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Intra-Articular Patient-Controlled Analgesia Improves Early Rehabilitation after Knee Surgery

Neli Vintar[1], Narinder Rawal[2], Maja Pohar[3] and Matjaž Veselko[4]

[1] Department of Anaesthesiology and Intensive Care, Clinical Center Ljubljana, Ljubljana, Slovenia
[2] Department of Anaesthesiology, University Hospital Örebro, Örebro, Sweden
[3] Institute of Biomedical Informatics, School of Medicine, Ljubljana University, Ljubljana, Slovenia
[4] Department of Traumatology, Clinical Center Ljubljana, Ljubljana, Slovenia

A B S T R A C T

The influence of patient-controlled intra-articular analgesia with ropivacaine, morphine and ketorolac (RMK) on postoperative pain relief and early rehabilitation after anterior cruciate ligament reconstruction was studied. Twenty six patients, randomized into two groups, were enrolled in a placebo-controlled, double-blind study. At the end of surgery a catheter was placed intra-articularly and connected to a patient-controlled pump, programmed to deliver 10 mL bolus and 60 min lockout interval. RMK group received 0.25% ropivacaine, morphine 0.2 mg/mL and ketorolac 1 mg/mL; P group saline. Pain was measured with 10 cm visual analog scale. At pain scores >3 cm, all patients were instructed to self-administer morphine intravenously using a patient-controlled pump. Daily rescue morphine consumption was noted and 48h rehabilitation programme was evaluated. Daily morphine consumption was significantly lower in the RMK group ($p<0.001$). At 24h after surgery, the patients in the RMK group experienced significantly less pain ($p<0.05$). The patients in the RMK group achieved higher maximum degree of knee flexion in supine ($p<0.001$) and in prone position ($p<0.05$) compared to placebo group and better pain free flexion with assistance on day 1 ($p<0.05$) and 2 ($p>0.05$). The results show that patient-controlled intra-articular analgesia with RMK combination provides effective pain relief following anterior cruciate ligament reconstruction and improves early physical rehabilitation.

Key words: *knee surgery, outcome, postoperative analgesia, intraarticular, Ljubljana, Slovenia*

Introduction

Anterior cruciate ligament (ACL) reconstruction is associated with moderate to severe postoperative pain[1]. Regional analgesic techniques such as epidural analgesia and femoral block provide successful analgesia, but may cause motor weakness which impaires active physiotherapy and also reduces muscular protection of the graft. Intra-articular use of local anesthetic drugs has been shown to be as effective as femoral nerve block for treating post-operative pain after ACL reconstruction and is an attractive technique avoiding motor block and allowing normal use of extremity[2,3].

The literature on intra-articular catheter analgesia is limited and its influence on early postoperative outcome has not been studied[4].

The aim of the present study was to compare the analgesic effect of intravenous morphine patient-controlled analgesia with intra-articular patient-controlled analgesia with ropivacaine, morphine and ketorolac and the impact of analgesic technique on early postoperative mobilization and rehabilitation in patients undergoing ACL reconstruction under spinal anesthesia.

Patients and Methods

The study was approved by the Institutional Ethical Committee. 26 adults, ASA class I–II, between 18 and 50 years of age, were consecutively enrolled in this prospective, randomized, double-blind study after obtaining written, informed consent. All patients were scheduled for elective arthroscopically assisted ACL reconstruction using quadriceps tendon autograft. The exclusion criteria were: hypersensitivity or known allergy to local anesthetics, nonsteroidal anti-inflammatory drugs (NSAIDs) or opioids, contraindications to regional anesthesia or

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the need for extended surgical procedure. Subjects were then assigned to two groups of 13 using a computer-generated list of random numbers.

Preoperatively, all patients were instructed in the use of the 10cm visual analog scale (VAS) with 0 and 10 labeled as »no pain« and »worst pain imaginable«, respectively, and in the use of a patient-controlled analgesia (PCA) pump. They were premedicated with midazolam administered intravenously (0.03 mg/kg).

A subarachnoid blockade was performed with a 25-G Sprotte needle through an introducer-cannula (Pajunk), inserted at the L3–L4 interspace using a median approach. Fifteen mg of plain 0.5% bupivacaine were injected (Marcaine spinal 0.5%, Astra Laboratories, Sweden).

All operations were performed by the same senior surgeon. The arthroscopic ACL reconstruction was performed using an autologous quadriceps tendon graft with adjacent bone block from the patella of the same knee. Before closing the wounds, a multiorifice epidural catheter (Portex G 18 epidural catheter with three lateral eyes) was placed intra-articularly through a Tuohy needle. Its position was confirmed arthroscopically. The catheter was secured to the skin by a sterile transparent dressing, flushed with 5 mL of saline and connected to a Microject® PCA pump (Sorenson Medical, West Jordan, Utah, USA), using a Microject® cassette with incorporated 1.2 ìm antimicrobial filter. The patients were instructed to self-administer the analgesic mixture (the pump was programmed to administer a bolus of 10 mL with a 60 min lockout interval). Analgesic mixtures were prepared in 100 mL plastic bags and coded. For the RMK group 0.25% ropivacaine was combined with 2 mg morphine and 10 mg ketorolac, for P group saline. Each patient also received 1g of paracetamol orally every 6 hours.

If the patient still experienced pain (VAS >3) 15 min after intra-articular bolus administration, the protocol included rescue analgesia by 2 mg *iv* self-administered boluses of morphine by a PCA pump. The lockout interval was 10 min.

To avoid confusion the IA PCA pump was marked with a green tape, the IV PCA pump with a red tape.

The number of intra-articular and intravenous boluses and total i.v. morphine consumption was noted.

Each patient was given a log book and asked to self-evaluate and record pain (on a 10 cm VAS) before and 15 min after an intra-articular bolus and before and after intravenous morphine dose. The patient was asked to evaluate and record pain at rest and during physiotherapy and to mark the time of self-adminstration. The following pain scores were included in the analysis: after regression of spinal block at rest about 4h after surgery, at 8 a.m. next morning about 16h after procedure, 24h after surgery, and during performing the first physiotherapy about 18h after surgery.

The presence of side effects (dizziness, nausea, vomiting, pruritus, urinary retention) was collected by a blinded observer who was not otherwise involved in the study.

The physiotherapist, blinded for the study, informed the patients about the rehabilitation programme.

The following parameters in patient's log book were analyzed: pain-free passive mobility exercises with the continuous passive motion device (CPMD) on the first and second postoperative day, pain-free flexion of the knee with assistance on day 1 and 2, knee flexion in prone position on day 2, sitting down without assistance on day 1 and 2, three-point gait using crutches with pain-free weightbearing on day 1 and 2.

Intra-articular catheter was removed 48 hours after surgery and the tip sent for microbiological analysis. Wound healing was assessed by the surgeon. Normal healing of the knee was considered when the knee was pale and the skin temperature was normal, infection of the knee when the knee was red, swollen, the skin temperature of the knee was elevated and/or patient's temperature was elevated.

Statistical analysis

The two groups were compared using the Student's t-test for numerical data and the χ^2-test for categorical data. The data are expressed as the mean (standard deviation). When no normality could be assumed, we used the Mann-Whitney test and the data summaries are presented using the median and interquantile range (IQR). Side effects and other categorical variables are presented in contingency tables. A p value <0.05 was considered statistically significant. The statistical analysis was performed using the statistical package R for Windows, version 2.1.

Results

There were 26 patients consecutively enrolled in the study. One patient from group P was not included in the data analysis because of accidental removal of the IA catheter. There were no statistically significant differences in age, body weight, sex and duration of procedure between the groups (Table 1).

The VAS pain scores at rest were similar at the time of the spinal block regression (4h after surgery) and 16h postoperatively (Figure 1). At 24h after the surgery the pain scores were significantly better in RMK group ($p=0.031$).

TABLE 1
DEMOGRAPHIC CHARACTERISTICS OF PATIENTS

Variables	Group RMK	Group P
Age (yr)	27 (9)	30 (7)
Weight (kg)	82 (11)	81 (18)
Sex (n) male/female	11/2	10/2
Duration of surgery (min)	88 (6)	94 (16)

Values are mean (SD), or numbers (n)
No significant differences were noted between the study groups

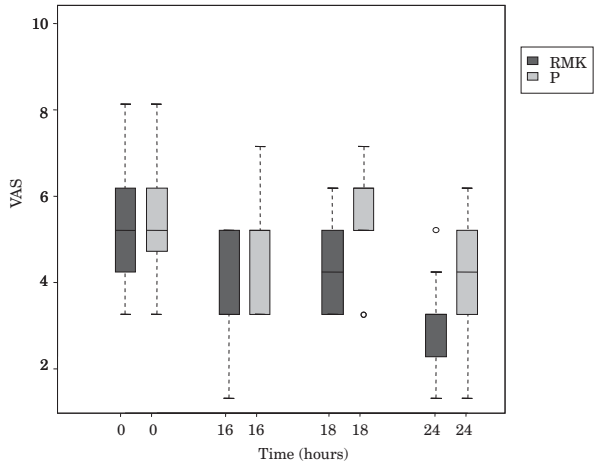

Fig. 1. Pain scores at rest at 4h – time 0, 16h and 24h postoperatively, and during movement 18h after surgery. VAS – visual analog scale. At time 24h, the difference is statistically significant (Mann Whitney p=0.031). The box represents 25th–75th percentiles and the median is represented by the firm line. The dotted lines are drawn from the end of the box to the largest and smallest observed values.

During the first physiotherapy 18h after the procedure, the differences in VAS scores between the groups were not statistically significant, but there was a tendency to lower pain scores in the RMK group.

The 48 h rehabilitation programme was completed by all patients of both groups. The RMK group patients were significantly more successful in performing pain-free passive mobility exercises with the continuous passive motion device (CPMD) on the first and second postoperative day (p<0.001), pain-free flexion of the knee with assistance on day 1 (p=0.0049) and day 2 (p=0.003), and knee flexion in prone position on day 2 (p=0.0014) (Table 2). In being able to sit-down from the laying position without assistance on day 1 and 2 there were no significant differences between the groups, but in using crutches with pain-free weightbearing on day 1 (p=0.02) and 2 (p=0.046) patients of the RMK group were significantly more successful (Table 2).

Daily rescue i.v. morphine total dose was significantly smaller in the RMK group (p<0.001). Morphine consumption over time is shown on Figure 2.

The incidence of side effects such as dizziness, vertigo, nausea, vomiting, pruritus, and urinary retention was not significantly different between groups (Table 3). More than one side effect was observed in 5 patients from the placebo group, but in none of the RMK group patients.

Microbiological analysis showed no bacterial growth, all catheter tips were sterile. No signs of local inflammation were noted in any of the patients. Wound healing assessed by the surgeon was considered normal in all patients.

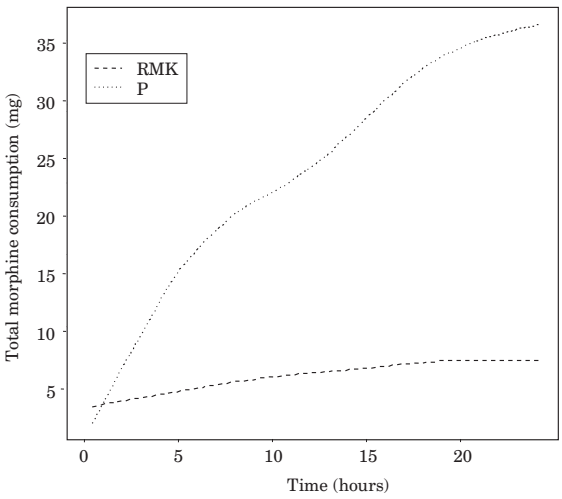

Fig. 2. Intravenous morphine consumption over time. Total amount of morphine consumption differs significantly between the groups (p<0.001).

TABLE 2
THERAPEUTIC EXERCISES PERFORMED DURING THE REHABILITATION PROGRAMME

Variables	Group RMK	Group P	p-values
Pain-free passive mobility using CPMD day 1 (°)	50 (6)	37 (3)	p<0.001
Pain-free passive mobility using CPMD day 2 (°)	90 (9)	75 (4)	p<0.001
Pain-free flexion with assistance day 1 (°)	45 (9)	33 (4)	p=0.0049
Pain-free flexion with assistance day 2 (°)	87 (8)	73 (6)	p=0.003
Knee flexion in prone position day 2 (°)	67 (8)	54 (6)	p=0.0014
Sitting down without assistance day 1 (n)	11	6	NS
Sitting down without assistance day 2 (n)	12	10	NS
Pain-free weightbearing using crutches day 1 (n)	8	2	p=0.02
Pain-free weightbearing using crutches day 2 (n)	12	7	p=0.046

CPMD – continuous passive motion device
° degrees of flexion or moving the leg from the relaxed extended position
Values are median (interquantile range (IQR)), or numbers (n)
NS – not significant

TABLE 3
INCIDENCE OF INDIVIDUAL SIDE EFFECTS

Side effects	Group RMK (N=13)	Group P (N=12)
No side effects	7	6
Dizziness	4	5
Vertigo	0	2
Nausea	1	3
Vomiting	0	2
Pruritus	0	1
Urinary retention	1	1

In 5 patients in the placebo group more than one side effect occured at the same time. There were no statistically significant differences between the groups

Discussion

The results of our prospective double-blind randomized study showed that intra-articular patient-controlled analgesia with a combination of ropivacaine, morphine and ketorolac provides effective postoperative pain relief after ACL reconstruction with significantly less daily morphine consumption compared to placebo. The range of motion of the knee joint was significantly better for the first two days in patients receiving intra-articular PCA.

I.v. opioid PCA is an effective method for postoperative analgesia. It can be associated with side effects such as dizziness, nausea/vomiting, and respiratory depression which may prevent early rehabilitation after surgery[5]. Regional analgesic techniques can provide effective analgesia with fast patient recovery and early mobilization[2,6–8]. Epidural analgesia has been an established method for successful postoperative analgesia after ACL reconstruction, but can be associated with motor blockade, urinary retention, pruritus, nause/vomiting, and even respiratory depression that can prevent the patient from active mobilization[1]. Femoral nerve block also decreases intravenous analgesic requirements after ACL reconstruction[7], but it requires additional time to perform and is often associated with motor blockade which can impair active physiotherapy and muscular protection of the graft. Some authors could not prove any advantages of femoral nerve block over intra-articular local anesthetic infiltration[2].

Morphine side effects are not only frequent but may be considered a limitation of intravenous morphine PCA. Postoperative nausea and vomiting (PONV) and sedation impair active mobilization and rehabilitation. A meta-analysis of 22 randomized controlled trials of PCA, morphine and NSAIDs showed that NSAIDs decreased the incidence of PONV and sedation[9]. The combination of nonopioid analgesics and /or regional analgesic techniques with opioid decreases morphine consumption and improves postoperative analgesia after severely painful surgery. Therefore, a multimodal approach has been developed to improve postoperative pain relief by acting on different pain pathways[10].

Alford and Fadale evaluated efficacy of intra-articular bupivacaine infusion after anterior cruciate ligament reconstruction (ACLR) and did not show statistically significant lower pain ratings compared with saline control group and the group with no catheters[11]. Similarly Parker studied intra-articular analgesic effects of bupivacaine and did not find significantly lower pain scores and analgesic use after ACL[12]. In both studies bupivacaine alone was not effective enough which also suggests a multimodal approach to intra-articular analgesia. Therefore we evaluated multimodal intra-articular analgesia. A combination of ropivacaine, morphine and ketorolac was shown to provide effective postoperative pain relief after ACLR and was superior to saline and to ropivacaine and morphine alone[13].

The conclusion of the study by Parker was that if only the visual analog scale pain scores and analgesic use were the rationale for justification, continuous intra-articular bupivacaine infusion after ACL reconstruction could not be supported[12]. This again suggests a multimodal approach and also the need for more outcome studies.

In an uncontrolled trial Rasmussen et al. showed that a continuous intra-articular injection of morphine and ropivacaine after total knee replacement led to a clinically relevant early improvement in the range of motion and shortened hospital stay[8].

In their studies Rasmussen et al.[8], Wagner et al.[14] and Capdevila et al.[15] showed that regional analgesic techniques improved early postoperative rehabilitation and shortened hospital stay after major knee surgery.

There is evidence that the source of pain after ACLR are articular surfaces but also subcutaneous tissues surrounding tendon donor graft area, what could justify the poor pain control in the early postoperative hours of intra-articular infusions alone[16]. In the Hoenecke study the catheter was placed subcutaneously at the donor site graft and pain scores were significantly reduced in the first 48 postoperative hours in the study group compared with the placebo group[17]. Further studies are needed to answer the question where to place the catheter to achieve most efficient pain relief: intraarticularly, subcutaneously or both.

The results of our study showed that patients with intra-articular PCA using ropivacaine, morphine and ketorolac achieved significantly more effective pain-free passive mobility with the continuous passive motion device (CPMD) on the first and second postoperative day, significantly better pain-free flexion of the knee with assistance and significantly better knee flexion in prone position on day 2. In sitting down without assistance on the first and second postoperative day there were no significant differences between the groups, but in using crutches the patients of the RMK group were significantly more successful.

Drains are regarded as an independent risk factor for wound infection, and are associated with an increase in

incidence of wound infection from 5% to 12%[9]. Therefore, concerns related to the risk of infection caused by intra-articular PCA are reasonable. In our study, microbiological analysis of all catheter tips showed no bacterial growth. The catheters were removed after 48h in our study, after 4 days in the report of Alford and Fadale[11] and after 72h in the study of Parker[12] and Rasmussen et al.[8]. None of these studies showed any evidence of infection related to intra-articular catheters. As there are few reports about continuous intra-articular analgesia available, further studies are needed to answer this question.

In conclusion, this randomized, double-blind study showed that intra-articular PCRA technique following ACL reconstruction with the combination of intra-articular ropivacaine, morphine and ketolorac was superior to intravenous morphine analgesia and enabled better rehabilitation in the early postoperative period.

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N. Vintar

Department of Anesthesiology and Intensive Care, University Medical Center, Zaloska 7, 1000 Ljubljana, Slovenia
e-mail: nvintar@gmail.com

INTRAARTIKULARNA SAMOKONTROLIRANA ANALGEZIJA POBOLJŠAVA RANU REHABILITACIJU NAKON OPERACIJE KOLJENA

SAŽETAK

Proučavan je utjecaj kontrolirane intraartikularne analgezije s ropivakainom, morfinom i ketorolakom (RMK) na postoperativno olakšavanje boli i ranu rehabilitaciju nakon anteriorne rekonstrukcije ligamenata. U studiju je bilo uključeno 26 pacijenata nasumično organiziranih u dvije skupine, s placebo-skupinom kao kontrolom. Na kraju operacije intraartikularno je ugrađen kateter i spojen na pumpu koju pacijent sam kontrolira. Pumpa je programirana da intravenozno otpušta 10 mL bolusa u intervalima od 60 minuta. RMK skupina je dobivala 0,25% ropivakaina, 0,2 mg/mL morfina i 1 mg/mL ketorolaka. Bol je mjerena s vizualnom analognom skalom od 10 cm. Kod razine boli >3 cm svi pacijenti su upućeni da samostalno intravenozno ubrizgaju morfin, koristeći pumpu. Bilježena je dnevna potrošnja morfina i procjenjivan je 48-satni rehabilitacijski program. Dnevna potrošnja morfina je bila značajno niža kod RMK skupine ($p<0.001$). 24 sata nakon operacije, pacijenti iz RMK skupine osjećali su značajno niže razine boli ($p<0.05$). Također, oni su postigli viši maksimalni stupanj fleksije koljena u usporedbi s placebo-skupinom, kao i bezbolniju fleksiju uz asistenciju prvi dan ($p<0.05$) i drugi dan ($p<0.05$). Rezultati su pokazali da intraartikularna samokontrolirana analgezija s RMK kombinacijom osigurava smanjenje bolova nakon anteriorne rekonstrukcije ligamenata i poboljšava fizičku rehabilitaciju.