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Effect of Intravenous Dexmedetomidine on the Action of Spinal Bupivacaine in Comparision with Intravenous Midazolam

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ABSTRACT
Background: *The present study was designed to evaluate the effect of intravenous dexmedetomidine on the action of spinal bupivacaine in comparision with intravenous midazolam.*
Materials and methods: *Study was done for a period of 8 months in total 50 patients, first group are of 25 patients receiving intravenous Dexmedetomidine 0.5 micrograms/kg (n = 25). The second group are controls of 25 patients receiving intravenous midazolam 0.05milligrams/kg (n = 25).*
Results: *Duration of sensory blockade and motor blockade was prolonged with the use of intravenous dexmedetomidine premedication in comparison with intravenous midazolam. Good sedation levels, patient's cooperation and better operating conditions for the surgeon without significant respiratory depression were achieved, intra operative risk of bradycardia was more clear and significant with dexmedetomidine than with midazolam. Post operative analgesia was significantly prolonged with the use of intravenous dexmedetomidine premedication than with intravenous midazolam.*
Conclusion: *Supplementation of spinal anesthesia with intravenous dexmedetomidine produces significantly longer sensory and motor block than intrathecal bupivacaine alone*
Key words: *Dexmedetomidine , Bupivacaine, Midazolam*

INTRODUCTION

Spinal anaesthesia is the technique most commonly employed in cases of Direct and indirect inguinal hernia repair. Different adjuvants have been used to prolong spinal anesthesia, with the possible advantages of delayed-onset of postoperative pain and reduced analgesic requirements. Dexmedetomidine, a highly selective α2-adrenoreceptor agonist, has been used for premedication and as an adjunct to general anaesthesia[1]. Intravenous Dexmedetomidine premedication before general anaesthesia provides preoperative sedation, analgesia, and hemodynamic stability and reduces requirements for intraoperative inhalational agents and postoperative analgesics. Also, it has been used safely as premedication or as a sedative agent in patients undergoing surgical procedures under regional anaesthesia[2].

Although a synergistic interaction between intrathecal Dexmedetomidine and local anesthetics has been observed in previous studies,

there are no clinical data regarding the effect of intravenous Dexmedetomidine premedication on the duration of sensory and motor block during spinal anaesthesia. This Randomized double-blind controlled clinical study is to assess the effects of intravenous Dexmedetomidine premedication on spinal block duration as well as on sedation and postoperative analgesia in patients undergoing repair of indirect and direct inguinal hernia.

To isolate dexmedetomidine's analgesic effects from its sedative effects, a comparison will be made with benzodiazepine, midazolam. It is recommended to administer dexmedetomidine over 10 min, as rapid administration might produce tachycardia or bradycardia, hypertension or hypotension. Furthermore, an evaluation of the analgesic effect of different doses of intravenous dexmedetomidine (0.25, 0.5, and, 1 micrograms /kg) on ischemic pain in healthy volunteers demonstrated moderate analgesia with a ceiling effect at 0.5 micrograms/kg.

Hencein this study dexmedetomidine at the dose of 0.5 micrograms/kg is used. Bolus administration of midazolam 0.05 milligrams/kg will be reported to give enough sedation and amnesia without any adverse effects on hemodynamics and respiration in patients aged 20-60 yr under spinal anaesthesia. Therefore, midazolam 0.05 milligrams/kg was administered to the patients in this study.

MATERIALS AND METHODS

It is randomized study conducted from june2014 to January 2015. A total 0f 50 patients with hernia posted for meshplasty under spinal anesthesia, after obtaining approval from Institutional Committee, and written informed consent obtained from each patient.

Inclusion criteria: Fifty patients classified as American Society of Anesthesiologists' (ASA) physical status I–II and undergoing under spinal anesthesia.

Exclusion criteria : use of any opioid or sedative medications in the week prior to surgery, a history of alcohol or drug abuse, known allergy to either Dexmedetomidine or bupivacaine, contraindication to spinal anesthesia (e.g., coagulation defects, infection at puncture site, pre-existing neurological deficits in the lower extremities), and cardiovascular, respiratory, neurological, psychological, hepatic, or renal disease.

Using a computer-generated randomization schedule, the patients were randomly divided into two groups, The first group are of 25 patients receiving intravenous Dexmedetomidine 0.5 micrograms/kg (n = 25). The second group are controls of 25 patients receiving intravenous midazolam 0.05milligrams/kg (n = 25).

After intravenous insertion of an 18-G catheter in the operating room, all patients received 10 ml/kg of lactated Ringer's solution intravascular volume loading before spinal anesthesia. Each group were premedicated 5 min before spinal anesthesia. The study drugs were premixed to a total volume of 5 mL in the 5 mL syringe and was administered intravenously over a 10 min period as a single dose. Five minutes after the end of the infusion, the patient placed in the lateral position and dural puncture was performed at the L3-4 interspace using a standard midline approach with a 25-G Quincke spinal needle. Bupivacaine 0.5% 3 ml was injected intrathecally and the patients received oxygen 4 L/min throughout the procedure. Both the patient and the anesthesiologist blinded to the treatment group, and all recordings were performed by an anesthesiologist blinded to group allocation.

Monitors included electrocardiography, noninvasive blood pressure measurement, pulse oximetry to measure peripheral oxygen saturation (SpO2)

Parameters observed are for **Haemodynamic status** as heart rate (HR), mean blood pressure (MAP), oxygen saturation (SpO2), and respiratory rate (RR) were recorded before premedication, 2 min after premedication, immediately before and after dural puncture, and every 5 min for 120 min after spinal anesthesia. Vasopressor requirements noted are Hypotension (defined by a decrease in MAP below 20% of baseline or systolic pressure <90 mmHg) treated with intravenous

Mephentermine 6 mg and additional lactated Ringer's solution (200 mL over a 5 min period). Bradycardia (HR\50 beats/min) was treated with intravenous atropine 0.5 mg.

In **Sensory blockade** Onset of action of Sensory blockade after spinal anaesthesia was assessed at every 2 min for the first 10 min and thereafter every 10 min during surgery and postoperatively using pinprick and loss of cold (iced tube) sensation bilaterally in the mid-axillary line. Time for maximum sensory level was observed. Duration of sensory blockade is defined as 2 segments regression of anaesthesia from the maximum level was observed. The time for the first request for analgesia and the number of patients who required supplemental analgesia were recorded.

In **Motor blockade**Onset of Motor block was assessed every 2 min for the first 10 min and thereafter every 10 min during surgery and postoperatively, Motor block duration was the time for return to Modified Bromage Scale 1.

Modified Bromage Scale

0 = no paralysis;

1 = unable to raise extended leg;

2 = unable to flex knee;

3 = unable to flex ankle,

Sedation score was re-evaluated every 10 min for up to 120 min. Excessive sedation was defined as a score greater than 4/6.

The Ramsay sedation score was used for sedation score

1 = anxious and agitated;

2 = cooperative and tranquil

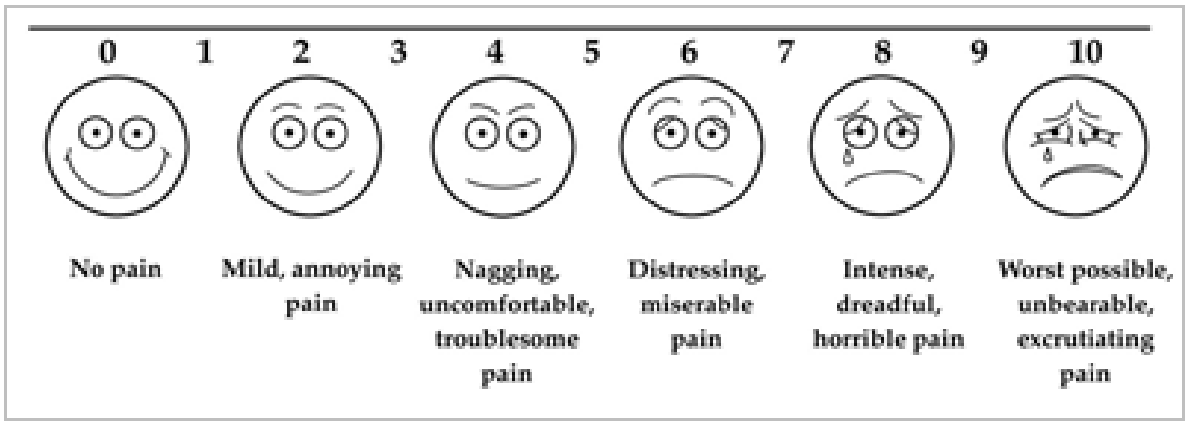
3 = drowsy but responsive to command

4 =asleep but responsive to a glabellar tap

5 = asleep with a sluggish response to tactile stimulation

6 = asleep and no response

Post operative pain was assessed by VAS scale



The presence of any complication in the preoperative and postoperative periods were noted, particularly in relation to respiratory or cardiovascular problems, nausea or vomiting, and headache.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS 15.0).P value is identified by paired t test. Probability values < 0.001 were considered as statistically significant.

RESULTS

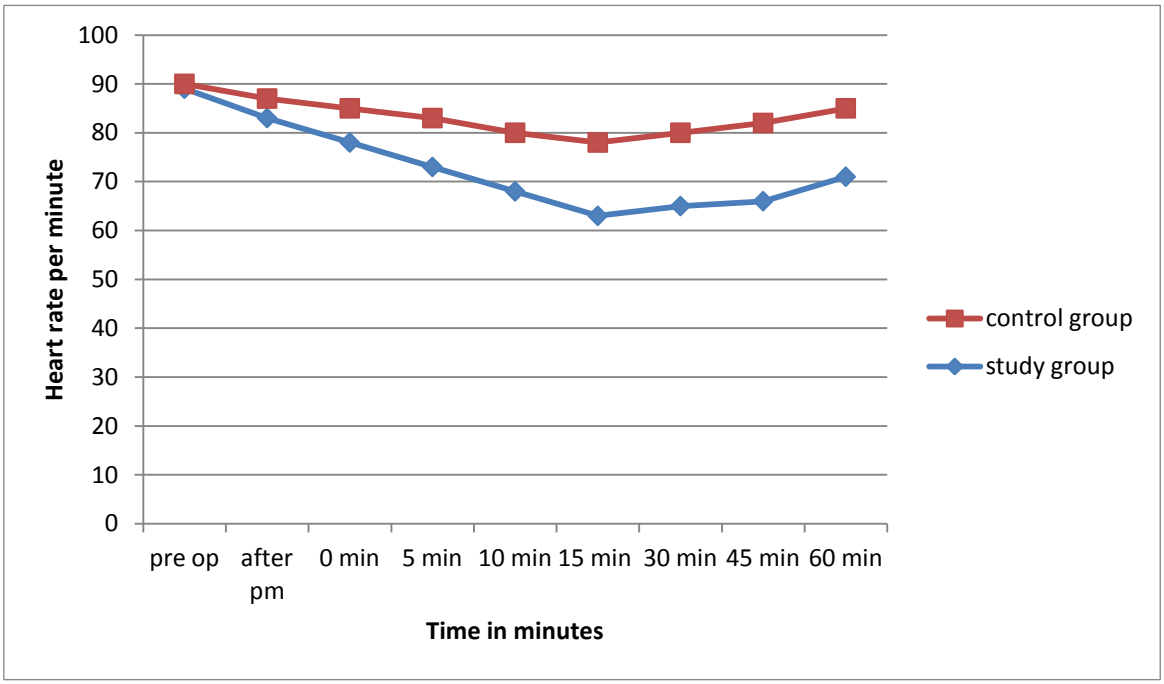
The two groups were comparable with respect to ASA status, age, weight height, as shown

TABLE – 1 : Demographic profile

	Study group 0.5mc/kgiv. Dexmedetomidine	Control group 0.05mg/kg iv Midazolam
Number of patients	25	25
Age	30.04±5.51	29.52±6.81
Weight	63.08±5.93	62.64±6.42
Height	160.96±6.19	161.72±5.99
ASA status	I / II	I / II

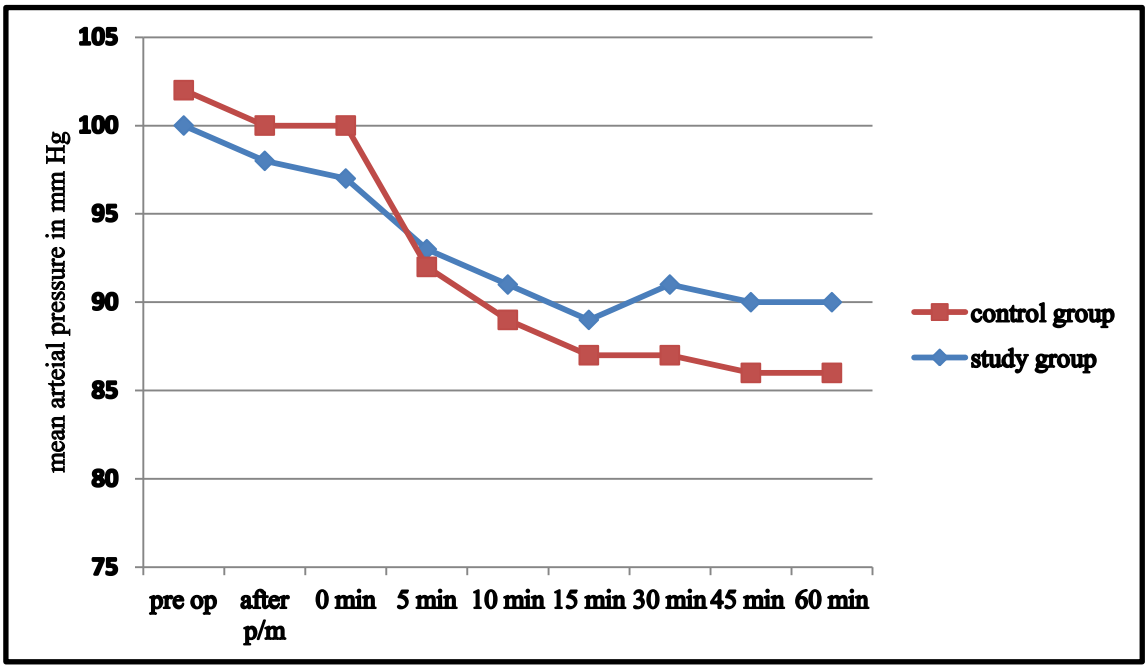
All patients were comparable for age, weight and height and the difference was stastistically not significant in both groups.

Figure-1: Line diagram showing Heart rate variation



Heart rate decreased in both the groups after spinal anesthesia but the fall in heart rate in study group was statistically significant in study group with the P value of 0.0088 .

Figure- 2: Line diagram showing mean arterial pressure changes



Mean arterial pressure decreased in both groups, but fall in mean arterial pressure is not statistically significant as P value was >0.001.

TABLE – 2 : Duration of duration of analgesia

Time in minutes (mean± S.D.)		
	CASES	**CONTROL**
Duration of motor blockade(to modified bromage scale 1)	180.48±3.39	151.4±2.23
Duration of post operative analgesia	200.72±2.35	140.88±2.26
Duration for two segment sensory regression)	130.92±2.46	105.24±2.53

Duration of motor blockade was prolonged in study group and was statistically significant with a P value<0.0001. Duration of post operative analgesia was prolonged and the time for first rescue analgesic dose was prolonged in study group and was statistically significant with a P value of <0.001. The two segment regression was prolonged in study group and was statistically significant with a P value<0.0001.

Quality of sensory blockade was good referring to no requirement of any analgesia support intra operatively. Quality of motor blockade was also good.

DISCUSSION

Different drugs have been used as adjuvant to local anesthesia in order to prolong the duration of spinal analgesia. The intravenous administration

of clonidine within 1 hr after the spinal block prolonged bupivacaine spinal analgesia for approximately 1 hour without adverse effect[3,4].

Dexmedetomidine has an onset of action of 30 min when the maintenance dose is used intravenously. Use of standard loading dose (1 μg/Kg/hr infused over 10 minutes) [76], decreases the time for onset of action. Side effects of dexmedetomidine, such as hypotension and bradycardia, are dose dependent. Infusion of loading dose over 10 min and then infusing the maintenance dose decreases the incidence of those side effects.

Jorm et al found that dexmedetomidine has an inhibitory effect on the locus ceruleus (A6 group) located at the brain stem[5,6.] Dexmedetomidine is known to have sedative effect[7] providing better conditions for the surgeon and the patient.Our results indicate that premedication with intravenousdexmedetomidine prolonged the duration of bupivacaine-induced sensory blockade during spinal anesthesia. In addition, dexmedetomidine increased the time until first request of analgesic for postoperative pain relief and decreased the requirement of supplemental analgesic. It also provided sedation comparable to midazolam premedication.

It is recommended to administer dexmedetomidine over 10 min, as rapid administration might produce tachycardia or bradycardia, hypotension [8].

Furthermore, previous studies describe an evaluation of the analgesic effect of different doses of intravenous dexmedetomidine (0.25, 0.5, and, 1 mcg/ kg) on ischemic pain in healthy volunteers demonstrated moderate analgesia with a ceiling effect at 0.5 mcg /kg.With this in mind, dexmedetomidine, 0.5 mcg /kg was given over 10 min in this study. Bolus administration of midazolam 0.05 mg/kg was reported to give enough sedation and amnesia without any adverse effects on hemodynamics and respiration in patients aged 30–70 yr under spinal anesthesia[9].Therefore, midazolam 0.05 mg/Kg was administered to the patients in this study.

Midazolam has been reported to have an antinociceptive effect through the neuroaxial pathway. However, the effects of midazolam on nociception may depend on the route of administration, with analgesia observed after spinal or epidural application, but not after systemic administration of this agent[10,11,12]. In our study also, intravenous administration of midazolam did not enhance the analgesic effect of intrathecal injection. Finally, the use of dexmedetomidine premedication before spinal anesthesia seems to offer clinical advantages compared with midazolam premedication, since dexmedetomidine provides additional analgesia. During spinal puncture, it is preferable that patients be able to alert the anesthesiologist of any paresthesia and pain on injection, both of which have been associated with postoperative neurologic deficit.

Midazolam may cause restlessness and disinhibition instead of sedation in some patients, and this is referred to as a paradoxical reaction[13].Thus, surgery will then become extremely difficult. In our study, no patients experienced a paradoxical reaction with midazolam. The sedation produced by dexmedetomidine differs from other sedatives, as patients may be easily aroused and remain cooperative[14].Midazolam has a potent anterograde amnesic effect, and dexmedetomidine infusion also may result in impairment of memory and psychomotor performance[16].However, the amnesic effect of midazolam rapidly diminished with time, and a comparable number of patients could remember the spinal puncture.

Rapid or bolus intravenous administration of dexmedetomidine produces sudden hypertension and bradycardia until the central sympatholytic effect dominates, resulting in moderate decreases in both MAP and HR from baseline. We observed no biphasic change or significant cardiovascular variability in this study consisting mainly of healthy patients[17].This might be attributed to sympathetic blockade associated with spinal anesthesia, slow administration of a low dose, and

sufficient preoperative hydration. However, further studies are needed to investigate the efficacy of dexmedetomidine in geriatric patients or medically compromised patient populations. In previous studies, it has been shown that dexmedetomidine caused no or minimal respiratory depression.

However, midazolam is known to cause apnea and arterial desaturation in sedative doses.In our study there was no respiratory depression in any patients and respiratory parameters remained within normal limits throughout the procedure. Nevertheless, it was concluded within the constraints of the present design that the addition of intravenous dexmedetomidine before spinal block provided similar pain relief with delayed-onset of postoperative pain and significantly less analgesic requirements.

In this study we have shown that a single dose of intravenous dexmedetomidine given as premedication prolonged the duration of sensory block of bupivacaine inducedspinal anesthesia. It also provided sedation andadditional analgesia.The heart rate decreased significantly after the start of intravenous infusion loading dose and extended in the PACU. This decrease in the heart rate was more clear and significant in study group in comparison with control group. The lower HR observed in study group could be explained by the decreased sympathetic outflow and circulating levels of catecholamines that are caused by dexmedetomidine[15,16.] Other studies support the finding that the bradycardia effect of dexmedetomidine is long lasting when used as a premedication drug.

CONCLUSION

Hence it is concluded that intravenous dexmedetomidine premedication prolongs the duration of sensory and motor blockade during the spinal anesthesia with Bupivacaine with good sedation and post operative analgesia than with intravenous midazolam premedication in patients undergoing repair of indirect and direct inguinal hernia.

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