Research Article

Ketamine versus Dexmedetomidine as adjuvants to epidural bupivacaine for abdominal hystrectomy

Nayera A. Muhammed, Ibrahim A. Youssef and Sohair A. Megalla
Department of Anaesthesiology and intensive care, El-Minya Faculty of medicine.

Abstract
Background and aims: Many studies have been conducted using dexmedetomidine as adjuvant to epidural bupivacaine in abdominal hysterectomy .We aimed to comparing the effect of dexmedetomidine and ketamine when added to epidural bupivacaine in patients undergoing elective abdominal hysterectomy, evaluating post operative analgesia, onset and duration of motor and sensory block, hemodynamic stability and side effects. **Patients and Methods:** This double blinded comparative study was conducted in 75 patients belonging to American Society of Anesthesiologist Physical Status (ASA) I or II, undergoing elective abdominal hysterectomy. The patients were randomly allocated into three groups of 25 each. Epidural anesthesia was performed in each group. While group (B) received bupivacaine15ml of 0.5% solution, group (BD) received epidural bupivacaine 15ml of 0.5% solution + Dexmedetomidine 0.5µg/kg in 1ml saline, (BK) received epidural bupivacaine 15ml of 0.5% solution + ketamine1ml (50mg). **Statistical analysis:** was done using ANOVA test, chi-square test and Paired t- testcomparison tests. **Results:** The demographic profile and hemodynamic variables were comparable in all three groups. Adding dexmedetomidine to epidural bupivacaine showed statistically significant improvement in block parameters **Conclusions:** A dose of 0.5µg / kg of dexmedetomidine showed clinically significant improvement in block characteristics with minimum undesirable effects like bradycardia and prolonged motor blockade.
Keywords: Dexmedetomidine, Ketamine,Bupivacaine, Epidural anesthesia, Hysterectomy.

Introduction
Abdominal hysterectomy (AH) is one of the most common surgeries performed in gynecology. AH is performed for malignant as well as benign indications. Hysterectomy can be performed in several different approaches: vaginal, laparoscopic and open abdominal .The level of pain associated with hysterectomy as well as the length of the period of convalescence depends on the surgical approach. The open abdominal hysterectomy is considered a major surgery and is associated with a medium to high pain level.

Epidural anesthesia is a central neuraxial block technique with many applications. Its versatility means it can be used as an anesthetic, as an analgesic adjuvant to general anesthesia, and for postoperative analgesia in procedures involving the lower limbs, perineum, pelvis, abdomen and thorax.

Neuraxial adjuvants are used to improve or prolong analgesia and to decrease the adverse effects associated with high doses of a single local anesthetic agent. In addition to their dose sparing effect, neuraxial adjuvants are also utilized to increase the speed of onset of neural blockade (reduce latency), improve the quality and prolong the duration of neural blockade.

Dexmedetomidine,an alpha-2 adrenergic receptor agonists have been the focus of interest for their sedative, analgesic, perioperative sympatholytic and cardio-vascular stabilizing effects with reduced anesthetic requirements. Inhumans, dexme-detomidine has also shown to prolong the duration of block and post-operative analgesia when added to local anesthetic in various regional blocks.

Ketamine, a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, inhibits sodium and potassium channels in nerve membranes, and thus, has local anesthetic properties.

Patients and Methods:

After obtaining institutional ethics committee approval, 75 female patients of ASA I/II , aged 35-75 years scheduled for elective abdominal hysterectomy were enrolled in this prospective, randomized, double blind,controlled study with written informed consent. Patients with hepatic or renal impairment, coagulopathy, known hypersensitivity to local anesthetics were excluded from the study.Patients were allocated into three groupsof 25 each (B), (BD) and (BK) usingclosed envelope technique.

The patients and the anesthesiologists performing blocks and assessing patients were blinded to the study groups. The drug solutions were prepared by an anesthesiologist blinded to the study groups and not involved in the study. On patient's arrival to the operating room, a 18 G intravenous cannula was inserted in a peripheral vein, patients were preloaded with lactated ringer solution 10ml\kg before the initiation of epidural block and standard monitoring commenced as Noninvasive blood pressure (NIBP), Electrocardiography (ECG), and Oxygen saturation (Spo2) (UltraviewSL2700,Spacelaps,USA) .

Epidural technique was used for anesthesia and postoperative analgesia. With the patients in the sitting position and under complete aseptic conditions, After local infiltration with 2% lidocaine, the epidural space was identified at the L3–L4 intervertebral level with an 18-G Tuohy needle (Perifix®) using the loss of resistance to saline technique. A 20-G epidural catheter was positioned 3-5 cm into the epidural space and secured in place for intraoperative and postoperative analgesia. The position of catheter was checked by aspiration for blood or CSF. A test dose of 3 ml of 2% lignocaine was administered to detect intrathecal or intravenous injection then patients turned to supine position.

After 3 minutes the patients received study solution according to randomization schedule at rate of 3 ml/10 seconds by epidural catheter. Surgery was allowed to start when sensory block level reached T4-T6.

Group (B) (control group) which receive 15 ml bupivacaine (0.5%) +1ml saline .Group (BD) which receive 15 ml bupivacaine (0.5%) + 1 ml saline(0.9%) +0.5 µg / Kg dexmeditomidine. Group (BK) which receive 15 ml bupivacaine (0.5%) + 1 ml saline (0.9%) +50mgketamine.

The sensory block was assessed by the bilateral pin-prick method using a short beveled sterile 26G hypodermic needle along the midclavicular line, bilaterally after giving the study drug at 5, 7, 10, 12, 15, 20min. Then every 20 min till the end of surgery. The time to achieve anesthesia up to T6-4 level was noted. **Motor blockade** was assessed by using Modified Bromage scale: 0. No motor block; **1** Inability to raise extended leg; able to move knees and feet. **2** Inability to raise extended leg or move knee but able to move feet. **3** Complete motor block of limb.

Motor blockade was assessed at 5, 10, 15, 20, 25 and 30 minutes intervals after the epidural administration of the drugs. Then every 30 minutes after complete establishment of sensory and motor block.

Grading of sedation was assessed using a five point scale: (1=alert and wide awake, 2=arousable to verbal command, 3=arousable with gentle tactile stimulation 4=arousable with vigorous shaking, 5=unarousable) Sedation scores were recorded just before the initiation of surgery and there after every 20 minutes during the surgical procedure.

Hemodynamic Monitoring: consisted of heart rate and noninvasive blood pressure monitoring in the three groups. The hemodynamic parameters were monitored continuously during the perioperative period and recordings were made every 5 min until 30 min and at 10 min interval, thereafter till the end of surgery.

Adverse effects: any adverse effects such as hypotension (i.e. 20% decrease relative to baseline), bradycardia (HR <60 beats/min), nausea, vomiting, sedation, back pain on injection, headache hallucination and shivering were noted.

A sample size of 20 patients in each group was determined to provide 99% power for onw way ANOVA test at the level of 5% significance using G Power 3.1 9.2 software

Results

The study included 75 patients, aged from (35-75) years, ASA I, II scheduled to undergo elective abdominal hysterectomy.

The studied groups were as age, sex, weight, ASA classification and operative time.

Hemodynamic data

found to be comparable with respect to **Patient characteristics** such Changes were presented in**figure**(1,2) baseline values of mean arterial blood presure of all groups were comparable except at 10, 40, 50, 60min and it was significantly lower in group (B) than the other groups.

Mean values of heart rate were significantly reduced in group (BD) than in group (BK) and group (B) through the study period**.**

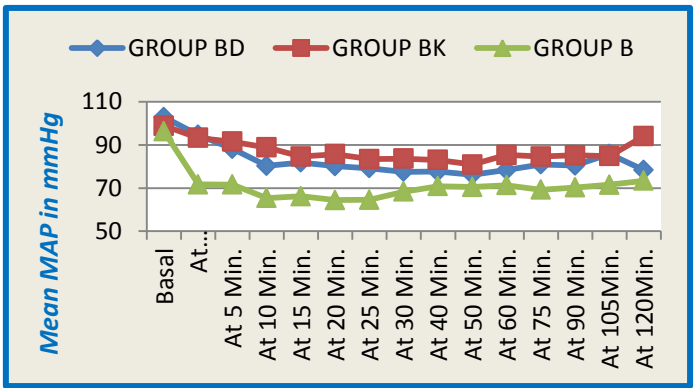

Figure (1):Mean arterial blood pressure among threegroups

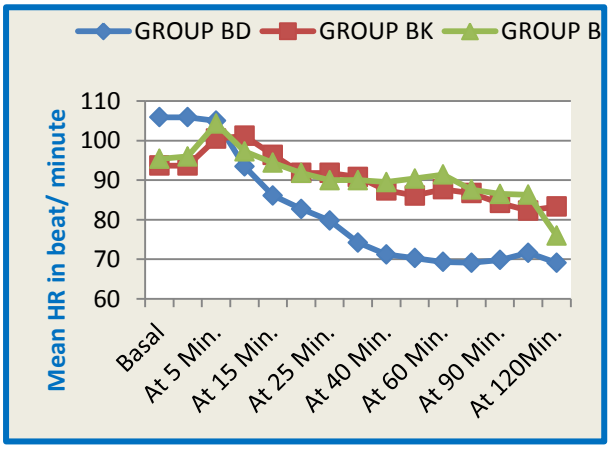

Figure (2): Mean changes in Heart rate among three groups.

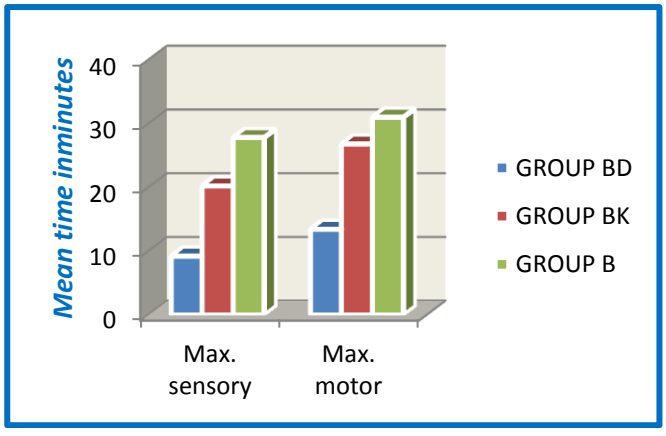

Figure (3): sensory and motor block

Characteristics of sensory and motor block are presented in figures (3): showing that the onset of sensory and motor block was faster in patients who received dexmedetomidine than patients who received ketamine and control groups**.**
The duration of sensory and motor block was found to be longer in group (BD) than in (BK) and (B), and group (BK) showed longer duration than (B).

The dexmedetomidine group experienced the prolonged pain free period as compared to ketamine group and control group.

Discussion

Dexmedetomidine is a α2-adrenoreceptor agonist with excellent analgesic properties and wide margin of safety. It has α2/α1 binding selectivity ratio of 1620:1 as compared to 220:1 for clonidine. This high selectivity for α2 receptors makes it more effective as a sedative and analgesic agent while minimising the unwanted effect of α1 receptor stimulation[1]. Singh et al., compared adding (1.5mcg/kg) of dexmedetomidine to epidural ropivacaine (0.75%) in abdominal hysterectomy and concluded that dexmedetomidine has increased the duration and characteristic of sensory and motor blockade. The mechanism by which dexmedetomidine affects the nerve block is multi-factorial. Peripherally, it acts by inhibiting the release of nor-epinephrine and also by direct effect on nerve action potential. Centrally, it acts by activation of α2-adrenoreceptors of locus coeruleusand by inhibiting the release of substance P.[2] Rastogi et al., showed that addition of dexmedetomidine 0.6 μg /kg in 1ml normal saline epidurally to 0.75% ropivacaine15ml resulted in earlier Onset of sensory block as compared to ropivacaine only and establishment of complete motor blockade was earlier in the ropivacaine with dexmedetomidine group. Postoperative analgesia was prolonged in the dexmedetomidine -ropivacaine. Sedation scores were also higher in the dexme-detomidine group.[3] In a study by Nupoor et al., a dose of 1mcg dexmedetomidine and fentanyl added to epidural bupivacaine in lower abdominal surgeries that was found Epidural dexmedetomidine with bupivacaine pro-duces a faster onset of sensory and motor blockade, with significantly prolonged sensory and motor blockade and lesser re-quirement of rescue analgesia compared to fentanyl with bupivacaine in lower abdominal and lower limb surgeries.[4] Karhade et al., used a smaller dose of 0.5mcg/kg of dexmedetomidine with epidural bupivacaine in vaginal hystere-ctomy and concluded thatFaster onset of action of local anesthetic agents, rapid establishment of both sensory and motor block, prolonged duration of analgesia in postoperative period, stable hemodynamics and minimal dose requirement make dexmedetomidine very effective adjuvant in epidural anesthesia. Dexmedetomidine reduces the dose of epidural bupivacaine, potentiates its action, and provides adequate surgical anesthesia and postoperative analgesia with a desirable level of sedation and minimal side‑effects.

Conclusion

In this double blinded comparative study, we compared comparing the effect of dexmedetomidine and ketamine when added to epidural bupivacaine in patients undergoing elective abdominal hysterectomy, evaluating post operative analgesia , onset and duration of motor and sensory block, hemodynamic stability. **We conclude** that 0.5 μg/kg epidural dexmedetomidine seems to be an attractive alternative as adjuvant to epidural bupivacaine for prolonged surgeries, with earlier onset time of sensory block, earlier achievement of complete sensory and motor blockade, prolonged sensory and motor blockade and good intraoperative sedation and excellent postoperative analgesia.

References

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