the time to first analgesic requirement was shorter in our postoperative tramadol group compared to the value (700.0±168.5 min) obtained by Alagöl et al. (2003). Various arthroscopic procedures included in their study may be the reason for the dis-

Table 5: Patient satisfaction (%).

Patient satisfaction	Group I (n=20)	Group II (n=20)	Group III (n=20)
2	11 (%55.0)	1 (%5.0)[a]	0 [a]
3	8 (%40.0)	12 (%60.0)	12 (%60.0)
4	1 (%5.0)	7 (%35.0) [a]	8 (%40.0) [a]

Patient satisfaction 2 = satisfactory/adequate, 3 = very good, 4 = excellent;
[a]: $p<0.05$ (compared to Group I)

crepency between two studies. Moreover, lower postoperative VAS values in the same study may indicate that less painful procedures were performed.

The total amount of analgesics utilized in the first 6,12 and 24 h after the operation, VAS pain scores at rest at all times postoperatively, VAS pain scores at movement at 1,2,4 and 12 h after the operation were statistically lower in Group II compared to Group I (Fig. 1 and 2). All these results indicated that tramadol administered intraarticularly provided significant analgesic effect.

The time to first analgesic request was statistically longer and the total amount of analgesics utilized in the first 6,12 and 24 h after the operation were statistically lower in Groups II and III, compared to Group I. These results demonstrate the analgesic effects of tramadol administered preoperatively in spite of articular lavage.

In the literature it was reported that total analgesic consumption was a better parameter than time to first analgesic request to demonstrate the preemptive effect (Mc Quay 1992). The total amount of analgesic consumption in the first 6,12 and 24 h and the number of patients requiring additional analgesics were statistically lower in Group III compared to Groups I and II. These findings suggest that ia tramadol administered preoperatively had preemptive effects.

Postoperative VAS pain scores at rest and with movement of the knee were lower in Group III compared to Group I, although no difference was obtained when compared to Group II.

Tourniquet is frequently used in knee arthroscopies in order to reduce bleeding and improve surgical vision (Strobel et al. 1992). In the orthopedics clinic of our hospital tourniquet is not routinely used. In order not to have differences with the use of tourniquet in some patients, tourniquet was deflated immediately after ia injection at the end of the operation. Undesired effects such as bleeding were not observed in any of our patients without tourniquets.

Intraoperative ia lavage may wash-out and remove the ia agents administered preoperatively and reduce their analgesic effects. To circumvent this, ia morphine was administered 20 min before the operation (Lundin et al. 1998) and 30 min before the operation (Reuben et al. 2001) in studies and successful results were obtained. Taking these studies into consideration, we injected tramadol intraarticularly 30 min before the operation in Group III. The failure to obtain statistically significant reduction in pain scores in the study of Fagan et al. may be attributed to the lower time interval of 15 min. Tramadol was injected in saline solution in the preemptive group rather than in combination with local anesthetics, in order to prevent their possible preemptive analgesic effects.

No statistically significant difference was found in the time to first analgesic request, VAS pain scores at rest and on movement of the knee and patient satisfaction in preemptive tramadol group (Group III) compared to postoperative tramadol group (Group II). However, the postoperative total analgesic consumption and the number of patients requiring additional analgesics were significantly lower in preemptive ia tramadol group. These findings indicate the effectiveness of intraarticularly administered preemptive tramadol as an analgesic.

In conclusion, ia tramadol and bupivacaine either applied preoperatively or postoperatively provided better pain control compared to ia bupivacaine alone and analgesic effect was more significant when tramadol was applied preemptively. Preemptive ia tramadol administration provided effective and safe postoperative analgesia in arthroscopic knee surgeries and may be preferred to postoperative ia tramadol administrations.

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