A Comparative Evaluation of Efficacy of Dexmedetomidine Vs Ketamine through Epidural Route in Lower Limb Surgeries

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Abstract

Background and Aims: The addition of adjuvants to local anesthetic (LA) agents through epidural route helps in lower limb surgeries by providing postoperative analgesia. We attempted to establish whether addition of Dexmedetomidine to Bupivacaine infusion provides better analgesia and hemodynamic stability than Ketamine as an adjuvant.

Methods: The study involved sixty patients undergoing lower limb surgeries, using either Dexmeditomedine (Group D [n=30]) or Ketamine (Group K [n=30]) as adjuvant along with primary LA (0.5% hyperbaric Bupivacaine) through epidural route with CSE (combined spinal epidural). Primary outcome measure was the VAS (visual analogue scale). Receding time for motor blockade, level of sedation, duration of analgesia, effects on hemodynamic parameters were among the secondary outcome parameters.

Results: VAS became significantly lower at 6 hours (p=0.002) and 12 hours (p=0.007) in Group D than Group K. The receding time for motor blockade was significantly (p=0.0001) higher in Group D (6.19±0.87 hrs.) than Group K (4.71±0.91 hrs.). The total LA drug used was significantly (p=0.0001) higher in Group K (209.40±20.58 ml) than Group D (168.13±10.34 ml). The level of sedation was level I in 86.7% patients in Group D and in all the patients of Group K. The duration of analgesia was significantly higher in Group D (8.78±0.41 hrs.) than Group K (6.37±0.64 hrs.) (p=0.04). Mean Systolic Blood Pressure (SBP) (p=0.001) and Mean Heart Rate (HR) (p=0.001) in Group D were significantly lower than Group K at all the time periods.

Conclusion: We conclude that using Dexmedetomidine as an adjuvant to LA through epidural route provides better postoperative pain relief and also reduces the requirement of LA.

Keywords: Dexmedetomidine, Ketamine, Epidural Analgesia.

Introduction

Sedation, stable haemodynamics and an ability to provide smooth and prolonged post-operative analgesia are the main desirable qualities of an adjuvant in neuraxial anaesthesia.[1] Epidural techniques are particularly effective at providing dynamic analgesia, allowing the patient to mobilize and resume normal activities unlimited by pain.[2] α-2 adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anaesthesia. Dexmedetomidine is a highly selective α-2 adrenergic agonist with receptor affinity 8 times greater than clonidine. This property makes it a much more effective sedative and analgesic agent than clonidine, with much less
unwanted cardiovascular effects from α1-receptor activation.\textsuperscript{[3],[4],[5],[6],[7],[8],[9]}

Ketamine is an NMDA receptors antagonist, and can inhibit this sensitization.\textsuperscript{[10]} It is the only hypnotic agent with analgesic properties. Analgesia induced by ketamine is mediated by the opiate receptors. The advantages of ketamine include a good analgesic effect and cardiovascular stability in a hypotensive state. Disadvantages include increased heart rate and blood pressure, emergence phenomenon, laryngospasm and apnea, increases in intracranial and intraocular pressure, and the lack of visceral anesthesia.\textsuperscript{[11]}

The objective of our study was to compare the efficacy of both these drugs as adjuvants to bupivacaine through epidural infusion in patients undergoing lower limb surgery.

**Material and Methods**

This Prospective Randomized Observational Study was conducted from January 2017 to November 2018.

After obtaining approval from the Institutional Review Committee and written informed consent from the patients, 60 ASA physical status I&II patients of either sex, aged 18 to 70 years undergoing lower limb orthopaedic procedures under Combined Spinal Epidural anaesthesia were included in this study. The anticipated duration of surgery was up to 2 hours. The exclusion criteria was Consent not available; Age <18 or >70 yrs; Weight < 40 or >70 kg ;Height less than 150 cm; ASA grade III and above; Any contraindication to epidural anaesthesia (Absolute or relative); Uncooperative patient; Patients using α2-adrenergic receptors antagonists, calcium channel blockers, angiotensin converting enzyme inhibitors; Patients having dysrhythmia evident by ECG.

The randomisation was achieved by a statistician through a computer-generated list of random numbers and sealed envelopes. The patients were divided into two groups, group K (n=30) patients received bupivacaine Ketamine and group D (n=30) patients received bupivacaine with Dexmedetomidine infusion by epidural route.

**Combined Spinal Epidural Technique**

All patients were wheeled into the operating room and prehydrated with 15ml/kg body weight of crystalloid solution via a peripheral IV cannula before administering combined spinal-epidural anaesthesia. All patients received 4 L/min of O2 by simple face mask during the surgery.

After recording baseline vitals, combined spinal-epidural (CSE) anaesthesia was performed under aseptic precautions using needle-through-needle technique. The epidural space was located using loss of resistance to air technique with an 18-gauge Tuohy needle. The dural puncture at L3-4 level was achieved with 27-gauge pencil-point needle. After confirmatory aspiration of cerebrospinal fluid, patients from both groups received 2.5 ml of 0.5% hyperbaric bupivacaine along with preservative free fentanyl 25 µg intrathecally. The spinal needle was withdrawn and a 20-gauge epidural catheter was inserted and fixed such that 5-7 cm remained in the epidural space. The catheter was then anchored in place on the back of the patient using adhesive tape and a test dose of 3 ml of 2% lignocaine hydrochloride solution containing adrenaline 1:200,000 was injected.

The bilateral pin-prick method was used to evaluate and check the sensory level after Sub Arachnoid Block.

A modified Bromage scale used to measure the motor blockade effect\textsuperscript{[1]}. 

- 0 = no block, 
- 1 = inability to raise extended leg, 
- 2 = inability to flex knee and 
- 3 = inability to flex ankle and foot.

Epidural drugs were given at sensory regression to T10 (which was considered as 0 hour) in the following manner:

Group K (n=30): Patients received bupivacaine 0.125% with Preservative Free Ketamine (0.5 mg/mL) infusion by epidural route.

Group D (n=30): Patients received bupivacaine 0.125% with preservative free Dexmedetomidine (1 µg/mL) infusion by epidural route. The drug preparation was done by an anaesthesia technician who was unaware of the randomization.

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Post-operative pain scores were recorded using visual analogue scale (VAS) ranging from 0 to 10 (0 - no pain, 10 - worst pain ever) at 0, 2, 6, 12, 24 and 48 hrs after starting epidural infusion.

Duration of analgesia (time from starting epidural infusion to the time of the first request for additional pain medication) were observed in both groups following epidural infusion.

Grading of sedation was evaluated by a five-point scale\[^{[12]}\]:

1. alert and wide awake,
2. arousable to verbal command,
3. arousable with gentle tactile stimulation,
4. arousable with vigorous shaking and
5. unarousable.

Sedation score was recorded just before the initiation of epidural infusion and thereafter at 2, 6, 12, 24 and 48 hrs.

Any untoward incident and side effects during the study period was carefully observed and recorded, and managed symptomatically.

Cardio-respiratory parameters were monitored continuously, and recorded just before the initiation of epidural infusion and thereafter at 2, 6, 12, 24 and 48 hrs.

Hypotension (defined as systolic arterial pressure falling more than 20% of baseline) was treated with inj. ephedrine 3–6 mg in bolus doses and heart rate <50 beats/min was treated with 0.6 mg of inj. atropine. Intravenous fluids were given as per body weight and operative loss requirement. During the surgical procedure, adverse events like anxiety, nausea, vomiting, pruritus, shivering, etc. were recorded. Nausea and vomiting was treated with 0.1 mg/kg of intravenous ondansetron. Patients with breakthrough pain received epidural top-up with 0.125% bupivacaine 1.5 mL/segment depending on the number of segments to be blocked. If the pain persisted (defined as VAS > 4), intravenous tramadol 50 mg was given. The requirement for supplementary analgesia was noted in the two groups.

**Statistical Method**

Sample size calculation was done by G* Power (Ver 3.2.1, Germany). Sample size was determined taking into consideration that a sample size of 30 patients per group was required to produce a difference of 35% between the two groups for the duration of analgesia and would give a power of 80% at an α-level of 0.05

All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA). The results were presented in frequencies and percentages and mean±SD. Chi-square test was used to compare the categorical variables between the groups. The Unpaired t-test was used to compare continuous variables between the groups. The Paired t-test was used to compare change in hemodynamic parameters from 0 hour to subsequent time periods. The p-value <0.05 was considered significant.

**Results**

Sixty-five patients scheduled for lower limb surgery were assessed for the study eligibility and 60 patients were eligible and involved in the study. Demographic data were similar between the two groups.

In our study, the comparison of VAS was done between the groups across the time periods (Fig-1). VAS became significantly lower at 6 hours (p=0.002) and 12 hours (p=0.007) in Group D than Group K.

The receding time for motor blockade was significantly (p=0.0001) higher in Group D (6.19±0.87 hrs.) than Group K (4.71±0.91 hrs.).

The total local anaesthetic drug used was significantly (p=0.0001) higher in Group K (209.40±20.58) than Group D (168.13±10.34) (Table-1).

The level of sedation was level I in 86.7% patients in Group D and in all the patients of Group K. There was significant (p=0.03) difference in the level of sedation between the groups. In our study, duration of analgesia was significantly higher in Group D (8.78±0.41 hrs.) than Group K (6.37±0.64 hrs.) (p=0.04) (Fig. 2).

We found that the incidence of PONV was nil in Group D and in 13.3% of Group K. There was significant (p=0.03) difference in the incidence of PONV between the groups. Rescue analgesia was not required in Group D, however, it was required...
in 13.3% of patients in Group K and the difference was statistically significant (p=0.03). MAP was significantly (p<0.05) lower at all the time periods in Group D than Group K except at 2 hours. Mean SBP in Group D was significantly lower than Group K at all the time periods (p=0.001). There was no statistically significant difference in the DBP amongst the two groups at any time period. Mean HR in Group D was significantly lower than Group K at all the time periods (p=0.001).

No further complications attributable neither to the epidural block nor to the block medications were detected in both groups within 2 week follow-up period.

Discussion
The current study revealed that epidural infusion of dexmedetomidine added to bupivacaine for patients undergoing lower limb surgery significantly reduced local anesthetic consumption, increased the time of motor blockade, increased the duration of analgesia, and decreased pain intensity during the first 48 hours postoperatively.

Dexmedetomidine is a potent and more selective α2 adrenoreceptor agonist. The Alpha-2 agonist provides sedation, anxiolysis, analgesia and sympatholysis. The antinociceptive effects of dexmedetomidine occurs at dorsal root neuron level, where it blocks the release of substance P in the nociceptive pathway and thorough action on inhibitory G protein, which increases the conductance thorough potassium channels.[13]

Dexmedetomidine has been used as an adjuvant to local anesthetics in a wide diversity of regional blocks. It has been administered intravenously in conjunction with spinal anesthesia and resulted in improvement of the quality of sensory and motor block and delayed the time to first analgesic supplementation.[14]

In our study, statistically significant difference was observed for median VAS at 6 and 12 hours which was in concordance with other studies.[15],[16] We noted that epidural dexmedetomidine prolonged post-operative analgesia and lowered the consumption of local anaesthetic postoperatively. Similar results have been found by other authors.[1],[3],[17]

We observed that dexmedetomidine with bupivacaine prolongs the duration of both sensory and motor blockade. Similar results were observed by Shaikh S.I. et.al.[17] They concluded that the prolongation of the motor block of local anesthetics may be the result of binding of α-2 adrenoreceptor agonists to the motor neurons in the dorsal horn.[13]

Dexmedetomidine is known to cause slight decrease in BP and modest reduction in HR while ketamine causes hypertension and tachycardia.[16],[18] In our study, MAP, SBP and HR in group D were significantly lower than in group k, however the values were within normal limits. Our results are in
concordance with other studies that observed lower values of haemodynamic parameters for epidural dexmedetomidine with insignificant hypotension and bradycardia.\[^{[15],[18]}\]

Adequate levels of sedation were seen in both the groups, however the incidence of PONV was higher in group K. Our study did not find any adverse neurological or cardiovascular side effects.

**Conclusions**

Thus, we conclude that using Dexmedetomidine as an adjuvant to LA through epidural route provides better postoperative pain relief and also reduces the requirement of LA.

**References**


