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Original Research Article

Comparative evaluation of clonidine versus fentanyl as adjuvants for epidural anaesthesia with 0.75% ropivacaine for day care knee arthroscopy: a double-blind study

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ABSTRACT

Background: Day care knee arthroscopy can be performed with general anesthesia, central neuraxial blockade and peripheral nerve blocks. The adjuvants to local anaesthetic may be used to enhance the duration of analgesia without increasing the duration of motor blockade. The present study compared the clinical efficacy of clonidine with fentanyl as adjuvants to epidural ropivacaine (0.75%) for day care knee arthroscopy.
Methods: Sixty adult patients of both gender of ASA physical status I and II scheduled for day care knee arthroscopy under epidural anaesthesia, were randomized into two groups of 30 patients each to receive either 15 ml of 0.75% ropivacaine with 1 ml of clonidine 50 µg (Group RC) or with 1 ml of fentanyl 50 µg (Group RF). Groups were compared for onset and duration of sensory and motor blockade and post-anesthesia discharge score (PADS) as primary end points. Intraoperative hemodynamic changes, time taken to void, total duration of hospital stay and any adverse effects were evaluated as secondary end points.
Results: The onset of complete sensory block to T10 (15.4±4.7 versus 17.5±3.8 minutes) and time to achieve complete motor block (23.7±3.3 versus 26.9±1.4 minutes) was earlier in patients of Group RC. Intraoperative hemodynamic changes were comparable. Time to achieve PADS was earlier in patients of Group RF (6.37±1.08 versus 7.11±0.49 hour) with no statistical significant difference. Total duration of hospital stays (7.81±1.31 versus 8.27± 1.18 hour) was also comparable.
Conclusions: Clonidine and fentanyl, both can be used as epidural adjuvant to 0.75% ropivacaine for day care knee arthroscopy as they could enhance the duration of analgesia without affecting the hospital stay.

Keywords: Clonidine, Day care surgery, Epidural anesthesia, Fentanyl, Knee arthroscopy, Ropivacaine

INTRODUCTION

Day care knee arthroscopy is performed as a planned, non-emergency surgical procedure on selected patients who will be returning home on the same day. Any anaesthetic agent or technique which could provide good surgical operating conditions with rapid induction, profound analgesia and anesthesia without depression of respiratory and cardiovascular system, followed by rapid smooth recovery, would be optimal for day care surgery. General anesthesia with newer short acting agents, regional anesthesia techniques or peripheral nerve blocks are appropriate choices.[1]

Epidural anesthesia is commonly performed for knee arthroplasty as it showed definite advantage over general anesthesia by blocking nociceptive impulses from the

operative site, reduce blood loss, decreased incidence of deep vein thrombosis, no respiratory depression or cardiovascular instability, patient's ability to communicate and reduced cost of drugs.[2] However there are few disadvantages as taking time for block initiation and its onset, needs active cooperation of patient, and urinary retention. There is possibility of local anaesthetic toxicity due to use of large volumes of epidural local anaesthetic solution, hence adjuvants like opioids or α 2 agonist can be incorporated to provide a dose sparing of local anaesthetics.

Ropivacaine showed favourable physiochemical profile with lesser systemic toxicity. It showed sensory- motor differentiation by blocking sensory nerve fibres more readily than motor fibre. Early recovery of motor function is associated with early postoperative mobilization, decrease incidences of deep vein thrombosis hence early hospital discharge.[3-5]

Clonidine acts on α 2 adrenoreceptors in the dorsal horn of spinal cord as agonist and prolongs the duration of sensory and motor blockade, but it does cause hypotension and bradycardia by virtue of its ability to decrease sympathetic outflow. Fentanyl is μ-opioid receptor agonist and enhances the analgesia without effecting the recovery.[6-8]

Considering the merits of ropivacaine, clonidine and fentanyl, the present prospective double blind randomized study was aimed to compare the clinical efficacy of clonidine with fentanyl as adjuvant to 0.75% epidural ropivacaine for day care knee arthroscopy.

METHODS

After approval by the Institutional Ethical Committee and written informed consent, 60 patients of American Society of Anesthesiologist (ASA) physical status I and II, aged 25 to 58 years of both genders and less than 110 kg, scheduled for elective knee arthroscopy under epidural anesthesia, were enrolled for this prospective double blind randomized study. All patients were subjected to pre-anaesthetic assessment prior to enrolment. Patients with history of severe cardiac or pulmonary disease, uncontrolled hypertension, hepatic or renal dysfunction, metabolic disorders, spinal deformity, skin infection at site of injection, bleeding diathesis or on any anticoagulant therapy, allergy to local anaesthetic or known sensitivity to clonidine or fentanyl, history of opioid dependence or neurological disorders and who did not have any competent accompanying person, were excluded from the study.

All selected sixty patients were randomized into two equal groups of 30 patients each according to computer generated random number, each receiving a sealed envelope of study medication. Patients of Group RC received epidural study solution of 15 ml of 0.75% ropivacaine with 1 ml of clonidine (50 μg) and patients of Group RF received epidural study solution of 15 ml of ropivacaine 0.75% with 1 ml of fentanyl (50 μg). The study drug was given by an anesthesiologist who was neither aware of study protocol nor further involved for data collection. The resident recording the data and caring the patient was also unaware of study protocol to ensure the blindness of study.

All patients were advised to take tab. Alprazolam 0.5 mg at night before surgery and their fasting was ensured on the day of surgery. After arrival of patient into operation theatre, routine monitoring of non- invasive blood pressure (NIBP), electrocardiogram (ECG), heart rate (HR), and finger pulse oximetry (SpO_2) was commenced. All patients were preloaded with lactate Ringer solution at rate of 10 ml kg-1 over 15 minutes before initiation of epidural blockade.

Under all aseptic condition, lumber epidural anesthesia was administered in the sitting position by midline approach at L2-3 or L3-4 inter-vertebral disc space using an 18 G Touhy needle and location of epidural space was confirmed by loss of resistance technique. With the bevel of Touhy needle in cephalic direction, a test dose of 3 ml of 2% lidocaine with epinephrine was given to detect intrathecal or intravenous injection. Three minutes after test dose, the patients were given study drug solution according to group allocation as single dose epidural injection and were aligned into supine position to achieve adequate level of anesthesia (T10). All patients were supplemented with 100% oxygen at rate of 4L/minute via vent mask during the surgery.

Epidural block characteristics

The sensory and motor block characteristics were assessed at 2 minutes interval till the surgical anesthesia was achieved. The segmental level of sensory blockade was assessed by bilateral pin prick method along the mid-clavicular line using a short beveled 26-G hypodermic needle. The onset of motor blockade of lower extremities was evaluated bilaterally by modified Bromage scale (0-3); 0- full motor activity and able to raise straight leg against resistance, 1- unable to raise extended leg at hip but able to flex knee, 2- unable to flex knee but able to move ankle joint, 3- unable to move hip, knee or ankle (no motor activity).

All time intervals were calculated from the time of end of epidural injection. The onset time of complete sensory block, maximum cephalic dermatome, time taken to achieve complete motor block and total recovery time from sensory and motor blockade was recorded. The surgical anesthesia was considered effective when T10 dermatome was anesthetized.

Hemodynamic parameters

The hemodynamic parameters of heart rate, systemic blood pressure, pulse oximetry and ECG were recorded

preoperatively and then at every 5 minutes intervals after initiation of epidural block, till end of surgery and followed by at every 15-minutes interval in the post anesthesia room. For the present study, hypotension was defined as a fall in systolic blood pressure of more than 20% of base line or less than 100 mm Hg. It was treated primarily by increasing the rate of lactate Ringer infusion and additionally with intravenous bolus of mephenteramine, 6 mg. Bradycardia was defined as heart rate less than 60 beats/minute, and was treated with intravenous atropine 0.6 mg.

Adverse events

All patients were observed for shivering, pruritus, sedation, nausea vomiting, respiratory depression, headache, backache, urinary retention or any other adverse effects. Respiratory discomfort was managed by increasing the oxygen flow. Nausea and vomiting was treated by intravenous ondansetron (4mg).

Postoperative care

At the end of surgery, the patients were shifted to post anesthesia recovery room and monitored for any changes in vital signs. The sensory and motor block levels were assessed at every 30 minutes intervals until normal sensations returned. Duration of sensory analgesia was taken from onset of epidural anesthesia to time of administration of first rescue analgesia with intramuscular diclofenac sodium 75 mg.

Patients were discharged on the same day according to post anesthesia discharge scoring system. (PADSS Annexure-1) These criteria included mental alertness, stable vital signs, absence of nausea, and control of pain, ability to ambulate and to void.[9,10] Total duration of stay in hospital was noted for each patient. After discharge, patient and doctor remained in contact with each other up to 48 hours.

Study population size and statistical analysis

The sample size was calculated with standard computer programme which computed that approximately 23 to 25 patients should be included in each group to detect at least clinically significant difference of 30 min in mean duration of analgesia between the groups for type I error of 0.05 with power of 80% and 95% confidence limit. Assuming a 5% dropout rate, the total number of patients was set at 60 for better validation of result.

All recorded data was compiled systematically in tabulated manner and expressed as mean±SD considering later being best predictor for statistical analysis. Data was analyzed using Stat graphic centurion, version 16 (Stat point Technologies INC, Warrenton, Virginia). The demographic data for categorical variables were compared using chi-square test and statistical significance in mean difference was done using analysis of variance (ANOVA). Epidural block characteristics were compared using Mann Whitney U test. A p value of less than 0.05 was considered statistically significant.

RESULTS

The present study compared the clinical efficacy of clonidine with fentanyl for day care knee arthroscopy, performed under epidural anesthesia with 0.75% ropivacaine on 60 adult consenting patients of both genders. The surgery was performed by one of the two orthopedic surgeon and mean duration of knee arthroscopy was less than120 minutes. There was no protocol deviation and study was successfully completed. Data of all patients were included for statistical analysis.

The demographic data for age, gender, weight, and American Society of Anesthesiologist (ASA) physical status were comparable between both the groups (Table 1).

Table 1: Demographic profile of patients.

Parameters	Group RC	Group RF	P value
Age (years)	56.6±2.8	54.9±4.2	0.361
Gender M/F	27/3	26/4	0.205
Weight (kg)	62.56±8.37	64.36±7.54	0.564
ASA physical status I/II	19/11	21/9	0.655
Duration of knee arthroscopy	105. 97±16.34	108.78±14.25	0.128

RC-Ropivacaine with clonidine; RF- Ropivacaine with fentanyl; ASA- American society of anaesthesiologist.

Sensory and motor block characteristics

The mean time required to achieve complete sensory analgesia at T10 dermatome was 15.4±4.7 minutes in patients of Group RC and 17.5±3.8 minutes in patients of Group RF with no statistically significant difference. The mean time to reach maximum cephalic dermatome level for sensory block was comparable between the groups. The mean time taken for complete motor block was 23.7±3.3 minutes in patients of Group RC while it took 26.9±1.4 minutes in patients of Group RF. The motor

block was of shorter duration than sensory analgesia in all patients. The total duration of motor blockade and sensory analgesia varied significantly between the groups (p=0.001) (Table 2).

Table 2: Sensory and motor blockade profile.

Parameters	Group RC	Group RF	P value
Onset of complete sensory block (minute)	15.4±4.7	17.5±3.8	0.063
Median maximal cephalic level	T7 (5-8)	T7 (5-7)	0.076
Time taken to achieve complete motor block (minute)	23.7±3.3	26.9±1.4	0.073
Total duration of sensory analgesia (minute)	178.7±9.6	136.7±12.3	0.001**
Duration of motor block (minute)	165.3±26	123.7±39	0.001**

Data are expressed as mean±SD or numbers; ** P value is highly significant.

Hemodynamic profile

The hemodynamic parameters of mean heart rate, mean systemic arterial pressure, respiratory rate and oxygen saturation at base line were comparable. After 15 minutes of epidural block the mean heart rate and mean systolic blood pressure showed gradual decline in patients of both groups, but the intraoperative mean values of heart rate and systolic blood pressure did not show statistically significant decline from the base values.

The heart rate was lower in patients of Group RC throughout the study period when compared to fentanyl group and 4 patients of Group RC suffered from manageable bradycardia. There was insignificant intragroup variation with respect to blood pressure, respiratory rate and peripheral oxygen saturation. The episodes of hypotension were negligible and no patient require any medical intervention. All patients were calm and easily arousable.

Table 3: Adverse events.

Adverse events	Group RC	Group RF
Total number of patients	30	30
Nausea/vomiting	-	-
Shivering	-	-
Pruritus	-	5
Urinary retention	-	-
Hypotension	-	-
Bradycardia	4	-

Adverse events

There was no incidence of shivering in any patient of either group. Mild pruritus was observed in 5 patients of Group RF which resolved by assurance and required no treatment.

The ventilatory frequency and peripheral oxygen saturation were comparable between groups. No patients suffered from post-epidural nausea, vomiting or urinary retention (Table 3).

Discharge after knee arthroscopy

There was no statistical difference between the two groups regarding the time to achieve post anesthesia discharge score (PADS) and total duration of hospital stay (Table 4) All patients were discharged on the same day.

Table 4: Time taken for hospital discharge.

Parameter	Group RC	Group RF
Time to achieve PADS (hours)	7.11±0.49	6.37±1.08
Mean total duration of hospital stay (hours)	8.27±1.18	7.81±1.31

DISCUSSION

Day care surgery was planned on non-resident patients either under general anesthesia or regional anesthesia to provide timely treatment with lower incidence of hospital acquired infection and an earlier return to normal activities. No dependence on the availability of hospital beds as all patients would be discharged from the hospital later on the day of procedure.

Many anesthetic options were sought to determine the ideal anesthetic technique for outpatient knee arthroscopy. Spinal anesthesia, epidural anesthesia, local infiltration, femoral-sciatic nerve blocks all are adequate techniques but with their inherited limitations. General anesthesia with propofol and sevoflurane or isoflurane can also be used satisfactorily. Recently, all proposed new regional anesthetic techniques are comparable with even short acting general anesthetics.[1]

The regional anesthesia is becoming popular due to safe, rapid and painless induction with lower postoperative morbidity but it needs active cooperation of patient and surgeon. The practice of epidural anesthesia is gradually gaining acceptance as patient is not rendered unconsciousness and retains spontaneous reflexes with cognitive responsiveness. It provides adequate duration of analgesia, short recovery period and minimal side

effects. On the contrary, the spinal anesthesia is associated with few incidences of post spinal puncture headache, transient nerve damage, nausea and vomiting, hemodynamic fluctuation and delayed ambulation. Awareness about anticoagulation schedules and necessary precautions has made epidural anesthesia, a valuable option.[2]

The present study evaluated the clinical efficacy of clonidine and fentanyl for day care knee arthroscopy performed under epidural anesthesia with 0.75% ropivacaine. Proving the efficacy of clonidine and fentanyl might incorporate the use of these medication in future. The present study showed adequate surgical anaesthesia with comparable intraoperative hemodynamic changes of systolic blood pressure, heart rate and peripheral oxygen saturation. There was no episodes of hypotension, nausea and vomiting, headache, shivering and urinary retention in any patients during the study. Only five patients of epidural fentanyl suffered with mild pruritus and four patients of epidural clonidine suffered from manageable bradycardia.

Patel et al compared favourably the general anesthesia to three-in-one femoral nerve block along with lateral femoral cutaneous nerve block for outpatient knee arthroscopy in terms of patient comfort and discharge times.[11] Mulroy et al compared spinal, epidural and general anesthesia with LMA and found similar patient satisfaction but longer recovery time in spinal anesthesia as compared with both epidural and general anesthesia.[12] Ben David et al reported the incidences of transient neurological symptoms in patients who were given spinal anesthesia.[13] Wong et al compared spinal anesthesia with general anesthesia for knee arthroscopy. They reported that despite similar discharge times, the patients of spinal anesthesia group showed less incidence of sore throat and less postoperative pain with few incidences of backache.[14]

Ropivacaine share many physiochemical properties with bupivacaine without its undesirable systemic toxic effects. The low lipid solubility of ropivacaine leads to greater sensory-motor differentiation and adequate duration of analgesia, thus can be used safely for epidural anesthesia for day care knee arthroscopy. The onset of sensory anesthesia begins at 10-25 minutes after epidural administration with 2 to 4-hours duration.[4] Peduto et al reported that epidural injection of 15 ml of either 0.5% levobupivacaine or 0.75% ropivacaine produced similar epidural blockade in patients undergoing lower limb surgery.[15]

The potency of epidural ropivacaine may be altered by adjuvants like opioids or α 2 agonist to fasten the onset and to increase the duration of sensory and motor blockade. The combination of local anaesthetic and adjuvants effectively inhibit multiple areas of neuronal excitability to provide a dose sparing effects of local anaesthetics and would also accelerate the onset time of sensory block. The synergistic interaction between local anaesthetics and opioids during epidural administration is reported in many previous studies.[8]

Fentanyl acts primarily as agonist at μ-opioid receptors to enhance the analgesia and possess a dose sparing effect of ropivacaine. It prolongs the epidural analgesia without prolonging recovery, but associated with incidences of pruritus, urinary retention, respiratory depression, nausea and vomiting. Clonidine decreases the sympathetic outflow by acting on pre-and post-synaptic sympathetic nerve terminal and central nervous system to cause sedation, analgesia, sympatholytic and hemodynamic effects. It enhances the effects of local anaesthetics without increasing the incidence of side effects of respiratory depression but can lead to hypotension and bradycardia. It is easily available and does not come under the narcotic act.

In the present study, the addition of clonidine or fentanyl with epidural ropivacaine has accelerated the onset of sensory and motor blockade. The sensory blockade profile was significantly better in patients with clonidine as compared to fentanyl and it is in concurrence with various other studies. The complementary action of local anesthetics and α-2 agonists accounts for their profound analgesic properties. The prolongation of motor block may be the result of binding of α-2 adrenoreceptors agonist to the motor neurons in the dorsal horn. Postoperative nausea and vomiting (PONV) is distressing symptoms and delayed the hospital discharge of patients. In the present study, there were no episodes of nausea and vomiting and all patients went home uneventfully.

Safe and timely discharge is main objective for efficient conduct of day care surgical cases. Fritz et al suggested that home nursing protocol may be utilized to allow day care surgery patients to be discharged prior voiding. Patients should drink fluids before discharge from day care surgery is under consideration.[16]

CONCLUSION

Epidural clonidine or fentanyl can be used as adjuvant to 0.75% ropivacaine for day care knee arthroscopy, as both could enhance the duration of postoperative analgesia without affecting the post anesthesia discharge score. Epidural clonidine was clinically more efficient than fentanyl due to potentiation of epidural block characteristics. All patients were calm and arousable.

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Annexure

Annexure- 1 Post anesthesia discharge scoring system (PADSS).

PADSS	
Vital sign	
Patient must be stable and consistent with age and preoperative base line	
BP and pulse within 20% of baseline	2
BP and pulse 20% to 30% of baseline	1
BP and pulse >30% of baseline	0
Activity level	
Patient must be able to ambulate at preoperative level	2
Steady gait, no dizziness or meets preoperative level	1
Unable to ambulate	0
Nausea and vomiting	
Patient should have minimal nausea and vomiting prior to discharge	
Minimal: Successfully treated with PO medication	2
Moderate: Successfully treated with IM medication	1
Severe: continuous after repeated treatment	0
Pain	
Patient should have minimal or no pain prior to discharge	

The level of pain should be acceptable to patient	
Pain should be controllable by local analgesics	
The location, type and intensity of pain should be consistent with anticipated postoperative discomfort	
Acceptability	
Yes	2
No	1
Surgical bleeding	
Postoperative bleeding should be consistent with expected blood loss for the procedure	
Minimal: does not require dressing change	2
Moderate: up to two dressing changes required	1
Severe: more than three dressing changes required	0