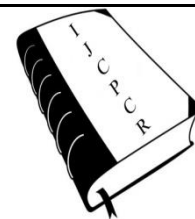




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COMPARISON OF INTRA ARTICULAR LOW DOSE SUFENTANIL, ROPIVACAINE, AND COMBINED SUFENTANIL AND ROPIVACAINE ON POST-OPERATIVE ANALGESIA OF KNEE SURGERY

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ABSTRACT

The impact of intra-articular injection of local anaesthetic (ropivacaine), opioid (sufentanil) and the combination of these two (ropivacaine combined with sufentanil) after single-bundle anterior cruciate ligament repair has been compared to the effect of combination local anaesthetic and opioid in post-operative analgesia. In a prospective randomized double-blind design, 120 patients undergoing isolated anterior cruciate ligament reconstruction under epidural analgesia were assigned randomly to 4 groups; group A (n = 30) received 30 mL of 0.9% saline as control group; group B (n = 30) received 10 mg of ropivacaine and 2 µg of sufentanil as control group. Group C (n = 30) obtained 10 mg of 0.9 percent saline in 30 mL. At the end of the procedure, ropivacaine obtained 2 µg sufentanil in 30 mL 0.9 percent saline, group D (n = 20) in 30 mL 0.9 percent saline. Pain was measured with the use of a 100-mm. Visual Analog Scale (VAS) tested at 6 and 24 h post-surgery. In successful straight leg raising exercise, the pain VAS ratings, the quality of sleep and the status of supplementary analgesia drugs administered during the first 24 h were also gathered. Each of the three experiment groups had significantly lower pain scores than the control group in each aspect. Group B (sufentanil ropivacaine) had a substantially lower pain score relative to group C (ropivacaine) and group D (sufentanil) at 6 and 24 h after surgery. Sleep characteristics were substantially better in patients in group B, C or D than in group A. Significantly more group A patients received supplemental analgesia relative to group B, C or D. In group B, no patient needed supplementary analgesia to obtain intramuscular dolantin. Intra-articular opioid (sufenta-nil) injection, local anaesthetic (ropivacaine) injection, or a combination of these two types of agents can significantly reduce pain after anterior cruciate ligament reconstruction. In conjunction with intra-articular opioid injection and local anaesthetic therapy, the analgesic effect was stronger than that of sufentanil or ropivacaine alone.

Key words Sufentanil, Ropivacaine, Reconstruction of anterior cruciate ligament, Intra-articular.

INTRODUCTION

Reconstruction of the anterior cruciate ligament (ACL) is a very common arthroscopic procedure. Since the operation involves digging bone tunnels, synovectomy and implant-in fixation devices et al., both patients and surgeons are often worried about post-operative pain. If not properly treated, pain can cause different psychophysiological symptoms and disorders [1, 2]. While pain after arthroscopic ACL reconstruction is not as important as open surgery and typically does not last for a

long time, control of pain is necessary for patient satisfaction and early post-operative recovery, especially within the first 24 hours after surgery. Effective pain management does not only alleviate the pain, and also the stress response, and keeps the patient in a stable state [3, 4].

Several strategies have been used to alleviate pain after arthroscopic knee surgery, such as non-steroidal anti-

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inflammatory medications, intramuscular and intravenous opioids, epidural narcotics, etc. Such approaches are either insufficient or have side effects. Intra-articular local anaesthetics may provide immediate onset, short-lived post-operative analgesia and continued instillation of intra-articular local anaesthetics may be at risk of chondrolysis [5, 6]. Furthermore, studies have shown that local anaesthetic has chondrotoxic effect. For example, 0.5 and 0.25 percent of bupivacaine and 0.5 percent of ropivacaine were both identified to have chondrotoxic effects. Low-dose local anaesthetic use has also been recommended.

A study reported that local opioid receptors are present in peripheral inflamed tissues and low-dose intra-articular morphine injection offers efficient post-surgical analgesia accompanying knee arthroscopy. Apart from local anaesthetic, morphine will not affect the survival of cells, their metabolism or apoptosis. Many subsequent experiments have been carried out on peripheral opioid receptors, but with controversial findings [7, 8]. The influence of mixed analgesic agents has also been investigated. When used in combination, local anaesthetics and opioids function by various mechanisms and may have synergistic action to provide longer analgesia. However, whether there are really synergistic effects or only plain summation of effects has not been confirmed. The direct comparison of these two mechanisms under epidural analgesia was recorded in rare studies because it normally takes several hours until the pain emerges after epidural analgesia, and at that point, the effect of local analgesia [9]. Several variables are thought to affect the intra-articular analgesia effect, such as different forms of anaesthesia, different types of procedure, degree of pain and tourniquet application. In this study, a prospective, double-blinded, randomized and controlled study was conducted to compare the clinical effectiveness and safety of intra-articular analgesic injection of low-dose sufentanil, ropivacaine and sufentanil in conjunction with ropivacaine following independent single-bundle ACL reconstruction under similar epidural anaesthesia procedure techniques [10, 11].

MATERIALS AND METHODS:

From July 2011 to February 2012, the study was a prospective, randomized, double-blind study performed in one hospital. The research was accepted by the Ethics Committee of the Institute and written informed consent was taken from patients. Ninety-two chronic patients with ruptured ACL were tested for eligibility. If they had a history of allergy to the study drug, or a history of significant systemic disease, patients were disqualified. Also disqualified were patients who were younger than 16 years of age or older than 65 years of age, and those whose surgery was not done under epidural anaesthesia and those with concomitant injury. All the patients were clarified by the linear visual analogue scale (VAS) and those who didn't even understand were not included in the study. The

exclusion of 15 patients resulted in the reconstruction of 120 adult patients undergoing arthroscopic isolated autograft single-bundle anterior cruciate ligament under epidural anaesthesia. These 120 patients were all from class I or II of the American Society of Anaesthesiologists and were randomized for the study. Randomization was performed with tools for computer based randomization. The same surgeon who conducted the procedure administered the study drug and was blinded to the drug. Patients were anesthetized with the traditional technique of epidural anaesthetic. Using 0.75 percent bupivacaine 2 ml with 10 percent glucose 1 ml, lumbar epidural anaesthesia at L2-3 level. The mean analgesia dermatomal amount was T10. During the surgery, epidural and parenteral opioids were prevented. During the surgery, a thigh tourniquet was placed at a pressure of 100 mm Hg above the patients' systolic blood pressure. In all the cases, one senior surgeon applied identical single-bundle ACL procedures.

First, arthroscopic testing was performed to assess the isolated ACL rupture. As an ACL graft, the semitendinosus and gracilis tendons were harvested. The femoral and tibial tunnels were carried out and ACL graft was inserted and fixed through the tunnels.

Patients were randomly assigned to four groups, group A (n = 30) received 30 mL of 0.9% saline as control group only, group B (n = 30) received 10 mg of ropivacaine and 2 µg of sufentanil in 30 mL of 0.9% saline, group C (n = 30) received 10 mg of ropivacaine in 30 mL of 0.9% saline, group D (n = 30) received 2 µg of sufentanil in 30 mL of 0.9% saline. The drug was injected intra-articular in each group at the end of the surgery and The tourniquet was released 10 minutes after the injection and at the end of the surgery. The fluid in the joint was dissolved by vacuum suction before the injection so that it would not reduce the concentration of the medication. Both patients were sent back to the ward after surgery and were assessed for a VAS pain score at 6 and 24 h post-surgery;

The hypothesis of this research is that combined sufentanil and ropivacaine can have a stronger analgesic effect than sufentanil or ropivacaine alone by intra-articular injection. An additional possibility is that there might be an association that is not only attributable to clear summation of these two kinds of analgesic agents. Independent investigators who have been blinded to group allocation have compiled all clinical data.

A 100-mm linear VAS ranging from 0, indicating no pain, to 100, representing the worst pain, was used to measure pain. In order to measure the quality of sleep, the five-point Likert scale was used: 5 suggesting failure to sleep, 4 indicating disturbed sleep, 3 indicating fair sleep, 2 indicating good sleep, and 1 indicating excellent sleep. Postoperative supplementary analgesia included 50 mg of intramuscular (IM) dolantin and oral somidon, which were provided by physicians who were not interested in the study on the basis of patient demand and status. Among the 4 classes, the VAS score, Likert sleep quality scale points

and the intake of the supplementary analgesia drug were compared.

STATISTICAL ANALYSIS:

Using the SPSS statistical analysis, statistics were performed (version 13.0, SPSS Inc.). Descriptive statistics on continuous variables have been carried out. Mean differences were rendered by study of variance (ANOVA) and an independent evaluation of samples t. Those frequencies were carried out in the 92 test. The Meaning A level of P\0.05 was set. The sample size was determined based of the hypothesis that the treatment groups were not different. The final

power of this analysis was greater than 0.80. For alpha error = 0.05, with 30 subjects in each sample.

RESULTS:

The demographics of patients (age, sex, height and weight) and length of the procedure were identical in 4 groups which are shown in Table 1 with no major variations. In all the classes, the influence of epidural analgesia dissipated completely within 4 h post-operatively. This was checked in order to detect the feeling at the level of the knee joint using the pin-prick process.

Table 1: Demographic details of patients and duration of surgery (mean ± SD)

Group	N (min)	Gender (M/F)	Age (years)	Height (cm)	Weight (Kg)	Duration of surgery
A	30	27/3	30.5± 7.5	174.2 ± 9.2	75.5 ± 17.6	57.4 ± 14.9
B	30	20/10	28.9±8.9	171.3 ± 7.6	73.9 ± 11.1	55.8 ± 14.1
C	30	28/2	29.5 ± 9.5	171.8 ± 7.7	72.0 ± 3.6	57.9 ± 16.3
D	30	25/5	28.8 ± 9.2	171.5 ± 5.5	71.3 ± 12.9	54.9 ± 15.9

A-control group, B- ropivacaine + sufentanil group, C- ropivacaine group, D-sufentanil group
 In all the categories, no association was observed between the pain score and the demographics of the patient. With respect to the quality of sleep in Table 2, groups B, C and D showed significantly better quality of sleep than group A (P \ 0.05) with respect to the 5-point Likert scale. No relevant side effects were found in the study patients; none of the patients had seizures, abdominal pain, pruritus, or any other drug-related adverse effects.

Table 2: Sleep status in the patients

	1	2	3	4	5
A	4*	1	2	5	8*
B	10	3	0	4	5
C	3	3	3	2	3

A = control group, B = ropivacaine + sufentanil group, C = ropivacaine group, D = sufentanil group
 * Represents the statistical difference between group A and group B, C, D, P \ 0.05.

DISCUSSION

The most significant finding of the present study was that after ACL reconstruction, combined intra-articular opioid injection and local anaesthetic produced a better analgesic effect than using sufentanil or ropivacaine alone, and synergistic interaction between opioid and local anaesthetic could exist. Although the effects of the intra-articular injection combination of opioid and local anaesthetic have been studied and considered to be better than local anaesthetic alone, comparison of the effects of opioid alone and in combination with local anaesthetic has rarely been studied. In this research, the impact of intra-articular injection of local anaesthetic drugs (ropivacaine), opioid drugs (sufen-tanil) and a mixture of the two drugs (ropivacaine combined) was examined. After the single-bundle ACL reconstruction, sufentanil) was compared. The research aimed to establish if the analgesic effect of the combination of sufentanil and ropi-vacaine was greater than that of the combination of

sufentanil or ropivacaine alone. Since these two analgesic agents work by separate mechanisms, it has also been examined whether the overall effect was only a clear description of the effects or synergistic interaction between the two mechanisms. Patients with isolated ACL reconstruction were selected as research artifacts in this study and similar techniques were applied. One surgeon performed all the procedures. Similar demographic period and surgery were obtained. We found that the pain following ACL reconstruction was very important, especially after the resolution of epidural anaesthesia, from the comparison of the control group and the experimental mental groups. The mean VAS score of the control group at 6 h post-operation could exceed 60 out of 100. Intra-articular injection of ropivacaine alone, sufentanil alone or in combination with these two agents could substantially reduce pain at 6 h post-surgery. At 24 h after surgery, the effect of ropivacaine vanished, while the other two groups still had a strong anal-gesia effect.

It is fair that even though ropi- vacaine is a long-lasting agent, the local anaesthetic could not sustain a long analgesia effect. It is also fair that an intra-articular opioid, consistent with previous studies, may be effective up to 24 hours after surgery.

This research has many limitations. First, there may be too few time points for the observation, and more observation points may more clearly illustrate the pattern of the VAS score. Secondly, the straight leg raising exercise was not a very accurate method, although the VAS score was tested in the recovery process. Third, the indication of flexible-mental intake was focused largely on the demand of the patient and the lack of objective assessment that could impair objectivity [12]. In addition, the experimental object's VAS score was still not at a low stage, so a higher opioid dose could be administered to achieve better control of pain. Finally, the research indicates that there might be a synergistic relationship between opioid and

local anaesthetic, however laboratory experiments without direct proof

It must be done in order to prove the mechanism. The clinical significance of this study is that low-dose opioid intra-articular injection is an effective, secure and easy analgesic tool to decrease post-operative pain, and if combined with local anaesthetic, the analgesic effect could be enhanced.

CONCLUSION

Intra-articular opioid injection (sufentanil), local anaesthetic injection (ropivacaine) or a mixture of these two forms of opioid injection. Following the repair of the anterior cruciate ligament, medications could greatly alleviate pain and could boost the quality of sleep and the potential for recovery. The anaesthetic effect of the combination of opioid and local anaesthetic was greater than that of sufentanil or ropivacaine alone.

REFERENCE

1. Brodner, G., Mertes, N., Van Aken, H., Möllhoff, T., Zahl, M., Wirtz, S., Marcus, M. A. E., & Buerkle, H. (2000). What concentration of sufentanil should be combined with ropivacaine 0.2% wt/vol for postoperative patient-controlled epidural analgesia? *Anesthesia and Analgesia*. <https://doi.org/10.1097/0000539-200003000-00027>.
2. Lilot, M., Meuret, P., Bouvet, L., Caruso, L., Dabouz, R., Deléat-Besson, R., Rousselet, B., Thouverez, B., Zadam, A., Allaouchiche, B., & Boselli, E. (2013). Hypobaric spinal anesthesia with ropivacaine plus sufentanil for traumatic femoral neck surgery in the elderly: A dose-response study. *Anesthesia and Analgesia*. <https://doi.org/10.1213/ANE.0b013e31828f29f8>.
3. Van De Velde, M., Dreelinck, R., Dubois, J., Kumar, A., Deprest, J., Lewi, L., & Vandermeersch, E. (2007). Determination of the full dose-response relation of intrathecal bupivacaine, levobupivacaine, and ropivacaine, combined with sufentanil, for labor analgesia. *Anesthesiology*. <https://doi.org/10.1097/0000542-200701000-00024>.
4. Wong, C. A. (2009). Advances in labor analgesia. In *International Journal of Women's Health*. <https://doi.org/10.2147/ijwh.s4553>.
5. Roelants, F., Rizzo, M., & Lavand'homme, P. (2003). The effect of epidural neostigmine combined with ropivacaine and sufentanil on neuraxial analgesia during labor. *Anesthesia and Analgesia*. <https://doi.org/10.1213/01.ANE.0000050480.73209.9C>.
6. De Cosmo, G., Congedo, E., Lai, C., Sgreccia, M., Amato, A., Beccia, G., & Aceto, P. (2008). Ropivacaine vs. levobupivacaine combined with sufentanil for epidural analgesia after lung surgery. *European Journal of Anaesthesiology*. <https://doi.org/10.1017/S0265021508004638>.
7. Dango, S., Harris, S., Offner, K., Hennings, E., Priebe, H. J., Buerkle, H., Passlick, B., & Loop, T. (2013). Combined paravertebral and intrathecal vs thoracic epidural analgesia for post-thoracotomy pain relief. *British Journal of Anaesthesia*. <https://doi.org/10.1093/bja/aes394>.
8. Levin, A., Datta, S., & Camann, W. R. (1998). Intrathecal ropivacaine for labor analgesia: A comparison with bupivacaine. *Anesthesia and Analgesia*. <https://doi.org/10.1213/0000539-199809000-00025>.
9. Qian, X. W., Chen, X. Z., & Li, D. B. (2008). Low-dose ropivacaine-sufentanil spinal anaesthesia for caesarean delivery: A randomised trial. *International Journal of Obstetric Anesthesia*. <https://doi.org/10.1016/j.ijoa.2008.01.018>.
10. Ortner, C. M., Posch, M., Roessler, B., Faybik, P., RÜtzler, K., Grabovica, J., Kimberger, O., & Gustorff, B. (2010). On the ropivacaine-reducing effect of low-dose sufentanil in intrathecal labor analgesia. *Acta Anaesthesiologica Scandinavica*. <https://doi.org/10.1111/j.1399-6576.2010.02254.x>.
11. Bremerich, D. H., Waibel, H. J., Mierdl, S., Meininger, D., Byhahn, C., Zwissler, B. C., & Ackermann, H. H. (2005). Comparison of continuous background infusion plus demand dose and demand-only parturient-controlled epidural analgesia (PCEA) using ropivacaine combined with sufentanil for labor and delivery. *International Journal of Obstetric Anesthesia*. <https://doi.org/10.1016/j.ijoa.2004.12.005>.
12. De Cosmo, G., Primieri, P., Adducci, E., Fiorenti, M., & Beccia, G. (2004). Epidural analgesia in abdominal surgery: 0.2% ropivacaine with sufentanil. *Minerva Anestesiologica*.