Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL4, ISSUE 04, 2013

Original research article

An evaluative study of morphine and intraarticular fentanyl for pain relief after arthroscopic surgeries of knee

Dr. Kushal Raj Kataria
Assistant Professor, Department of Anaesthesia, Major S.D. Singh Medical College & Hospital, Baikunthpuri Bewar Road Fatehgarh, Farrukhabad, Uttar Pradesh, India

Corresponding Author:
Dr. Kushal Raj Kataria

Abstract

Background: Several approaches for adequate pain control in patients undergoing knee surgeries have been investigated, from the systemic administration of non-hormonal anti-inflammatories (NSAIDs) to systemic and spinal opioids, and patient-controlled analgesia, exposing the patient to the inherent risks of invasive procedures and adverse effects of systemic analgesics.
Aims and Objectives: To compare the analgesic effect of intra-articular administration of morphine, fentanyl and placebo following arthroscopic surgery of knee.
Material and Methods: Our study was conducted in the Department of Anaesthesia, Major S.D. Singh Medical College & Hospital, Fatehgarh, Farrukhabad, UP, India. A retrospective, randomised, placebo controlled, double blind comparative study conducted in 63 patients of either sex, who underwent arthroscopic surgery of knee, between the age group of 18 and 65 years and of ASA class II physical status and I were included in the study. Patients were randomly assigned equally to one of the 3 groups of 21 each by a sealed envelope method. The groups were Group A-Patients receiving IA Fentanyl 50mcg in 20 ml normal saline. Group B-Patients receiving IA Morphine 3mg in 20 ml normal saline. Group C-Patients receiving IA 20 ml normal saline as placebo. Parameters monitored were degree of analgesia along with hemodynamic parameters and side effects. Data were analysed using student's t-test for continuous variables and Chi-Square test was used to find out the association between categorical variables.
Results and Observations: Pain scores at one, two, four and eight hours were greater at all times in placebo group. Pain scores for fentanyl and morphine were similar at one hour, but thereafter less (p<0.001) for IA-Fentanyl group.
Conclusion: However, Intra-articular fentanyl provided effective post-operative pain relief and reduced rescue analgesic requirement in the first 8 hours following arthroscopic knee procedures. It also revealed that fentanyl is better intra-articular analgesics than morphine. While intra-articular morphine was found to provide good pain relief during early post-operative period, it lacked analgesic efficacy in the later half of our observation period. Intra-articular 50-mcg fentanyl provided better post-operative analgesia than 3mg morphine.
Keywords: Knee surgeries, post-operative analgesia, morphine, intraarticular, analgesia, opioids, arthroscopy, fentanyl, arthroscopic surgeries, knee injuries

Introduction

Several approaches for adequate pain control in patients undergoing knee surgeries have been investigated, from the systemic administration of non-hormonal anti-inflammatories (NSAIDs) to systemic and spinal opioids, and patient-controlled analgesia, exposing the patient to the inherent risks of invasive procedures and adverse effects of systemic analgesics [1, 2, 3]. At the end of the surgery, local hemostasia was performed followed by placement of a suction drain through a different opening than the surgical wound, and synthesis of the wound planes. Before complete skin closure, the solution specified for the case was injected in the intra-articular space. In all patients, the drain was opened after 15 minutes. Postoperative pain is the acute inflammatory pain that begins with the trauma of surgery and ends with the healing of the tissue. This pain has deleterious effects on organ systems and may lead to pathophysiological changes in the pulmonary/cardiovascular system. Pain is a common human experience, a symptom frequently encountered in clinical practice that is usually associated with actual

ISSN:0975 -3583,0976-2833 VOL4, ISSUE 04, 2013

or impending tissue damage. “Failure to relieve pain is morally and ethically unacceptable.” Adequate pain relief could be considered a basic human right. Pain is not a straightforward sensory “perception”. It is an “experience” as the physiological sensation is inseparable from the associated emotional distress. Pain after orthopaedic surgery depends on thesite and extent of surgery. Arthroscopic procedures are routinely performed on outpatient basis and have spared patients large incisions and decreased morbidity compared with open incisions but has not eliminated pain. At present, several techniques are available to treat pain following arthroscopic surgeries; these include the use of opioids (either providing peripherally or centrally mediated analgesia), local anaesthetics, non-steroidal anti-inflammatory drugs, corticosteroids, clonidine and cryotherapy. The evidence of synovial opioid receptors supports the use of intra-articular (IA) opioids to achieve a peripheral opiate receptor-mediated analgesia. A number of such studies have demonstrated effective and prolonged analgesia from small intraarticnlar (LA) doses of morphine [4-11]. In contrast, other investigators have failed to demonstrate an analgesic effect of IA morphine [12-18]. Morphine is the most frequently used opioid analgesic. Better postoperative analgesia was reported with intra- articular fentanyl when compared to morphine. Various direct and indirect measures had evaluated the effects of intra-articular application of opioids on postoperative pain relief. Here we sought to compare the analgesic efficacy of intra-articular administration of morphine and fentanyl following arthroscopic surgery of knee.

Material and Methods

The study designed was a prospective, randomised, placebo controlled, double blind comparative study was conducted in the Department of Anaesthesia, Major S. D. Singh Medical College & Hospital, Fatehgarh, Farrukhabad, UP, India. 63 patients of either sex, who underwent arthroscopic surgery of knee; between the age group of 18 and 65 years and of ASA class, I and II physical status were included in the study. Patients of ASA III and IV physical status and patients on chronic medications were excluded from the study. After approval from the hospital ethics committee, 63 patients were randomly assigned equally to one of the three groups of 21 each by a sealed envelope method.

Group A: Patients receiving IA Fentanyl 50mcg in 20 ml normal saline.
Group B: Patients receiving IA Morphine 3mg in 20 ml normal saline.
Group C: Patients receiving IA 20 ml normal saline as placebo.

The randomized assignment was sealed in an envelope and handed over to a senior anaesthesia technician, who would verify the group on the day of surgery and prepared the bolus solution of drug with 20ml 0.9% Normal saline under aseptic precautions. This was injected intra-articularly at the end of the arthroscopic surgery by the operating surgeon. The patient, the operating surgeon, the anaesthesiologist conducting the case and the nursing staff who assessed the pain and delivered rescue medication were blinded regarding the drug used.

Anaesthetic technique and performance

All patients were premedicated with H-2 blocker (Ranitidine 150 mg) and benzodiazepine (Alprazolam 0.5mg). Postoperative pain intensity was assessed by visual analogue scale which is a “0 to 10” cm Scale, with score 0 as “No Pain”, upto 3 mild bearable pain, “3 to 5” as “Moderate Pain”, greater than “5” as “Severe Pain” and “10” as “Worst Pain”. All patients were explained about VAS before surgery and written informed consent was obtained. After shifting the patient to operation theatre, an 18G intravenous cannula was secured and connected to intravenous fluid. Pre-induction monitoring included pulse-oximeter, non-invasive blood pressure monitoring and continuous electrocardiography. Injection midazolam 1mg and injection glycopyrrolate 0.01mg/kg was administered intravenously. After pre-oxygenation for 3 minutes with 100% oxygen, anaesthesia was induced with injection fentanyl 2mcg/kg and injection propofol 2mg/kg intravenously. After loss of consciousness and eyelash reflex, appropriate size laryngeal mask airway (LMA) was placed. After confirming proper placement of LMA, patient’s ventilation was assisted or left breathing spontaneously if found satisfactory with continuous capnography monitoring. Oxygen, nitrous-oxide combination was administered in 1:2 ratios with isoflurane 0.6% to 2% concentration throughout the procedure. No further analgesics or sedative medications were given for the duration of the procedure. At the end of the surgical procedure, before tourniquet was released the surgeon injected study drug intra-articularly and patient was extubated.

Pain assessment and data collection

Post-operative pain intensity scores and hemodynamic data (heart rate and blood pressure) were recorded 15 min after extubation and noted as the score at 0 hour, further pain scores were recorded at 1, 2, 4 and 8 hours by the bedside nursing staff who was explained about visual analogue scale and rescue analgesia. Any VAS>3 were given injection tramadol 50mg intravenously as rescue analgesia. The staff recorded the time of first rescue analgesia and total dose of rescue analgesia during 8 hours. Side effects like nausea, vomiting, pruritis, urinary retention and respiratory depression were specifically looked for during the observation period.

ISSN:0975 -3583,0976-2833 VOL4, ISSUE 04, 2013

Methodology

The study sample size was determined to be at least 21 patients in each of the 3 groups studied, which would provide 80% power for detecting a significant difference in analgesic effect. The student t – test was used both to assess homogeneity and to compare the main results and to find difference between the groups for continuous variables. Data were analyzed using SPSS 11.0 software. A descriptive statistical tool such as mean was used to represent the continuous data. Differences within the groups were analyzed using analysis of variance and Post Hoc test was used to test the difference between individual groups. Chi-Square test was used to find out the association between categorical variables. In all cases, the level of statistical significance (P value) was less than 0.05.

Observations and Results

During the period of April 2011 and March 2012, 63 patients in age group of 18-65 years were studied. Distribution of patients in each of the three groups was similar with respect to demographics, diagnosis and operative procedures.

Age and Sex distribution

The mean age in the study population was 35 years. The age comparison was done by student t test, which demonstrated no significant difference in its distribution among 3 groups.

Table 1: Mean Age+/SD distribution in three groups

	A (Fentanyl)	B(Morphine)	C(Placebo)
Age(Years)	33.3+/-10.5	36.8+-12.0	34.0+/-10.4

Table 2: Sex distribution in three groups

Sex	A (Fentanyl)	B(Morphine)	C(Placebo)
Female	3	5	3
Male	18	16	18

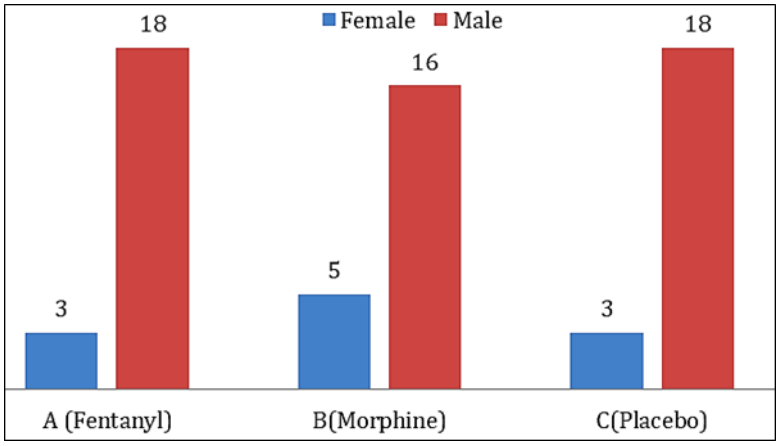

Fig 1: Sex Distribution in three groups

52 male and 11 female patients were enrolled in this study as given in (Table 2) and (Figure 1). The group comparison was done by student t test, which demonstrated no significant difference in its distribution among 3 groups with regard to distribution of sex and also there was no difference between groups in terms of ASA (p-0.951). The group comparison was done by student t test, which demonstrated no significant difference in its distribution among 3 groups with regard ASA physical status.

Table 3: Surgeries in three groups

Surgery	A(Fentanyl)	B(Morphine)	C(Placebo)
ACL Reconstruction	12	11	14
Menisectomy	4	3	5
Partial Menisectomy	0	2	0
Synovectomy	5	5	2

There is no difference between groups in terms of surgeries (p-0.846).

Comparison of analgesia: Visual analogue scores assessed at 0, 1, 2, 4, and 8 hours were compared with chi-square test for statistical difference among the groups. Visual Analogue Score with respect to groups at 0 hour;

ISSN:0975 -3583,0976-2833 VOL4, ISSUE 04, 2013

Table 4: Vas at 0 hour

VAS	A(Fentanyl)	B(Morphine)	C(Placebo)
0	21	21	0
3	0	0	2
4	0	0	10
5	0	0	6
6	0	0	3

Table 5: Comparison of analgesia at 0 hour

	A(Fentanyl)	B(Morphine)	C(Placebo)
VAS<3	21	21	0
VAS>3	0	0	21

VAS<3-Inadequate analgesia, VAS>3-inadequate analgesia.

Mean visual analogue scores analysed during the 0 hour were lower (VAS-0) in A and B groups, when compared to group (C) (Table 5). There was statistically significant difference among 3 groups with respect to VAS at 0 hour (p-0.000). Pain intensity scores were higher in-group (C) when compared with other 2 groups. However, there was no statistical difference among A and B groups (p0.944). All Placebo group patients received rescue analgesia during 0 hour (VAS > 3) which indicated inadequate analgesia (Table 6), while none in other 2 groups. Visual Analogue Score with respect to groups at 1.

Table 6: Vas at 1 hour

VAS	A(Fentanyl)	B(Morphine)	C(Placebo)
0	21	21	0
3	0	0	0
5	0	0	5
6	0	0	11
7	0	0	5

Table 7: Comparison of analgesia at 1 hour

	A(Fentanyl)	B(Morphine)	C(Placebo)
VAS<3	21	21	0
VAS>3	0	0	21

Visual analogue scores compared at 1 hour (Table 6, Table 7) had high scores in placebo in comparison with A and B groups. There was significant difference (p-0.000) between placebo and the drug groups. However, there was no significant difference (p-0.944) between the two drug groups. Visual Analogue Score with respect to groups at 2 hours;

Table 8: Vas at 2 hours

VAS	A(Fentanyl)	B(Morphine)	C(Placebo)
0	21	9	0
1	0	7	0
2	0	5	0
3	0	0	0
4	0	0	1
5	0	0	5
6	0	0	11
7	0	0	4

Table 9: Comparison of analgesia at 2 hours

	A(Fentanyl)	B(Morphine)	C(Placebo)
VAS<3	21	21	0
VAS>3	0	0	21

At 2nd hour VAS score (Table 8) showed significant difference between placebo and other two groups (p0.000). Pain intensity scores was significantly different (p-0.002) between group A and B. Even though morphine had significant p values when compared to fentanyl, none of the patients received rescue analgesia (Table 9). Visual Analogue Score with respect to groups at 4 hours;

ISSN:0975 -3583,0976-2833 VOL4, ISSUE 04, 2013

Table 10: Visual analogue score at 4 hours

VAS	A(Fentanyl)	B(Morphine)	C(Placebo)
0	12	2	0
1	6	2	0
2	3	11	0
3	0	6	1
4	0	0	7
5	0	0	8
6	0	0	1
7	0	0	3
8	0	0	1

Table 11: Comparison of analgesia at 4 hours

	A(Fentanyl)	B(Morphine)	C(Placebo)
VAS<3	21	15	0
VAS>3	0	6	21

At 4 hours, there was significant difference with respect to VAS score among all 3 groups (Table 10). Placebo had high scores (p-0.000). A and B groups differed significantly as 6 patients (morphine) (p-0.04), had inadequate analgesia with VAS>3. Visual Analogue Score with respect to groups at 8 hours;

Table 12: Vas at 8 hours

VAS	A(Fentanyl)	B(Morphine)	C(Placebo)
0	11	0	0
1	1	0	0
2	8	0	0
3	1	4	0
4	0	11	3
5	0	5	9
6	0	1	7
7	0	0	2

Table 13: Comparison of analgesia at 8 hours

	A(Fentanyl)	B(Morphine)	C(Placebo)
VAS<3	20	0	0
VAS>3	1	21	0

At 8 hours, P values were significantly different among 3 groups. Placebo was significantly different (p-0.000) from A and B groups, in terms of VAS score (Table 12). However, the number of patients with inadequate analgesia (VAS>3) was same in morphine and placebo group (Table 13). VAS score in morphine group showed significant difference when compared to fentanyl. (Table 13). Heart Rate with respect to groups from 0 to 8 hour.

Table 14: Comparison of Mean +/-SD of heart rate from 0 to 8 hour

Time	A(Fentanyl)	B(Morphine)	C(Placebo)
Hour-0	70.7+/-10.6	75.15+/-7.3	80.05+/-5.9
Hour-1	69.85+/-8.9	72.25+/-4.8	86.55+/-4.6
Hour-2	71.2+/-9.0	75.5+/-4.7	88.45+/-4.2
Hour-4	71.15+/-9.1	78.75+/-5.2	83.25+/-5.0
Hour-8	74.75+/-7.6	84.6+/-5.6	84.65+/-4.0

Table 15: Comparison of Mean +/-SD of Mean Arterial Pressure (MAP) from 0 to 8 hour

Time	A(Fentanyl)	B(Morphine)	C(Placebo)
Hour-0	90.3+/-6.3	90.4+/-5.5	94.1+/-5.7
Hour-1	87.6+/-6.3	86.8+/-3.9	98.6+/-3.7
Hour-2	88.6+/-4.2	85.2+/-4.0	101.8+/-4.4
Hour-4	89.6+/-4.6	86.3+/-3.4	96.8+/-5.1
Hour-8	89.7+/-3.9	87.2+/-4.2	98.4+/-3.1

Heart rate and MAP was higher in the placebo group when compared to A and B group (Table 15) throughout observation period and was statistically significant (p-0.01). Nevertheless, there was no significant difference between the other 2 drug groups (p-0.00).
And also time first rescue analgesia in 0 to 7 hours in Fentanyl group is 0 in 8th hour it's 1,

ISSN:0975 -3583,0976-2833 VOL4, ISSUE 04, 2013

Similarly in Morphine group 0 to 3hours it's 0 in 4th, 5th 6th, 7th 8th hours respectively 6, 8, 5, 2, 0 doses of rescue analgesia.
In Placebo group in 0 hour 21, highest dose of rescue analgesia, and in remaining hours it's 0.
Therefore, Patients in Placebo group had highest dose of rescue analgesia followed by morphine group, while fentanyl group had none or least respectively. None of the patients in any of the group had any of these side effects during the observation period.

Discussion

A study suggested that tissue binding and, therefore, the efficacy of the local anesthetic, could be increased by maintaining longer the tourniquet in place after the IA injection. The author demonstrated, when evaluating the pharmacokinetics of this drug, an increase in plasma concentration with a reduction in the time between the intraarticular injection and the release of the tourniquet, possibly by increasing local blood flow, leading to greater systemic absorption of the drug. Multimodal analgesia protocol may increase analgesic activity. Severe pain can be treated with intravenous opioids and NSAIDs used as patient-controlled analgesia (PCA), epidural local anesthetics and/or opioids, techniques called peripheral nerve blocks, or different combinations of drugs. The knee is a joint in which arthroscopy has the greatest IA 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 intervention. Many nerve fibers, for example, are non-responsive under normal conditions but react after inflammation, therefore, there is a potential for acute injury or inflammation to sensitize nerves such that they respond even when the original stimuli is removed. Hence, just like any other surgical procedure, the arthroscopic intervention of the knee joint can cause considerable postoperative pain that limits ambulation and combined with a stress induced hypercoaguable state, may contribute to an increased incidence of deep vein thrombosis. Postoperative analgesia following arthroscopic knee surgery can be provided either by systemic administration of narcotic and non-narcotic analgesic drugs or IA administration of local anaesthetic drugs [19], non-narcotic analgesic drugs (ketorolac) [20] and narcotic analgesic drugs (morphine [21], pethidine and fentanyl). Intermittent systemic analgesic administration cannot keep the patient totally pain free for all times where as IA route requires specialized technique, possible only when patient undergoes surgical procedure. However, IA route provides qualitatively better analgesia without major side effects, e.g. respiratory depression. In our study we sought to evaluate the analgesic efficacy and the need for rescue analgesia with 3mg morphine and 50mcg fentanyl were compared with a placebo (20 ml 0.9% normal saline) when administered intra-articularly following arthroscopic knee surgery. We found that in immediate postoperative period at 0 and 1 hour fentanyl and morphine had good and equal analgesic effect as none of the patients required rescue analgesia. In contrast, all 21 patients in placebo group had moderate to severe pain and all required supplementary analgesics. These results were similar to inferences of Kazemi *et al*. [22], Mandal P *et al*. [23], Varrassi *et al*. [24] and Varkel *et al*. studies. Further comparing the analgesic efficacy at 2 hours postoperatively all 21 patients had no pain in fentanyl group indicating good analgesic effect. Even though morphine provided analgesia, 12 patients had mild pain but did not require rescue medication. This was significantly different from fentanyl. This was similar to study by Rosseland *et al*., who concluded that postoperative analgesic effect of IA morphine was found only in subgroup of patients with higher pain intensity in the immediate post anaesthetic period. The possible reasons quoted were lack of inflammation that was prerequisite for peripheral opioid analgesia, lack of expression of opioid receptors and due to weak pain stimulus. At 4 hours, the analgesic efficacy of morphine was wearing off with six patients having moderate pain and requiring analgesics supplementation. Nevertheless, this was better than placebo group, where everyone had moderate pain even after rescue analgesia. In comparison with morphine and fentanyl, fentanyl had good analgesic effect with 9 patients having mild pain, but without requiring analgesics. This was demonstrated by Varkel *et al*. with similar doses of morphine and fentanyl as in our study and concluded that postoperative analgesia with IA fentanyl was better when compared with morphine during 8 hours of observation. At 8 hours, morphine did not from that of placebo group as all 21 patients had inadequate analgesia and required supplementary analgesics. This was similar to the conclusion drawn by Heard *et al*. who considered IA morphine no better than placebo, except for prolonging the time of first analgesic request and for its systemic effect. Fentanyl was a better analgesic than morphine when administered intra-articularly and differed significantly in terms of pain scores and rescue analgesic requirement in comparison to morphine. This was consistent with study of Mandal P *et al*. [25] who inferred 50mcg fentanyl provided longer duration of totally pain Free State without any supplementary analgesic therapy and fentanyl was better analgesic than morphine at 8 hours duration. We compared the hemodynamic data in which the placebo group had higher heart rate and mean arterial pressure than the other two drug groups and this was statistically significant. This could be due to pain and anxiety causing sympathetic stimulation. However, no significant difference with hemodynamic data among the two drug groups. We also noted the time of request for first rescue analgesia, with placebo group requiring analgesics in the immediate postoperative period itself. With better early analgesic effect

ISSN:0975 -3583,0976-2833 VOL4, ISSUE 04, 2013

only one patient requiring first rescue analgesia at 8th hour of observation in fentanyl group, while Six patients required first rescue analgesia at 4th hour of observation in morphine group. The total dose of analgesic consumption in 8 hours showed placebo group requiring highest dose (2050 mg of tramadol intravenously for 21 patients), followed by morphine group (1000mg of tramadol) while fentanyl group hardly required any analgesic dose. None, in any of the three drug groups, had significant side effects during 8-hour observation period. It is known that the postoperative period of total knee arthroplasty is very painful, and patients often require analgesics and present elevated pain scores resulting in important morbidity [26-27].

Conclusion

However, Intra-articular fentanyl provided effective post-operative pain relief and reduced rescue analgesic requirement in the first 8 hours following arthroscopic knee procedures. It also revealed that fentanyl is better intra-articular analgesics than morphine. While intra-articular morphine was found to provide good pain relief during early post-operative period, it lacked analgesic efficacy in the later half of our observation period.

Source of support: None.
Conflict of interest: None.

References

1. Sitsen E, Van Poorten F, Van Alphen W, *et al*. Postoperative epidural analgesia after total knee arthroplasty with sufentanil 1 microg/ml combined with ropivacaine 0.2%, ropivacaine 0.125% or levobupivacaine 0.125%: a randomized, double-blind comparison. Reg. Anesth. Pain Med. 2007;32:475-480.
2. Sites BD, Beach M, Biggs R, *et al*. Intrathecal clonidine added to a bupivacaine-morphine spinal anesthetic improves postoperative analgesia for total knee arthroplasty. Anesth Analg. 2003;96:1083-1088.
3. Good RP, Snedden MH, Schieber FC, *et al*. Effects of a preoperative femoral nerve block on pain management and rehabilitation after total knee arthroplasty. Am J Orthop. 2007;36:554-557.
4. Stein C, Comisel K, Haimerl E, *et al*. Analgesic effect of intraarticular morphine after arthroscopic knee surgery. N Engl. J Med. 1991;325:1123-6.
5. Likar R, Schiifer M, Paulak F, *et al*. Intraarticular morphine analgesia in chronic pain patients with osteoarthritis. Anesth Analg. 1997;84:1313-7.
6. Joshi GP, McCarroll SM, Cooney CM, Blunnie WP, O'Brien TM, Lawrence AJ. Intra-articular morphine for pain relief after knee arthroscopy. J Bone Joint Surg (Br). 1992;74:749-51.
7. Joshi GP, McCarroll SM, O'Brien TM, Lenane P. Intraarticular analgesia following knee arthroscopy. Anesth Analg. 1993;76:333-6.
8. Dalsgaard J, Felsby S, Juelsgaard P, Froekjaer J. Low dose intra-articular morphine analgesia in day case knee arthroscopy: a randomized double-blinded prospective study. Pain. 1994;56:151-4.
9. Allen GC, St. Amand MA, Lui ACP, Johnson DH, Lindsey MP. Post-arthroscopy analgesia with intraarticular bupivacaine/morphine. Anesthesiology. 1993;79:475-80.
10. Heine MF, TiUet ED, Tsueda K, *et al*. Intra-articular morphine after arthroscopic knee operation. Br J Anaesth. 1994;73:413-5.
11. McSwiney MM, Joshi GP, Kenny P, McCarroll SM. Analgesia following arthroscopic knee surgery. A controlled study of intra-articular morphine, bupivacaine or both combined. Anaesth Intensive Care. 1993;21:201-3.
12. Laurent SC, Nolanf P, Pozo JL, Jones CJ. Addition of morphine to intra-articular bupivacaine does not improve analgesia after day-case arthroscopy. Br J Anaesth. 1994;72:170-3.
13. Khoury GF, Chen ACN, Garland DE, Stein C. Intraarticular morphine, bupivacaine, and morphine/bupivacaine for pain control after knee video-arthroscopy. Anesthesiology. 1992;77:263-6.
14. Raja SN, Dickstein RE, Johnson CA. Comparison of postoperative analgesic effects of intraarticular bupivacaine and morphine following arthroscopic knee surgery. Anesthesiology. 1992;77:1143-7.
15. Heard SO, Edwards~Ferrari D, *et al*. Analgesic effect of intra-artictdar bupivacaine or morphine after arthroscopic knee surgery: a randomized, prospective, double-blind study. Anesth Analg. 1992;74:822-6.
16. Badner Nit, Bourne RB, Rorabeck CH, Doyle JA. Does not improve analgesia following knee joint replacement. Keg Anesth. 1997;22:347-50.
17. Kalso E, Trainer MR, Carroll D, MeQuay HI, Moore RA. Pain relief from intra-articular morphine after knee surgery: a qualitative systematic review. Pain. 1997;71:127-34.
18. Dierking GW, (Gstergaard HT, Dissing CK, Kristensen JE, Dahl JB. Analgesic effect of intra-articular morphine after arthroscopic meniscectomy. Anaesthesia. 1994;49:627-9.
19. Scott S Reuben, Sklar J. Pain management in patient who undergo outpatient Arthroscopic surgery

ISSN:0975 -3583,0976-2833 VOL4, ISSUE 04, 2013

of the knee. The Journal of Bone and Joint surgery. 2000;82-A(12):1754-1765.
20. Gupta A, Axelison K, Allvin R, *et al*. Postoperative pain following knee arthroscopy. The effects of intraarticular ketorolac and/or morphine. Regional anaesthesia pain medicine. 1999;24:225-230.
21. Likar R, Kapral S, Steinkellner H. Dose dependency of intra-articular morphine analgesia. British Journal of Anaesthesia. 1999;83:241-244.
22. Kazemi APS, Rezazadeh H, Ranjbar Gherachec. Intraarticular sufentanyl compared to morphine for pain relief after arthroscopic knee surgery. Journal of research in medical sciences. 2004;4:168-172.
23. Mandal P, Saudagar AH. Intra-articular fentanyl for analgesia following arthroscopic knee surgery. Indian Journal of Anaesthesia. 2002;46(2):107-110.
24. Varkel V, Volpin G, Ben-David B, Said R, Grimberg B, Simon K, Soudry M. Intra-articular fentanyl compared with morphine for pain relief following arthroscopic knee surgery. Canadian Journal of Anaesthesia. 1999;46:867-887.
25. Tanaka N, Sakahashi H, Sato E, *et al*. The efficacy of intra-articular analgesia after total knee arthroplasty in patients with rheumatoid arthritis and in patients with osteoarthritis. J Arthroplasty. 2001;16:306-311.
26. Pitimana-Aree S, Visalyaputra S, Komoltri C, *et al*. An economic evaluation of bupivacaine plus fentanyl versus ropivacaine alone for patient-controlled epidural analgesia after total-knee replacement procedure: a double-blinded randomized study. Reg. Anesth. Pain Med. 2005;30:446-451.
27. Klasen JA, Opitz SA, Melzer C, *et al*. Intraarticular, epidural and intravenous analgesia after total knee arthroplasty. Acta Anaesthesiol Scand. 1999;43:1021-1026.