VILNIUS UNIVERSITY

Saulė Švedienė

EVALUATING THE EFFICACY OF INTRA-ARTICULAR AND PERINEURAL ANALGESIA METHODS FOR THE ARTHROSCOPIC RECONSTRUCTION OF ANTERIOR CRUCIATE LIGAMENT OF THE KNEE

Summary of Doctoral Dissertation

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VILNIAUS UNIVERSITETAS

Saulė Švedienė

INTRASĄNARINĖS IR PERINEURINĖS ANALGEZIJOS METODŲ VEIKSMINGUMO NUSTATYMAS ATLIEKANT ARTROSKOPINES KELIO PRIEKINIO KRYŽMINIO RAIŠČIO REKONSTRUKCINES OPERACIJAS

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CONTENT

LIST OF ABREVIATIONS

ACL – anterior cruciate ligament

BMI – body mass index

CFNB – continuous femoral nerve block

ECG – electrocardiography

gauge – comparing outer diameter of the needle

h – hours

i/a – intra-articular

iv – intravenous

L – litre

M – morphine

mA – milliampere

mg – milligramme

min – minute

ml – millilitre

N – neostigmine

NRS – numeric rating score

P – placebo

PCA – patient-controlled analgesia

SD – standard deviation

SFNB – single-shot femoral nerve block

Th – thoracic

vs – *versus* (lat.) – as compared with

1. INTRODUCTION

The arthroscopic reconstruction of the knee anterior cruciate ligament (ACL) requires a close postoperative pain management since more than 60% of patients report moderate to severe pain. Thus, search continues for the anesthetic technique that would provide optimal postoperative analgesia allowing early functional recovery with minimal side effects for these patients. Numerous methods and their combinations have been put to test during the last decade.

Regional anesthesia is currently a strategy of choice for inpatient ACL repair surgery. Postoperative regional analgesia may improve functional recovery and shorten in hospital stay as compared with opiate analgesia. Moreover, post-operative management costs after regional anesthesia are lower than after general anesthesia. The conventionally used spinal block is more and more frequently replaced by the nerve blocks. The single-shot femoral nerve block (SFNB) is associated with an improved side-effect profile and is less likely to cause severe neuraxial complications while providing a comparable intraoperative and close postoperative analgesia.

Perineural infusions of analgesics such as used in continuous femoral nerve block (CFNB), and especially in a patient-controlled analgesia (PCA) pump manner, can provide the most efficient postoperative analgesia so far. This technique affects pain at the site of its origin, limits the spread effects and is less associated with complications such as local anesthetic toxicity, hematoma, nerve injury or infection. CFNB provides better analgesia and allows a significant reduction of opiate consumption in comparison with intra-articular (i/a) or wound infusion of a local anesthetic after ACL repair. A high patient satisfaction can be achieved by providing them with instructions and observing their ability to use the technique.

Intra-articular analgesia with local anesthetics is less effective than nerve blocks, but it has no systemic effects and does not induce motor blockade. Reports addressing the intra-articular co-administration of local anesthetics and systemic drugs such as morphine are scarce and sometimes controversial. Addition of morphine to the intra-articular injection of bupivacaine was reported to be safe and providing a significant reduction in systemic opiate consumption after ACL repair. However, other reports raised a concern that the effectiveness of i/a morphine is dose-dependent and has an additional systemic analgesic effect. Earlier, McCarty and colleagues investigated the use of i/a morphine in addition to general anesthesia combined with SFNB for the ACL repair surgery. The use of i/a neostigmine has been even less investigated.

The synergistic postoperative analgesic effect provided by a combination of SFNB and intra-articular analgesics expands to the postoperative period, potentially reducing the need for systemic opioids such as tramadol and non-steroidal anti-inflammatory drugs such as diclofenac. However, the obturator nerve might contribute to postoperative pain and is frequently missed by traditional 3-in-1 approach. Thus, a combination of spinal block, SFNB, and intra-articular injection of morphine or neostigmine seems a clinically justified aiming for the optimization of perioperative pain management, especially in settings where more efficient methods such as CFNB are not available. However, the choice between morphine and neostigmine for intra-articular injection in ACL repair patients needs further investigation because data in the literature are inconclusive so far.

2. THE AIM AND OBJECTIVES OF THE STUDY

The aim of our study was to assess the most effective and safe method of perioperative regional analgesia after arthroscopic anterior cruciate ligament repair surgery.

Objectives:

1. To evaluate and compare the impact of intra-articular injection of morphine (SFNB + M), neostigmine (SFNB + N) or placebo (SFNB + P) on the postoperative pain management; also, patient satisfaction after arthroscopic ACL reconstruction performed under spinal block, followed by SFNB with 0.5% isobaric bupivacaine.
2. To compare the first two strategies with the presumably more efficient postoperative pain management that deploys continuous femoral nerve block with a patient-controlled analgesia infusion pump (CFNB + PCA).
3. To compare the two preset regimens (R1 and R2) of the PCA pump operation in the CFNB + PCA protocol subjects.
4. To evaluate the rate of side effects or complications related to regional analgesia techniques or used medications.

3. SCIENTIFIC NOVELTY OF THE RESEARCH WORK

The arthroscopic ACL reconstruction of the knee is currently one of the most frequently performed operations in orthopedic practice. Adequate pain control for patients after surgery is very important for the effective rehabilitation and better functional outcomes. Thus, the search continues for the postoperative analgesia technique that would be cost-effective and facilitate fast recovery with minimal side effects. Previous observations have shown that SFNB is more effective than intravenous or intra-articular postoperative analgesia, but it still remains insufficient for an adequate pain control after ACL repair surgery.

We decided to accomplish this prospective randomized double-blind placebo-controlled trial to determine finally the most effective and safe method of postoperative regional analgesia for these patients. We compared the intra-articular injections of analgesics (morphine and neostigmine) in never before investigated doses as well as their combination with regional analgesia. In contrast to conventional practice, these agents were diluted in normal saline.

We also investigated two new patient-controlled analgesia regimens through a perineural femoral catheter. In the present study, a lower concentration of bupivacaine was used and no additives were employed. One of our objectives was to compare the both strategies mentioned above.

It is the first research in Lithuania to investigate this type of perioperative analgesia management.

4. PATIENTS AND METHODS

Approval was granted from the Lithuanian Ethics Committee (ID number 31; 6B-8-393). Written informed consent was obtained from 95 adult ASA physical state class I–II patients with the body mass index ≤ 30 kg/m^2, scheduled for arthroscopic ACL reconstruction (Figure 1). All patients were eligible for spinal block followed by SFNB and intra-articular morphine or neostigmine, also being eligible for the application of CFNB with a PCA infusion pump. Subjects were randomized by a computer-generated sequence into 5 groups: (I) SFNB + M, *n=20;* (II) SFNB + N, *n=20*; (III) SFNB + P (placebo), *n=20;* (IV) CFNB + PCA R1, *n=16*; (V) CFNB + PCA R2, *n=19.*

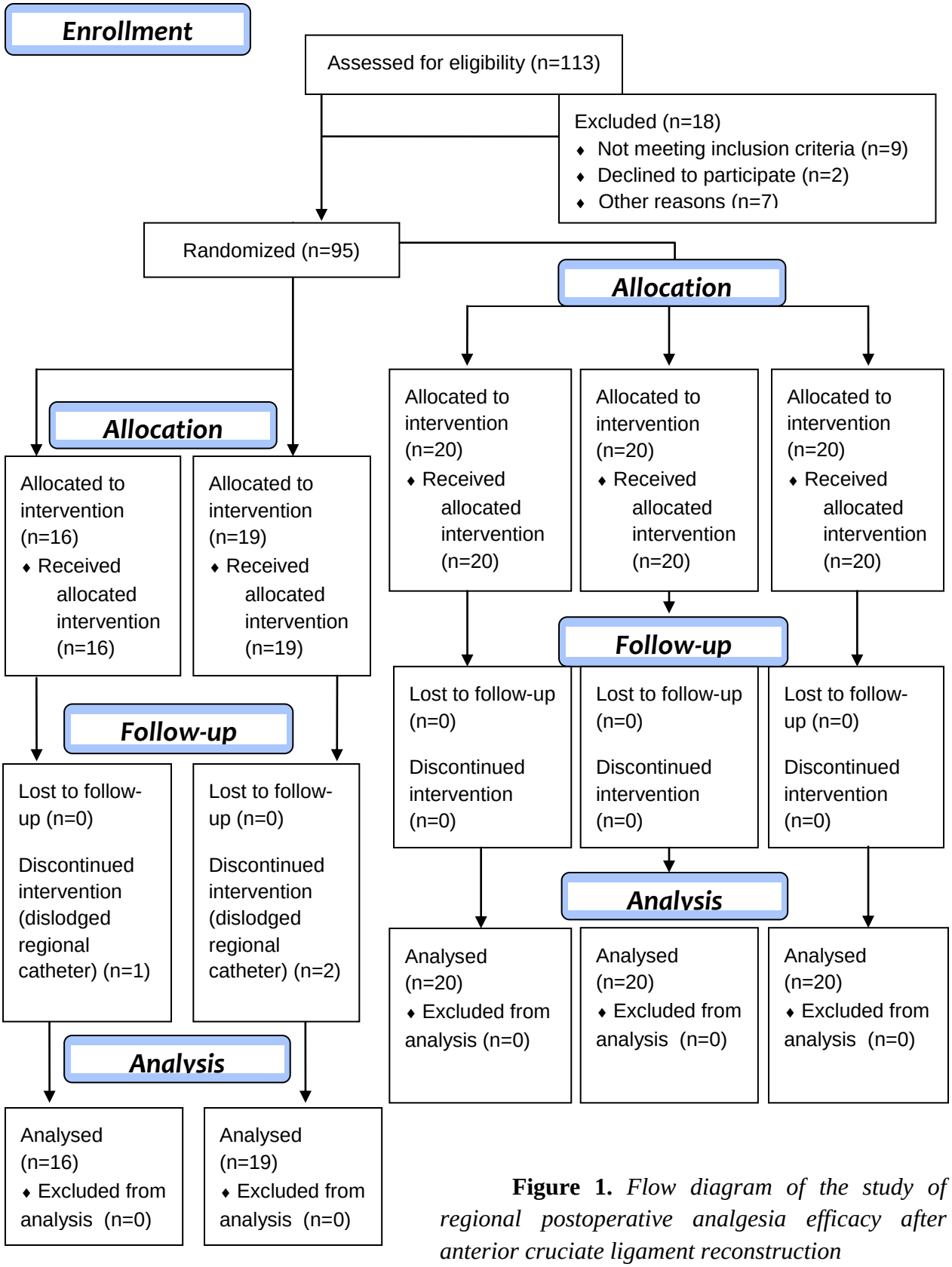

Figure 1. *Flow diagram of the study of regional postoperative analgesia efficacy after anterior cruciate ligament reconstruction*

4.1 Intraoperative period

Before anesthesia induction, all patients had been premedicated with 0.1 mg of iv fentanyl and 10 mg of iv diazepam. Groups I, II and III received a single-shot femoral nerve block by 20 ml of 0.5% bupivacaine (100 mg) with epinephrine (1 : 200,000); a 21-gauge stimulating needle was used. For the last-mentioned tree groups at the end of the operation (10 min before the tourniquet release), the surgeon injected into the articular cavity 6 mg of morphine (SFNB + M group) with 10 ml of 0.9% normal saline, 0.5 mg of neostigmine (SFNB + N group) with 10 ml of 0.9% normal saline or placebo (SFNB + P group) – 10 ml 0.9 % normal saline sole. The continuous femoral nerve catheter placement was accomplished after skin disinfection and sterile draping of the inguinal region of the involved limb; a local anesthesia was made with 2 ml of 1% lidocaine. An insulated stimulating needle (50 mm, 18-gauge) was inserted at a 40° in a cephalic direction. Quadriceps contraction and patellar elevation via nerve stimulation with a minimum current of between 0.6 and 0.3 mA were used to confirm the exact location of the femoral nerve. A 20-gauge catheter was introduced through the needle and advanced for 5 to 10 cm beyond the needle tip. The needle was withdrawn, and the catheter was fixed. The initial bolus of 20 ml of 0.5% bupivacaine (100 mg) with epinephrine (1 : 200,000) was injected through the catheter. The infusion of 0.1% bupivacaine for these patients was previewed to start via a perineural catheter upon the motor block reaching the Bromage scale 2 (just able to flex knees with a free movement of feet), before leaving the post-anesthesia care unit by using a PCA infusion pump. Pumps were preset to run till 48 hrs, and preprogrammed with two PCA infusion regimens: (a) regimen R1 (CFNB + PCA R1) applies the basal rate of 5 ml/hr with allowed patient controlled addition of 5 ml boluses if needed with a refractive period of 30 minutes; (b) regimen R2 (CFNB + PCA R2) applies only a patient-controlled bolus of 5 ml with a refractive period of 15 min without basal infusion. The total allowed dose of bupivacaine did not exceed 5 mg/kg in 24 h.

The spinal block was induced in a sitting position for all subjects immediately after completing the femoral block procedure. After skin disinfection and sterile draping of the procedure site, the spinal block was performed in lumbar 3–4 interspace. A 27-gauge needle (type *Quincke*) with 15^0 cephalad angulation was advanced until a specific click was felt. After a free flow of the cerebro-spinal fluid had been observed, the 0.5% isobaric bupivacaine was injected, aiming to obtain a sensory block to Th8. Patients were then returned to a supine

position and given to breathe a mixture of air and oxygen (3 L/min) via a facial mask. A continuous observation of pulse oximetry data was applied, and the basic hemodynamic parameters (ECG, non-invasive arterial blood pressure) were evaluated every 5 min in the operating theatre, every 15 min in the post-anesthesia care unit, and also every 6 hrs during the 48-h postoperative period.

4.2 Postoperative rescue pain management

The numeric rating pain scores (NRS) [0–10] were evaluated every 6 hours by the nursing staff asking unified questions. The following adjuncts were administered on the needed basis: intramuscular diclofenac 75 mg was given when the NRS pain score was 1–3, and/or iv tramadol 50 mg when NRS $\geq$ 4.

4.3 Data collection

The study personnel who collected data were blinded to the group allocation of the subjects. The postoperative motor block of the operated leg was recorded by using the Bromage scale [1–4]. The pain intensity of the operated leg at rest and especially motion (treading down) was collected at three timepoints during the 48 postoperative hours – at 12, 24, and 48th hour after the surgery: a patient was asked about the most painful score at rest and at motion during the last 24 hours. The consumption of NSAIDs and opiates was registered at the same timepoints. The quality of postoperative analgesia was also assessed by the difference between demanded and administrated PCA boluses of bupivacaine. The patient satisfaction was evaluated at the end of the trial by asking subjects to provide the overall evaluation in a scale from 0 to 10. The adverse events included hypotension (with or without nausea/vomiting), postoperative bladder catheterization, and postdural puncture headache. The study persons' age, BMI, surgery and motor blockage duration, and the length of hospital stay were also reported.

4.4 Statistical analysis

We had not performed the prospective power calculation while planning our research as no reference data on these specific methods were available. Descriptive summaries are presented

as frequencies and percentages for categorical data (sex and ASA) and as mean values and standard deviations for continuous variables (age and others). The analysis of variance one way ANOVA and nonparametric Kruskal–Wallis test were applied in investigating the difference among the groups. For all pairwise comparisons among the mean values Duncan‘s test was used. For comparing groups in pairs, the Wilcoxon–Mann–Whitney test for two independent samples was used. The percentage among the groups was compared by the chi-square or Fisher’s exact tests. The value $p \leq 0.05$ was considered significant in all tests. Analysis was performed in a sequence as follows: first, following the primary purpose of the study, differences among the SFNB protocol groups I, II and III were assessed; then, following the secondary purpose N1, the SFNB protocol groups I and II (placebo excluded) were compared with CFNB + PCA groups IV and V. Finally, following the secondary purpose N2, the CFNB + PCA groups IV and V were compared.

5. RESULTS

The baseline characteristics of the subjects were similar considering sex (p=0.65), the ASA physical state class (p=0.64), age (p=0.57), and body mass index (p=0.78) (Table 1).

Table 1. *Baseline characteristics*

	I (n=20)	II (n=20)	III (n=20)	IV (n=16)	V (n=19)	p(ANOVA)
Age, year	**30.5**±9.5	**29.05**±7.94	**30.5**±7.9	**33.38**±10.01	**32.8±4**9.81	0.57
BMI, kg/m^2	**25.15**±3.15	**25.5**±2.87	**24.9**±3.28	**25.0**±3.56	**24.26**±1.94	0.78
Surgery duration, min	**66.55**±15.95	**76.5**±18.14	**71.0**±22.4	**79.69**±16.17	**89.74**±18.67	0.15
Motor blockade duration, h	**6.84**±2.23	**6.17**±1.99	**5.62**±1.17	**6.1**±1.57	**6.21**±1.724	0.32
Sensory blockade duration, h	**8.38±**3.41	**7.96**±3.42	**7.98**±2.09	**8.76**±2.36	**8.19**±2.14	0.89
Hospital stay, days	**3.65**±0.75	**3.3**±0.8	**3.7**±0.73	**3.69±3.69**	**3.58**±0.84	0.46

Data are reported as a mean ± SD (standard deviation).

5.1 Postoperative pain

Day 0. Pain at rest (NRS)

There was no significant difference among the mean NRS values in the SFNB protocol groups I, II, and III (ANOVA p=0.92, Kruskal–Wallis p=0.96) (Table 2). Meanwhile, considering groups I, II, IV, V, they were significantly different (ANOVA p<0.001, Kruskal–Wallis p=0.001). The reason is a significant difference between the SFNB and CFNB + PCA protocol subjects and subjects in the CFNB + PCA protocol groups IV and V: it was better in group IV than in group V (Mann–Whitney p=0.002) (Table 3). Also, although pain control was worse in groups I and II than in group IV (Mann–Whitney p<0.021), it was better than in group V (Mann–Whitney p<0.019) according to the analysis of pairs (the placebo group excluded).

Table 2. *Pain intensity in I–III groups, NRS [0–10]*

	I (n=20)	II (n=20)	III (n=20)	p (ANOVA or Kruskal–Wallis*)
Day of operation (12 h)	**4.85**±1.42	**4.9**±1.45	**5.05**±1.96	0.92 (0.96)
1st day (24 h) at rest	**0.7**±1.08	**0.45**±0.76	**0.75**±0.91	0.59*
1st day at motion	**3.4**±2.01	**3.65**±2.06	**3.9**±2.02	0.74 (0.76)
2nd day (48 h) at rest	**0.45**±0.69	**0.15**±0.37	**0.4**±0.68	0.29*
2nd day at motion	**1.95**±1.19	**1.45**±1.36	**2.3**±1.17	0.103 (**0.05)**

Data are presented as mean ± SD.

* Kruskal–Wallis test only was used, because the normality assumption was not valid in this case.

Table 3. *Pain intensity in IV–V groups, NRS [0–10]*

	IV (n=16)	V (n=19)	p (t–test or MW*)
Day of operation (12 h)	**3.63**±2.16	**6.37**±2.09	**0.001 (0.002)**
1st day (24 h) at rest	**0.44**±0.89	**1.1**±0.94	**0.02***
1st day at motion	**2.25**±1.77	**3.79**±1.51	**0,009 (0.006)**
2nd day (48 h) at rest	**0.13**±0.34	**0.21**±0.42	0.51*
2nd day at motion	**0.94**±0.77	**1.58**±1.02	**0.047** (0.059)

Data are reported as mean ± SD.
* Mann-Whitney test only was used because normality assumption was not valid in this case.

Day 1. Pain at rest (NRS)

There was not significant difference between the mean NRS values in the SFNB protocol groups I, II and III (ANOVA p=0.55, Kruskal–Wallis p=0.59). Also, considering groups I, II, IV, V, they were also not significantly different (ANOVA p= 0.106, Kruskal–Wallis p=0.045). Since the p values were not high, the comparison of pairs was expected to show possible differences among the groups. It revealed that pain control at rest was better in group IV than in group V (Mann–Whitney p=0.02), and in group I it was similar to that of group IV and V (Mann–Whitney p>0.104). Also, group II performed better than group V (Mann–Whitney p=0.017), but similarly to group IV (Mann–Whitney p=0.65).

Day 1. Pain at motion (NRS)

There was no significant difference between the mean NRS values in the SFNB protocol groups I, II, and III (ANOVA p=0.74, Kruskal–Wallis p=0.76). Also, considering groups I, II, IV, V, they were also not significantly different (ANOVA p= 0.076, Kruskal–Wallis p=0.039). A comparison of pairs revealed that pain control at motion was better in group IV than in group V (Mann–Whitney p=0.006). Group I was similar to groups IV and V (Mann–Whitney p>0.051), but it was significantly closer to the latter, which in turn was significantly worse than group IV.

Group II performed worse than group IV (Mann–Whitney p=0.021), but similarly to group V (Mann–Whitney p=0.58).

Day 2. Pain at rest (NRS)

There was no significant difference between the mean NRS values in the SFNB protocol groups I, II and III (ANOVA p=0.21, Kruskal–Wallis p=0.24). Also, considering groups I, II, IV, V, they were also not significantly different (ANOVA p= 0.15, Kruskal–Wallis p=0.27). A comparison of pairs confirmed the same: pain control was similar in groups IV and V (Mann–Whitney p=0.51), in I and IV or V (Mann–Whitney p=0.109, p=0.28), also in II and IV or V (Mann–Whitney p=0.83, p=0.63).

Day 2. Pain at motion (NRS)

Although there was no significant difference among the SFNB protocol groups I, II, and III (ANOVA p=0.103, Kruskal–Wallis p=0.05), a comparison of pairs revealed that pain at motion was significantly better in group II than in group III (Mann–Whitney p=0.018), while differences were not significant between groups I and II, also I and III (Mann–Whitney p=0.13, p=0.34, accordingly). Also, pain control was similar in group IV and V (Mann–Whitney p=0.059, t–test p=0.047), and in groups I and V (Mann–Whitney p=0.44), but in the former it was significantly worse than in group IV (Mann–Whitney p=0.008). Group II performed similarly to groups IV and V (Mann–Whitney p=0.25, p=0.41).

5.2 Adjunctive pain management

Day 0. Diclofenac

The consumption of diclofenac was not significantly different in the SFNB groups I, II, and III (chi-square p=0.85, Fisher's exact p=1)**,** and it was not significantly different among groups I, II, IV, V (chi-square p=0.15, Fisher's exact p=0.54). A comparison of pairs confirmed that pain control was similar in groups IV, I (Mann–Whitney p=0.36), and II (Mann–Whitney p=0.12), also in V, I (Mann–Whitney p=0.08), and II (Mann–Whitney p=0.06). The difference was not significant among the CFNB + PCA groups IV and V (chi-square p=0.43).

Day 0. Tramadol

The consumption of tramadol was not significantly different among the SFNB groups I, II, and III (Fisher's exact p=0.62), while in the CFNB + PCA groups tramadol wasn't used at all (p=1). The mean consumption of tramadol was significantly different in groups I, II, IV, V (Fisher's exact p<0.0001). More specifically, tramadol consumption was lower in group IV than in groups I and II (Fisher's exact p<0.001, p<0.001), as well as in group V than in groups I and II (Fisher's exact p=0.0012, p<0.001).

Day 1. Diclofenac

The consumption of diclofenac was not significantly different among the SFNB groups I, II, and III (chi–square p=0.41, Fisher's exact p=0.52)**,** but it was significantly different among groups I, II, IV, V (chi-square p=0.0006, Fisher's exact p<0.0001). The reason lies in the significant difference between SFNB and CFNB + PCA protocol subjects since the consumption was lower in group IV than in groups I and II (chi-square p=0.0015, p=0.035), as well as in group V than in groups I and II (chi-square p=0.0005, p=0.017). Meanwhile, the consumption of diclofenac in CFNB + PCA groups IV and V was similar (chi–square p=0.85).

Day 1. Tramadol

The consumption of tramadol was not significantly different among the SFNB groups I, II, and III (Fisher's exact p=0.72), while it was significantly different among groups I, II, IV, V (Fisher's exact p=0.011). The reason lies in the significant difference among the SFNB and CFNB + PCA protocol subjects, while there was no difference among the CFNB + PCA groups (Fisher's exact p=0.46). More specifically, the demand of tramadol was lower in group V than in groups I and II (Fisher's exact p=0.02, p=0.02), while there was no significant difference between group IV and groups I and II (Fisher's exact p=0.104, p=0.104).

Day 2. Diclofenac

The consumption of diclofenac was not significantly different among the SFNB groups I, II, and III (chi-square p=0.9, Fisher's exact p=1)**,** and it was not significantly different among groups I, II, IV, V (chi-square p=0.65, Fisher's exact p=0.17). The difference between SFNB and CFNB + PCA protocol subjects was not significant: IV vs I and II (chi-square p=0.24, p=0.41,

Fisher's exact p=0.36, p=0.61), also V vs I and II (Fischer's exact p=0.11, p=0.23). The consumption of diclofenac in the CFNB + PCA groups IV and V was also similar (chi-square p=0.46).

Day 2. Tramadol

The consumption of tramadol was not significantly different among the SFNB groups I, II, and III (p=1) and in CFNB + PCA groups (p=1). Also, the mean consumption of tramadol was not significantly different in groups I, II, IV, V (Fisher's exact p=0.61).

5.3 Patient satisfaction at the end of trial

There was no significant difference between the mean values of patient satisfaction in the SFNB protocol groups I, II and III (Duncan's p=0.28; Mann–Whitney p>0.32) (Fig. 2). Meanwhile, as for groups I, II, IV, V, they were significantly different (ANOVA p=0.001, Kruskal–Wallis p=0.003). The reason lies in the significant difference between the SFNB and CFNB + PCA protocol subjects, while there was no significant difference between the CFNB + PCA protocol groups IV and V (Duncan's p=0.35; Mann–Whitney p=0.32). More specifically, patient satisfaction was significantly better in group IV (CFNB + PCA R1) than in group I (SFNB + M) (Mann–Whitney p=0.006) and group II (SFNB + N) (Mann–Whitney p=0.002) according to the analysis of pairs (the placebo group excluded). Group V was very close to being significantly different from group I (Mann–Whitney p=0.061), and it was significantly better than group II (Mann–Whitney p=0.016) (Figure 2).

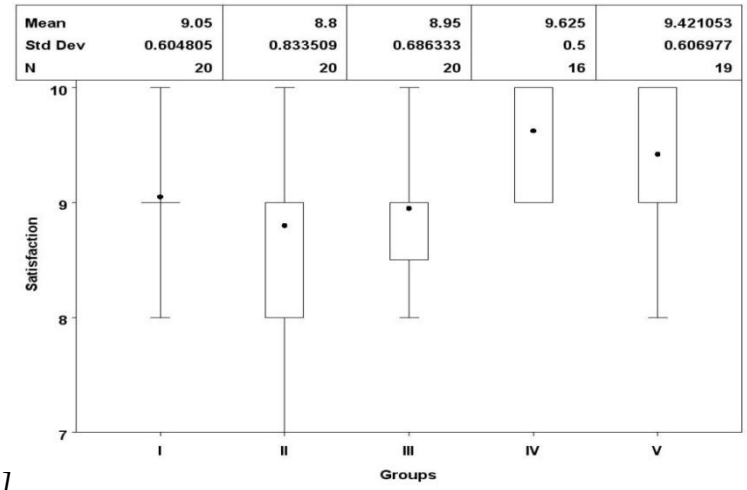

Figure 2. *Patient satisfaction [0–10]*

5.4 Bupivacaine consumption

The mean consumption of bupivacaine (Table 4) in group V was lower than in group IV during the first 24 h (Mann–Whitney p=0.0001) and the whole trial (Mann–Whitney p=0.0001). There were no differences among the groups in demanded and administered PCA boluses (Mann–Whitney p=0.3, p=0.71).

Table 4. *Bupivacaine (mg) consumption in CFNB + PCA groups*

	CFNB + PCA R1 IV (n=16)	CFNB + PCA R2 V (n=19)	p (Mann–Whitney)
First 24 h	**94.19**±23.29	**47.28**±16.74	**0.0001**
All 48 h	**182.04**±31.14	**79.56**±36.34	**0.0001**
Mean dose/h	**5.45**±0.77	**2.32**±1.32	**0.0001**
D/A* 0–24 h	**81.23**±19.84	**89.22**±12.43	0.3
D/A* 0–48 h	**97.00**±6.75	**95.5**±9.3	0.711

Data are reported as mean ± SD.

*D/A: difference of demanded and administered PCA boluses (%).

To summarize: there was only one significant difference among groups I, II, and III found during the study period: there was a significantly better pain control at motion at the end

of the trial in group II than in group III (p=0.018). ***Patient satisfaction*** in group IV was significantly higher than in groups I and II (p=0.006, 0.002), while there was no difference between groups IV and V (p=0.32). Although ***pain control on the day of surgery*** in groups I and II was worse than in group IV (p<0.021), it was better than in group V (p<0.019). However, the consumption of adjunct analgesics was higher in the former group. That day's pain control was better in group IV than in group V (p=0.002) with no difference in adjunct consumption. ***On postoperative day 1, pain control at rest*** was better in group II than in group V (p=0.017), and similar to that in group IV (p=0.651), but it had a higher adjunct consumption (p<0.035). The latter can contribute to the same day's pain at motion since it was similar in groups I, IV, and V (p>0.51). Also, pain control was better in group IV than in group V (p=0.006).

5.5 Complications

The adverse events were mostly related to the spinal anesthesia technique (urine retention 6.32%; postdural puncture headache 7.37%; hypotension 13.68%; and backache 8.42%). Also, 4.2% of patients had paresthesias in the femoral nerve area. There was no significant difference among the groups. However, no complications related to the use of intra-articular medicaments or bupivacaine infusion were observed.

6. DISCUSSION

In contrast to conventional practice, in our trial, the intra-articular morphine or neostigmine were diluted in normal saline rather than mixed with bupivacaine solution. We expected that intra-articular morphine (group I) would be associated with a better pain control after the ACL repair surgery during the whole trial (48 postoperative hours). However, we didn't observe its significant analgesic effectiveness. Our study revealed that the difference was only observed on Day 2. It was associated with the primary endpoint (pain at motion), and it was observed between two groups, since only intra-articular neostigmine (group II) demonstrated an advantage over the placebo (group III). Several mechanisms may explain this peripheral cholinergic antinociception. They may be related to hyperpolarization of neurons, reduction in the release of pronociceptive neurotransmitters, or activation of the nitric oxide-cyclic guanosine monophosphate pathway by elevating endogenous acetylcholine. A possible explanation why

there were no differences on Day 1 is the residual analgesic effect of SFNB, since the allowed force of treading down was similar in all groups at the time of evaluation.

Numerous reports in the literature do not show significant advantages of intra-articular morphine (1–5 mg) alone or in combination with bupivacaine over bupivacaine alone. Moreover, a qualitative systematic review of well-controlled trials compared postoperative pain intensity and reported no additive analgesic effect of intra-articular morphine compared to saline. Our study is probably the first to compare in a placebo-controlled manner the efficacy of the end-surgery injection of intra-articular morphine and nesotigmine without local anesthetics in addition to spinal anesthesia combined with SFNB. Neither did a rather similar study by McCarty and colleagues also find support for intra-articular injection of morphine (5 mg) after arthroscopic ACL reconstruction in addition to general anesthesia combined with SFNB. We used a bigger dose of morphine (6 mg) aiming for a more pronounced analgesic effect. According to literature reports, the adverse systemic reactions of intra-articular morphine and neostigmine are a reasonable concern. However, we did not observe the side effects such as nausea, bradycardia, miosis, pruritus, hypersalivation or confusion; but we did not evaluate the systemic action of morphine or neostigmine by measuring their levels in circulation.

The present prospective randomized clinical trial discovered that patient-controlled perineural femoral infusion of on-demand 0.1% bupivacaine boluses combined with basal infusion provided a more efficient postoperative pain control than on-demand boluses alone during 48 h after ACL reconstruction. The scarce literature reports in patients after ACL reconstruction describe that a PCA regimen with on-demand boluses of bupivacaine was associated with a lower consumption of local anesthetics than a regimen with basal infusion plus on-demand boluses, and there was no difference in the quality of analgesia. In the present trial, a lower concentration of bupivacaine was used and no additives were deployed; nevertheless, the consumption of bupivacaine during the postoperative 48 h was lower. This is a clinically important finding, since it argues that the use of a lower-concentration bupivacaine solution without additives results in a lower overall bupivacaine dosage. Such strategy would be cost-effective with a lower systemic toxic effect of bupivacaine. In addition, the low concentration of bupivacaine facilitates a selective sensory block, which is very important for performing the rehabilitation exercises. This is also important for the investigating the possibility to continue the use of PCA pumps at home after day-case surgery. The good overall satisfaction of all

participants of the present trial and their comments that they felt comfortable with the use of PCA pumps and found them easy to operate is also encouraging. However, the possibility to continue the use of PCA devices at home has to be investigated, including numerous other aspects such as patient safety and education and the cost–benefit ratio in the specific healthcare system. The lockout intervals of 15–30 min between the on-demand boluses in the present trial complied with the conventional clinical practice aiming to minimize the overdose possibility. No manifestation of systemic toxicity was observed in the present trial; however, the plasma concentration and/or bupivacaine clearance were not measured.

As expected, in CFNB + PCA groups IV and V there was a significantly better patient satisfaction and pain control during the whole trial with a logical significant prevalence of group IV over group V. When the SFNB groups provided pain control close to CFNB + PCA, such cases were associated with a higher consumption of adjunct analgesics.

Most of the adverse events observed in the present trial had an inherent association with spinal anesthesia. The occurrence of paresthesia in the femoral nerve area was within the common average incidence of 0.5–20% in association with peripheral nerve blocks. The postoperative fever could be related to surgical stress response, since there were no signs of local inflammation or infection. Serious infection in association with the short-term perineural catheters had not been reported before. The reasons for exclusion of a few subjects from the study were the unsuccessful insertion of a perineural catheter or its malfunction. This complies with the common incidence of similar events reported in literature.

The peripheral nerves such as sciatic and obturator may probably contribute to the postoperative pain. Thus, in our trial, there was a need for adjunct analgesics to contest with mild-to-moderate pain during 48 hrs after ACL reconstruction in all groups. In the present trial, the use of adjunctive analgesics (diclofenac and tramadol) was different from similar studies which used IV ketoprofen and morphine or IV propacetamol followed by 10–20 mg of IM piritramide, which is a synthetic l-agonist opioid. Such diversity did not allow a reliable comparison of the analgesic efficacy among different studies.

There are a few deficiencies in the present study. The operations were performed according to the same methodology but by different surgeons. Thus, differences in postoperative surgical stress response could be present. An obvious weak point is that the actual length of hospital stay was recorded instead of evaluating the fitness to discharge. The actual hospital stay

was determined by institutional regulations. The average stay of three-and-a-half days after ACL reconstruction was the clinical standard at the present trial's site where the biggest annual number of such operations in the region was performed.

The present trial is too small for ambitious conclusions in declaring the advantage of one strategy's over another. Nevertheless, the findings encourage further investigations aimed to establish the optimal regimens of the perineural infusion of local anesthetics as part of multimodal postoperative analgesia after ACL reconstruction.

7. CONCLUSIONS

1. Our results show that there was only a single difference among intra-articular-SFNB groups found on the 2nd postoperative day: a significantly better pain control at motion in neostigmine (0.5 mg) group than in the placebo group. There was no additive analgesic effect of i/a morphine (6 mg).
2. Also, we observed a significantly better pain control and patient satisfaction in continuous femoral perineural block PCA groups during the whole trial.
3. There was a significant prevalence of the PCA analgesia regimen which implies the preset basal rate of 0.1% bupivacaine: a 5 ml bolus with a lockout period 30 min and basal infusion 5 ml/h (group IV).
4. Neither side effects nor complications related to regional analgesia techniques or the medications were observed.

8. PRACTICAL RECOMMENDATIONS

Upon evaluating the results of our prospective randomized study, for the perioperative pain management during arthroscopic anterior cruciate ligament repair surgery we could recommend:

- spinal anesthesia (Th8 level) + femoral nerve block with 20 ml of 0.5% bupivacaine;
- postoperatively: continuous femoral perineural infusion of 0.1% bupivacaine (48 hrs);
- PCA regimen: bolus 5 ml/ 30 min + basal infusion 5 ml/h.

As an alternative (if there is no possibility of perineural catheterization), the 2nd choice of the postoperative analgesia method could be:

- single-shot femoral nerve block with 20 ml of 0.5% bupivacaine (100 mg);
- end-surgery intra-articular injection of 0.5 mg neostigmine with 10 ml 0.9 % normal saline.

We propose and encourage the investigation of the possibility to continue the use of PCA pumps at patient's home after day-case surgery.

9. LIST OF AUTHOR'S PUBLICATIONS

1. Svediene S, Andrijauskas A, Ivaskevicius J. Intra-articular morphine or neostigmine does not assure better pain relief. Cent Eur J Med 2011; 6(5): 645–51.
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3. Svediene S, Ivaskevicius J. Good medical practice for regional block procedures. Acta Medica Lituanica 2012; 19(3): 187–90.

10. PRESENTATIONS

1. "Paciento kontroliuojamos tęstinės regioninės analgezijos metodo taikymas". Vilniaus ir Kauno kraštų ortopedų traumatologų ir anesteziologų draugijų konferencija. Vilnius, 2008 spalis.
2. "The advantages of the continuous femoral nerve block as a postoperative regional PCA in extended knee arthroscopic surgery". 4th International Baltic Congress of Anesthesiology and Intensive Care. Latvia, Ryga, 11–13 Dec 2008.
3. "The advantages of the continuous femoral nerve block as a postoperative regional PCA in extended knee arthroscopic surgery". 28th Annual Congress of the ESRA and Pain Therapy. Austria, Salzburg, 9–12 Sept 2009.
4. "Alternatives of regional anesthesia techniques for extended arthroscopic knee surgery". ESRA and Latvian Association of Anesthesiologists and Reanimatologists. Latvia, Ryga, 20–22 May 2010.
5. "Neurological disorders following regional blocks". 5th International Baltic Congress of Anesthesiology and Intensive Care. Estonia, Tartu, 21–23 Oct 2010.
6. "Good medical practice for regional block's procedures". 6th International Baltic Congress of Anesthesiology and Intensive Care. Lithuania, Vilnius, 18–20 Oct 2012.

7. “Nuskausminimo metodų palyginimas, atliekant artroskopines kelio operacijas”. Lietuvos anesteziologų-reanimatologų draugijos mokslinė praktinė konferencija. Vilnius, 22 02 2013.

11. CURRICULUM VITAE OF THE AUTHOR

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2009–2013 Doctoral (Ph. D.) studies at the Vilnius University Faculty of Medicine

2003 – University diploma – Faculty of Medicine of Vilnius University – doctor anesthesiologist-reanimatologist

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12. SUMMARY IN LITHUANIAN
SANTRAUKA LIETUVIŲ KALBA

Įvadas

Lietuvoje kasmet atliekama daugiau kaip 5000 kelio artroskopinių operacijų, iš kurių maždaug 500 yra kryžminių raiščių rekonstrukcijos. Priekinio kryžminio raiščio (PKR) plyšimas būdingas jauniems sportininkams ar darbingiems pacientams, kuriems gyvybiškai svarbu išsaugoti kelio funkciją bei fizinį aktyvumą dar ilgus metus. Reabilitacija po operacijos stengiamasi pasiekti kuo palankesnių rezultatų, kuriems didžiulę reikšmę turi perioperacinio skausmo malšinimo efektyvumas. Skausmo malšinimo būdų yra daug ir įvairių, bet tinkamai pasirinktas metodas lemtų ne tik efektyvią reabilitaciją bet ir sutrumpintų gydymo ligoninėje trukmę, sumažintų išlaidas. Visame pasaulyje iki šiol ieškoma efektyviausio ir saugiausio perioperacinės analgezijos metodo. Tiriami įvairūs asocijuotos sisteminės analgezijos deriniai – intraveniniai ir peroraliniai būdai su intrasąnarine ar regionine anestezija. Pacientai tampa vis reiklesni, todėl jų pasitenkinimui skiriamas ypatingas dėmesys.

Šiuo metu atliekant artroskopines PKR rekonstrukcines operacijas dažniausiai pasirenkama regioninė anestezija. Po centrinių nervų blokadų (spinalinės ir epiduralinės) ir bendrosios nejautros atsigavimo laikas yra panašus, tačiau taikant blokadas nepasitaiko tokių komplikacijų, kaip kvėpavimo funkcijos nepakankamumas ir aspiracija, o vėmimo ir pykinimo atvejų būna rečiau. Be to, jos pasižymi pooperacine analgezija, kurią galima pagerinti ir pailginti naudojant specialius kateterius, tačiau gali sukelti šlapimo susilaikymą, niežulį, pykinimą, euforiją ar mieguistumą, širdies ir kraujagyslių sistemos sutrikimus (hipotenziją iki 20 %, bradikardiją), sensomotorinę blokadą, problemiška derinti su trombozių profilaktika.

Periferinių nervų blokados yra galingesnė technika nei intrasąnarinės injekcijos, jos ypač tinka tokioms operacijoms kaip PKR rekonstrukcija, nes sukelia chirurginę anesteziją, pooperacinę analgeziją ir palengvina pacientų reabilitaciją bei išrašymą. Periferinės blokados yra daug retesnė rehospitalizacijos priežastis nei kitos anestezijos technikos. Atlikus regioninę nejautrą, pacientas išlieka sąmoningas, mažėja metabolinis ir endokrininis organizmo atsakas į operaciją, mažiau įvyksta tromboembolinių komplikacijų, poveikis žarnyno motorinei funkcijai yra palankus, pooperacinis laikotarpis ramus, reikia mažiau slaugos, įmanoma pasiekti gerą pooperacinę analgeziją (ypač naudojant perineurinius kateterius ir paciento kontroliuojamą

analgezijos režimą). Žinoma, regioninė nejautra turi ir trūkumų, kurie nėra būdingi bendrajai nejautrai: regioninei nejautrai atlikti reikia gerų įgūdžių ir praktikos, reikia ilgokai palaukti anestezijos pradžios, ne visada pavyksta sukelti norimą analgeziją; yra toksinių reakcijų ir neurologinių komplikacijų pavojus. Tačiau po nervų blokadų pooperacinės slaugos išlaidos yra mažesnės nei po bendrosios nejautros.

Intrasąnarinė analgezija galbūt mažiau veiksminga nei nervų blokados, bet neturi sisteminio poveikio ir nesukelia motorinės blokados. Literatūros duomenys apie intrasąnarinį morfino ar neostigmino vartojimą yra skurdūs ir prieštaringi. Teigiama, kad jų efektyvumas priklauso nuo dozės. Manome, jog sinerginis pooperacinis vienkartinės periferinės nervo blokados ir intrasąnarinių injekcijų poveikis leistų sumažinti papildomų analgetikų suvartojimą.

Galutinė analgezijos schema priklauso nuo chirurginio veiksmo, operatoriaus įpročių, galimybių ir paties paciento. Siekdami nustatyti optimalų skausmo malšinimo būdą pacientams, kuriems atliekama kelio artroskopinė PKR rekonstrukcija, nutarėme atlikti skirtingų regioninės analgezijos metodų (intrasąnarinio ir perineurinio) derinių palyginimą.

Darbo tikslas

Tyrimo tikslas – nustatyti efektyviausią ir saugiausią perioperacinio skausmo malšinimo metodą atliekant artroskopines kelio PKR rekonstrukcines operacijas.

Darbo uždaviniai

Vertinant skausmo stiprumą ramybėje ir reabilitacijos metu, papildomų analgezinių vaistų suvartojimą ir paciento pasitenkinimą, palyginti:

1. Intrasąnarinio morfino ir neostigmino efektyvumą, derinant su vienkartine šlauninio nervo blokada.
2. Intrasąnarinio ir tęstinio perineurinio analgezijos metodų veiksmingumą.
3. Skirtingus tęstinio perineurinio paciento kontroliuojamo skausmo malšinimo režimus.

4. Nustatyti su taikytais regioninės anestezijos metodais ar vartotais vaistais susijusių komplikacijų bei šalutinių reiškinių dažnį.

Mokslinis naujumas

Artroskopinė priekinio kryžminio raiščio rekonstrukcija – viena iš dažniausiai dabar atliekamų ortopedinių operacijų pasaulyje. Adekvati skausmo kontrolė yra labai svarbi siekiant efektyvios ankstyvos reabilitacijos ir gerų funkcinių rezultatų, sutrumpinant gydymo ligoninėje trukmę. Vis dar ieškoma optimalios regioninės anestezijos technikos, kuri palengvintų atsistatymą po operacijos, neturėtų šalutinio sisteminio poveikio.

Pastebėjome, jog vienkartinė šlauninio nervo blokada yra veiksmingesnė už intraveninį ar intrasąnarinį skausmo malšinimą, tačiau neužtikrina tinkamos kelio sąnario analgezijos bei paciento pasitenkinimo reabilitacijos metu. Todėl nutarėme, glaudžiai bendradarbiaudami su ortopedais-traumatologais, modifikuoti mūsų ligoninėje taikomą perioperacinio skausmo malšinimo protokolą atliekant kryžminių kelio raiščių operacijas ir pritaikyti pasirinktus naujus analgezijos metodus.

Atlikome randomizuotą perspektyvųjį dvigubai aklą placebu kontroliuojamą tyrimą ir panaudojome dar netirtą intrasąnarinių vaistų (morfino ir neostigmino) dozę, derindami su vienkartine šlauninio nervo blokada. Taip pat tyrėme tęstinį skausmo malšinimą šlaunies perineuriniu kateteriu, taikydami du dar netyrinėtus paciento kontroliuojamos analgezijos režimus tikėdamiesi, kad skausmo valdymas bus optimalus. Taikėme mažesnę vietinio anestetiko koncentraciją, siekdami selektyvesnės sensorinės blokados, mažesnės paros dozės, mažiau toksinių reakcijų. Tikrinome, ar tęstinis skausmo malšinimas perineuriniu kateteriu yra veiksmingesnis nei vienkartinė nervo blokada su intrasąnarinėmis analgetikų injekcijomis: į tyrimą įtraukėme ir šių dviejų metodų palyginimą.

Tiriamieji ir metodai

Randomizuotas perspektyvusis tyrimas atliktas 2007–2010 metais Respublikinės Vilniaus universitetinės ligoninės (RVUL) Anesteziologijos-operaciniame ir Ortopedijos-traumatologijos skyriuose. Protokolą patvirtino Lietuvos bioetikos komitetas 2007 m. liepos 13 d. ir išdavė leidimą (Nr. 31; B-8-393) atlikti biomedicininį tyrimą.

Dalyvauti tyrime buvo atrinkti 95 suaugę pacientai, kuriems numatoma atlikti artroskopinę kelio PKR rekonstrukcinę operaciją. Visi pacientai pagal ASA atitiko I–II klasę, jų kūno masės indeksas neviršijo 30 ir jie neturėjo pasirinktos regioninės anestezijos taikymo kontraindikacijų.

Pacientai suskirstyti į penkias grupes (1 lentelė). Visi buvo operuojami sukėlus spinalinę nejautrą (SA). I–III grupių tiriamiesiems buvo atlikta vienkartinė šlauninio nervo blokada (VŠNB) bei skirtingos intrasąnarinės injekcijos papildomam pooperacinio skausmo malšinimui. IV–V grupių pacientams pooperacinis skausmas buvo malšinamas perineuriniu šlaunies kateteriu – taikyta tęstinė infuzija skirtingais paciento kontroliuojamos analgezijos (PKA) režimais.

1 lentelė. *Tiriamųjų grupių detalus aprašymas*

Grupės	Regioninio skausmo malšinimo metodika
I grupė (VŠNB + M) n=20	SA + **VŠNB** 100 mg bupivakaino (0,5 % 20 ml) + **6 mg morfino** į sąnarį (i/**s**) (skiesta 10 ml 0,9 % NaCl fiziologinio tirpalo)
II grupė (VŠNB + N) n=20	SA + **VŠNB** 100 mg bupivakaino (0,5 % 20 ml) + **0,5 mg neostigmino** i/**s** (skiesta 10 ml 0,9 % NaCl)
III grupė (kontrolinė) (VŠNB + P) n=20	SA + **VŠNB** 100 mg bupivakaino (0,5 % 20 ml) + **placebas** i/**s** (10 ml 0,9 % NaCl)
IV grupė (TŠNB R1) n=16	SA + **šlaunies perineuriniu kateteriu** priešoperacinis boliusas 100 mg bupivakaino (0,5 % 20 ml) + pooperacinė tęstinė bupivakaino 0,1 % infuzija režimu R1: **bazinė infuzija 5 ml/val. ir PKA boliusai 5 ml/30 min.**
V grupė (TŠNB R2) n=19	SA + **šlaunies perineuriniu kateteriu** priešoperacinis boliusas 100 mg bupivakaino (0,5 % 20 ml) + pooperacinė tęstinė bupivakaino 0,1 % infuzija režimu R2: tik **PKA boliusai 5 ml/15 min.**

Atvykusiems į operacinę premedikuotiems pacientams atliekama vienkartinė šlauninio nervo blokada, ir IV–V grupių pacientams paliekamas perineurinis kateteris. Jeigu pacientas priskiriamas I, II ar III grupei tiriamųjų, operacijos pabaigoje 10 min. prieš atleidžiant šlaunies veržiklį, chirurgas pro dreną į sąnario ertmę suleidžia steriliai paruošto 10 ml analgezinio tirpalo (konkreti sudėtis nei jam, nei tiriančiajam, nei tiriamajam nežinoma). Perineurinė PKA infuzija pradedama poanestezinės priežiūros palatoje, motorinei blokadai sumažėjus iki 2 balų pagal *Bromage* skalę. Papildomam skausmo malšinimui, jei pacientas skausmo stiprumą pagal NRS skalę nurodo $\leq$ 3 balai, suleidžiama 75 mg diklofenako; jeigu skausmas siekia $\geq$ 4 balus, skiriama 50 mg tramadolio.

Pooperacinis skausmingumas ramybėje ir reabilitacijos metu per visą tyrimą buvo registruojamas trimis etapais: 12, 24 ir 48 val. nuo anestezijos pradžios. Papildomas nesteroidinių vaistų nuo uždegimo ir opioidų suvartojimas buvo fiksuojamas tais pačiais momentais, t. y. 3 kartus per visą tyrimą. Pacientų pasitenkinimas vertintas tyrimo pabaigoje, prašant nurodyti skalės balais nuo 0 iki 10 didėjančio pasitenkinimo kryptimi.

Pacientai buvo stebimi dėl galimų komplikacijų, susijusių su regioninės anestezijos technika ar vartotais vaistais. Perineurinio tęstinio skausmo malšinimo grupėse (IV ir V) papildomai fiksuotas bupivakaino (mg) suvartojimas.

Statistiniai metodai panaudoti remiantis matematinės statistikos metodine medžiaga. Statistinės hipotezės reikšmingumo lygmuo visiems testams pasirinktas 0,05. Gautų duomenų analizė buvo atliekama šia tvarka: pirmiausiai buvo vertinami skirtumai tarp intrasąnarinių vaistų grupių (I, II ir III); toliau pirmosios dvi (placebo neįtraukiant) buvo lyginamos su kateterinėmis grupėmis (I, II, IV ir V) poromis; galiausiai buvo ieškoma reikšmingo pranašumo tarp skirtingų perineurinio skausmo malšinimo režimų (IV ir V grupėse).

Rezultatai ir jų aptarimas

Buvo patvirtintas visų penkių tiriamųjų grupių homogeniškumas.

Vienintelis skirtumas tarp I, II ir III grupių, nustatytas per visą tyrimo laiką – tai reikšmingai geresnė skausmo kontrolė antrą parą krūvio metu II-oje (intrasąnarinio neostigmino) grupėje nei III (placebo) grupėje (p=0,018).

IV grupės pacientų pasitenkinimas buvo patikimai didesnis nei I ir II grupių (p=0,006, 0,002); V grupės beveik išsiskyrė nuo I (p=0,061) ir turėjo patikimai didesnį pasitenkinimą nei II grupės pacientų (p=0,016); tačiau patikimai reikšmingo skirtumo tarp IV ir V grupių pasitenkinimo nebuvo (p=0,32).

Skausmo kontrolė operacijos dieną I ir II grupių pacientų buvo blogesnė nei IV grupės (p<0,021), tačiau nors ir geresnė nei V grupės (p<0,019), papildomų opioidinių analgetikų suvartojimas abiejose intrasąnarinėse grupėse buvo didesnis (p<0,012). Operacijos dieną patikimai geresnę analgeziją gavo IV grupės pacientai, palyginti su kitu PKA režimu be bazinės infuzijos – V grupe (p=0,002), o papildomų analgetikų šiose grupėse buvo suvartota panašiai.

Pirmą pooperacinę parą ramybėje II grupės NRS balai buvo žemesni nei V (p=0,017) ir panašūs kaip IV (p=0,061). Tačiau II grupėje tiek papildomų NVNU (p<0,035), tiek opioidų (p=0,02) suvartota daugiau. Tą pačią – pirmąją dieną krūvio metu skausmingumas buvo panašus I, IV ir V grupių (p>0,051), bei II ir V grupių (p=0,58), o II net didesnis nei IV grupės pacientų (p=0,021). Tarp kateterinių grupių – IV grupėje skausmo kontrolė buvo patikimai geresnė nei V grupėje (p=0,006).

Antrą pooperacinę parą ramybėje NRS balai visose tiriamųjų grupėse buvo panašūs. Krūvio metu nedidelį privalumą turėjo IV (perineurinio skausmo malšinimo su PKA boliusais ir bazine infuzija) grupė (p=0,047).

Apibendrinant teigtina, kad analgezijos kokybė ir pacientų pasitenkinimas per visą tyrimą buvo žemesnis I, II ar III (intrasąnarinių) grupių nei V ir ypač IV (perineurinio skausmo malšinimo) grupių, pastarosiose beveik visai neprireikė papildomų opioidų injekcijų viso stebėjimo laiku.

Atliekant tyrimą, vertintas ir vietinio anestetiko bupivakaino suvartojimas perineurinei infuzijai per pirmą ir antrą stebėjimo parą, apskaičiuota vidutinė valandos dozė. IV grupės pacientams bupivakaino suleista reikšmingai daugiau nei V grupės per pirmąsias 24 valandas

(*Mann–Whitney* p=0,0001), taip pat per visą tyrimo laiką (*Mann–Whitney* p=0,0001). Analizuoti skirtumai tarp paciento pareikalautų ir infuzinės pompos suleistų boliusų – šis rodiklis patikimai neišsiskyrė tarp grupių nei pirmą, nei antrą tyrimo parą (*Mann–Whitney* p=0,3; p=0,71). Bupivakaino paros dozė neviršijo 5 mg/kg.

Didžioji dalis šalutinių reiškinių buvo susijusi su spinalinės anestezijos taikymu. Šlapimo susilaikymas pasireiškė 6,32 %, popunkciniai galvos skausmai – 7,37 %, hipotenzija – 13,68 %, nugaros skausmas – 8,42 % pacientų. Šlauninio nervo srityje parestezijas jautė 4,2 % pacientų. Lyginant šių komplikacijų pasikartojimą atskirose grupėse, reikšmingų skirtumų negauta. Jokių komplikacijų, susijusių su intrasąnariniu morfino bei neostigmino ar vietinio anestetiko bupivakaino vartojimu, savo tyrime nenustatėme.

Mūsų studija tikriausiai pirmoji palygino placebu kontroliuojamu metodu morfino ir neostigmino intrasąnarines (i/s) pooperacines injekcijas, derinamas su spinaline anestezija ir vienkartine šlauninio nervo blokada. Mūsų tyrime morfinas ir neostigminas nebuvo leidžiami į sąnarį maišant su vietiniu anestetiku (VA), bet skiedžiami NaCl 0,9 % tirpalu. Dabar siūloma atsisakyti VA leisti į sąnarį dėl toksiškumo chondrocitų mitochondrijoms. Neostigmino periferinę cholinerginę antinocicepciją paaiškintų neuronų hiperpoliarizacija, pronocicepcinių neurotransmiterių atsipalaidavimo redukcija bei ciklinio guanozino monofosfato aktyvacijos kelias, galintis padidinti endogeninio acetilcholino koncentraciją. Pirmą parą skirtumai tarp intrasąnarinių grupių neišryškėjo dėl liekamojo vienkartinės šlauninio nervo blokados (0,5 % bupivakaino 100 mg) poveikio. Kitų kojos nervų – sėdmeninio ir užtvarinio įnervacijos zonos taip pat tikriausiai turėjo įtakos pooperaciniam kelio sąnario skausmingumui: tai galėjo būti papildomų analgetikų poreikio priežastis, nepaisant intrasąnarinių injekcijų. Taigi, per visą mūsų tyrimo laiką (48 val.) sisteminio skausmo gydymo reikėjo visose intrasąnarinėse grupėse.

Tyrimas atskleidė, kad PKA režimas, kai taikomi 0,1 % bupivakaino boliusai su bazine infuzija, geriau užtikrina pooperacinio skausmo malšinimo kokybę nei vien tik boliusai 48 val. laikotarpiu po PKR operacijų. Negausūs literatūros duomenys rodo priešingai, kad taikant vien tik PKA boliusų režimą, suvartojama mažiau VA, tačiau analgezijos efektyvumas panašus, kaip ir režimo su bazine infuzija. Mes tyrėme mažesnę bupivakaino koncentraciją (0,1 %) ir be adjuvantų klonidino ar adrenalino, skirtingai nei anksčiau minėtose studijose. Mūsų 48 val. bei vidutinė 1 val. bupivakaino dozė suvartota netgi mažesnė, nei nurodo kiti tyrėjai. Tai kliniškai reikšmingas radinys, nes naudojant mažesnę bupivakaino tirpalo koncentraciją gaunama

selektyvesnė sensorinė nervo blokada, ypač svarbi reabilitacijos procesui, ir sisteminio toksiškumo rizika yra mažesnė.

Pacientai jautėsi patenkinti per visą tyrimą, naudojimasis PKA infuzinėmis pompomis nesudarė jokių sunkumų. Tai skatina išplėsti metodo pritaikymą: ateityje jį būtų galima naudoti paciento namuose, anksčiau išleidus po dienos chirurgijos operacijų.

Išvados

1. Intrasąnarinių grupių (derinant su vienkartine šlauninio nervo blokada) pacientų skausmo kontrolė ramybėje, papildomų analgetikų suvartojimas ir pacientų pasitenkinimas buvo panašūs.

   Intrasąnarinis morfinas (6 mg) turėjo panašų analgezinį poveikį kaip ir neostigminas (0,5 mg) paciento krūvio metu per visą tyrimo laiką (48 val.); tačiau neostigminas buvo patikimai efektyvesnis už placebą antrą pooperacinę dieną.

2. Skausmo kontrolė ramybėje ir krūvio metu bei pacientų pasitenkinimas per visą tyrimą buvo geresni perineurinio skausmo malšinimo grupėse negu intrasąnarinėse.

   Intrasąnarinių grupių pacientų analgezijos efektyvumui priartėjus prie kateterinių grupių, nustatydavome didesnį papildomų analgetikų suvartojimą pirmosiose.

3. Skausmo malšinimas 0,1% bupivakaino infuzija šlaunies perineuriniu kateteriu, taikant paciento kontroliuojamos analgezijos režimą boliusais 5 ml/30 min. kartu su nuolatine bazine infuzija 5 ml/val., buvo efektyvesnis už vien tik paciento kontroliuojamus boliusus (5 ml/15 min.) 48 val. pooperaciniu laikotarpiu.

   Abiejose perineurinio skausmo malšinimo grupėse pacientų pasitenkinimas nesiskyrė.

4. Komplikacijų, susijusių su regioninės anestezijos taikymu, dažnis nesiskyrė nei tarp mūsų tirtų grupių, nei nuo literatūroje skelbiamų duomenų.

   Komplikacijų, susijusių su intrasąnariniu morfino ir neostigmino ar vietinio anestetiko bupivakaino vartojimu, savo tyrimo metu nenustatėme.

Praktinės rekomendacijos

Įvertinę tyrimo rezultatus, artroskopinėms PKR plastinėms operacijoms siūlome taikyti tokį standartizuotą skausmo malšinimo protokolą:

- Atlikus premedikaciją (benzodiazepinu ± opioidu): spinalinė anestezija operacijos metu 0,5 % izobariniu bupivakainu (168 cm ūgiui – 15 mg, pridedant po 1,5 mg/15 cm), kad būtų pasiekta sensorinė blokada iki krūtininio VIII segmento lygmens.

- Šlaunies perineurinis kateteris: priešoperacinis boliusas 20 ml 0,5 % bupivakaino (100 mg); pooperacinėje palatoje: tęstinė perineurinė 0,1 % bupivakaino infuzija paciento kontroliuojamos analgezijos režimu (pradedama, kai motorinė blokada sumažėja iki 2 balų pagal *Bromage* skalę, ir tęsiama 48 val.).

- PKA režimas: bazinė infuzija 5 ml/val. + paciento kontroliuojami boliusai 5 ml/30 min.

Pooperacinio skausmo malšinimui pagerinti, jeigu nėra galimybės pacientui palikti perineurinio kateterio ir neturima PKA skirtų infuzinių priemonių, atliekant tokias chirurgines intervencijas alternatyva galėtų būti:

- SA + VŠNB bupivakaino (100 mg) + neostigmino (0,5 mg i/s).

Siūlome pradėti kurti specialią priežiūros sistemą ir esant galimybei tęsti pooperacinį infuzinį paciento kontroliuojamą skausmo malšinimą jo paties namuose.