

Original Article

Intra-Articular Sufentanil Compared to Morphine for Pain Relief After Arthroscopic Knee Surgery

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Abstract

Background: Prevention of postoperative pain by injecting opioid into the knee joint is believed to support the hypothesis of peripheral opioid receptor activation in inflammation. Main outcomes were reduction of pain intensity and need for supplementary analgesics. The aim of the present study was to evaluate the analgesic effects of intra-articular sufentanil in comparison with morphine, after arthroscopic procedures of knee joint.

Methods: In this prospective, double-blind study, 45 patients were randomized in three equal number groups to receive either sufentanil 5 µg (group s), morphine 3 mg (group M) or normal saline 20 cc as placebo (group p), intra-articularly at the end of arthroscopic knee surgery, under general anesthesia, which was same in all three groups. Pain levels at rest were measured by Visual Analog Scale (VAS) at intervals of 1,2,4,8,12,14 hours and during movement of knee at discharge time .

Results: Significant difference between the groups ($p < 0.001$) were found. Pain scores were statistically lower in the S and M groups in comparison with the P group, but intra-articular sufentanil was more effective than morphine.

Conclusion: Intra-articular injection of morphine and sufentanil both reduce the post arthroscopic knee procedure's pain and need for supplementary analgesics, but sufentanil, 5 µg is more effective than morphine (3 mg).

Keywords: Postoperative analgesia, intra-articular opioids, sufentanil, Morphine, Knee arthroscopy.

Pain control after surgery has always been an important issue and With the relatively recent advent of outpatient surgery, its importance has been magnified. Several clinical studies have demonstrated that failure to control pain caused unnecessary, suffering, delayed recovery, prolonged hospitalization and increased medical bills¹.

Arthroscopic procedures of the knee are commonly performed on an outpatient basis. In many studies the intra-articular injections of different agents, including opioids and nonopioid analgesics, have been evaluated for relief of post operative pain such as morphine²⁻⁶, ketoralac⁷, clonidine⁸, and bupivacaine^{2 6}.

Opioids administered intra-articularly produce conflicting data with respect to their analgesic efficacy: some reports showed intra-articular opioids

to be ineffective^{9, 10}, other reported a significant positive effect on postoperative analgesia^{11,12}.

The aim of the present study is to evaluate the analgesic effects of intra-articular sufentanil compared to morphine for pain relief after arthroscopic knee surgery. The choice for sufentanil was made on the basis of its greater lipophilic characteristics, which should provide a faster onset of analgesia than morphine¹³.

Materials and Methods

We studied 45 patients from August 2002 to May 2003 in Chamran Orthopaedic Hospital, affiliated to Shiraz University of Medical Sciences, Iran.

Patients who were ASA physical status I and II and scheduled for arthroscopic knee surgery

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[diagnostic arthroscopy, debridement-shaving, meniscectomy (partial, subtotal, total), and biopsy] enrolled in this study (table 1). Patients younger than 17 years and older than 70 years, with a significant cardiac, respiratory, metabolic, psychiatric disease or substance abuse, known drug allergy or arthroscopic procedure lasting more than 90 minutes, and patients who need for post operative intra articular drainage were not included in this study. The procedure was carefully explained to the patients and a written consent was obtained. All patients were admitted directly from the outpatient clinic and were not premedicated.

The study was a double blind randomized clinical trial. Patients were allocated randomly to one of three groups (15 patients in each group):

Group S=Sufentanil 5 μ g (Janssen Pharmaceutica) in 20 ml of normal saline.

Group M= Morphine 3 mg (Daru Pakhash Iran) in 20 ml of normal saline.

Group P= normal saline 20 ml as Placebo.

The test solutions were prepared in three sterile syringes and coded by the anesthesia nurse. The content of these syringes were unknown to anaesthesiologist and the surgeon who performed the study. The codes were not revealed until completion of the study. at the end of arthroscopic procedure the test drug was injected into the knee joint.

During anaesthesia, standard monitoring including continuous electrocardiogram and non-invasive blood pressure were assessed every 5 minutes. Continuous capnography and pulse oximetry was used. Anaesthesia was induced with Midazolam (0.05 mg/kg) IV, Morphine 0.1 mg/kg, and Thiopentone 5 mg/kg. Tracheal intubation was facilitated with 0.8 mg/kg atracurium IV. Anaesthesia was maintained with isoflurane (end tidal 1.3%), 50% O₂ and nitrous oxide.

At the end of surgical procedure one of test drug solutions (sufentanil 5 μ g, morphine 3 mg or normal saline 20 ml) was injected intra-articularly by the surgeon.

Pain assesment and data collection

After a stay of 3 hours in recovery room, the patients were transfered and admitted in ward. Patients were instructed in the use of Visual Analogue Scale (VAS with 0=no pain, 100 mm=

unbearable pain) before operation. Pain intensity was recorded at 1, 2, 4, 8, 12 and 24 hours during rest. Pain during movement was recorded only at 24 h after the end of surgery.

Any patient complaining of slight or moderate pain were given 1-2 acetaminophen codeine tablets orally while patients complaining of severe to unbearable pain received 25-50 mg pethedine IV. Total consumption of orally or intravenously analgesics was recorded for each patient.

The data are presented as mean \pm SD. Quantitative data were compared between groups using Kruskal Wallis H test. Statistical significance was determined at the level of $p < 0.05$.

Results

A total of 45 patients enrolled. The base line characteristics were compared among the three groups and no statistical differences were found when comparing age, sex, and operation time (table1). The operative procedures consisted of meniscectomy (partial subtotal, total), diagnostic arthroscopy, loose body removal, cartilage resection, shaving and biopsy. All of the 45 arthroscopies were performed by the same experienced surgeon. All procedures were under general anesthesia and therefore the 0 to 90 minutes interval was used as a baseline period. Demographic data and duration of anesthesia are summarized in table 1.

The pain intensity scores measured by the Visual Analog Scale were significantly different between three groups ($p < 0.001$) at interval of 1, 2, 4, 8, 12, 24 hours (figure 1).

Mean VAS scores in groups S and M were significantly lower than group P at 1 and 24 h post operatively. Pain intensity scores declined for all of groups after 8 h but this decrease in pain intensity was more significant in group S and M compared with group P. In group S only one patient received pethedine 25 mg IV, in group M three patients received pethedine 25 mg IV and two patients (13.3%) received acetaminophen codeine 2 tablets orally. In group P six patients received pethedine 25 mg IV and five patients received acetaminophen codeine 2 tablets orally. Analgesic consumption was represented as total dose in 24 h. In addition we also checked the intensity of pain during knee motion at the time of discharge (24 hours post

operatively) and found no patient complained of pain in group S and M, but all patients in group P had slight pain during motion.

Discussion

Arthroscopic surgery has been progressed rapidly in past ten years. The knee is a joint in which arthroscopy has the greatest intra-articular surgical application. There is rich innervation to articular capsule, tendons, ligaments, synovium and periosteum via a mixture of free nerve endings and receptors. These sensory nerves respond to mechanical stimuli such as stretching of the joint capsule as well as intra-articular surgical instrumental intervention⁷. Many fibers, for example, are non-responsive under normal conditions but react after inflammation, therefore, there is potential for acute injury or inflammation to sensitize nerves such that they respond even when the original stimuli is removed¹⁴. Hence, just like any other surgical procedure, the arthroscopic intervention of the knee joint can cause considerable postoperative pain, that limits postoperative ambulation combined with a stress induced hypercoagulable state may contribute to an increased incidence of deep vein thrombosis^{15, 16}. This postoperative knee joint pain can be controlled successfully by intra-articular injection of opioids^{11, 12}. In fact, peripherally administered opioids produce significant analgesia due to binding to peripheral receptors. Experimental studies of inflamed tissues have demonstrated pronounced antinociceptive effect of locally applied opioids¹⁷.

The receptors involved in the peripheral opioid effect are mu, kappa, and delta. Animal studies revealed the existence of these peripheral opioid binding sites, which appears to become specially active in the presence of inflammation^{18, 19}. These first observation have been confirmed in human clinical trials^{19, 20}. The action of the peripheral opioids (intra-articular injection) are characterized

by two properties: first, the effects are naloxane-reversible emphasizing that the drug action are mediated by an opioid receptor, and is not local anesthetic effect²⁰, secondly, the peripheral actions are most clearly manifested in inflamed state, when a well defined hyperalgesia is present^{21, 22}.

In this study we found that sufentanil and morphine injected intra-articularly at the end of knee arthroscopic procedures resulted in excellent analgesia postoperatively and the day after surgery which was evidenced by significantly lower pain scores (figure 1) and decreased supplementary requirement for analgesis in group S and M in comparison to group P (placebo). It is further noted that the analgesic effect of intra-articular sufentanil 5 µg is more pronounced and starts earlier than intra-articular morphine 3 mg for the first two hours postoperatively (figure 1). This earlier appearance of profound analgesic effect of sufentanil can be attributed to its high lipophilicity. The results of our study are similar to the study performed by Vranken et al¹³. In our study, we detected a fast onset of analgesia with the effect lasting until the morning after surgery. In contrast, the analgesic effect after intra-articular administration of local anesthetic, particularly bupivacaine, last for a shorter period⁵. The combination of morphine and bupivacaine administered intra-articularly, result in controversial analgesic effect^{22, 23}. Intra-articular administration of opioids such as fentanyl or meperidine did not result in a significant analgesic effect as compared to intra-articular morphine²¹.

It can be concluded that intra-articular sufentanil is a simple, effective, safe and well-tolerated analgesic technique for outpatients undergoing knee arthroscopic procedures.

Table 1. Demographic data (Mean ± SD) and type of surgery.

	Group S (N=15)	Group M (N=15)	Group P (N=15)
Male/Female	13/2	12/3	14/1
Age (year)	31 ± 11	30 ± 12	26 ± 10
Duration of anesthesia (min)	47 ± 14	40 ± 12	46 ± 13
Meniscectomy	7	4	6
Diagnostic arthroscopy	4	6	5
Cartilage resection, shaving	4	3	3
Biopsy	0	1	0
Removal of loose body	0	1	1

S=Sufentanil, M=Morphine, P= Normal Saline

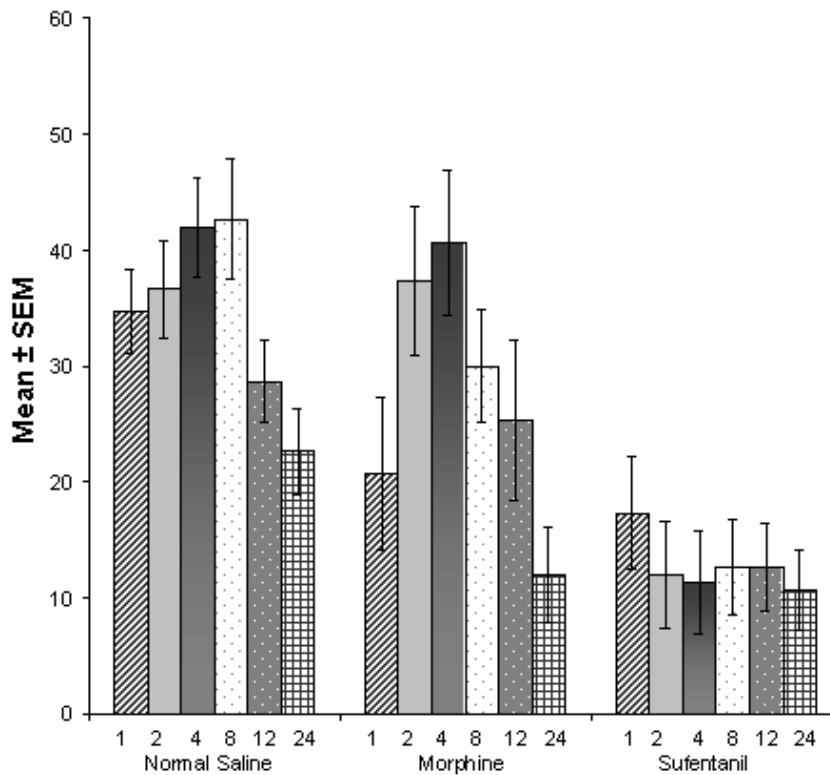


Figure 1. Average visual analog scale scores for Sufentanil, Morphine, Normal Saline groups, at 1, 2, 4, 8, 12 and 24 hour periods. The 24-hour visual analog scales score was significantly lower in the Sufentanil group VAS1: P=0.013, VAS8: P=0.001, VAS2: P=0.003, VAS12: =0.031, VAS4: P=0.000, VAS24: =0.032

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