Sedative and Analgesic Effect of Intravenous Dexmedetomidine in Patients Undergoing Meshplasty for Inguinal Hernia Repair under Spinal Anaesthesia: A Prospective Study.

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ABSTRACT

Background: We studied the sedative and analgesic effect of intravenous dexmedetomidine in patients posted for meshplasty for the repair of inguinal hernia under subarachnoid block with 0.5% hyperbaric bupivacaine. **Methods:** Fifty patients of the American Society of Anaesthesiologists (ASA) physical status I or II of either sex (20 – 50 years) presenting for meshplasty for inguinal hernia were included in the prospective double-blind randomized study. All patients received 2.5 ml of 0.5% hyperbaric bupivacaine intrathecally. Patients were randomly allocated on the basis of a sealed envelope technique to receive one of the following after subarachnoid block: Group D (n=25) - Loading dose of 1 µg kg^{-1} dexmedetomidine over 10 minutes started 20 minutes after spinal block + maintenance dose of 0.4 µg kg^{-1} hr^{-1} dexmedetomidine till the end of surgery; Group P (n=25) - same calculated volume of normal saline as a loading dose over 10 minutes + maintenance till end of surgery. Data regarding the VAS score, duration of analgesia were recorded. **Results:** Patients in group D had a significantly higher sedation score than those in group P ($p< 0.001$). Dexmedetomidine significantly reduced the requirement of diclofenac injection for pain relief in 24 hours postoperative period ($p< 0.001$). **Conclusion:** Intravenous dexmedetomidine resulted in significant prolongation of time to VAS ≥ 4, reduced postoperative analgesic requirement and produced good sedation levels without significant haemodynamic compromise.

Keywords: Adjuvant, dexmedetomidine, subarachnoid block.

INTRODUCTION

Spinal anaesthesia is a commonly used technique for inguinal hernia surgery as it is very economical and easy to administer. However, intraoperative anxiety and postoperative analgesia need special concern. Dexmedetomidine belongs to the imidazole subclass of α_2-receptor agonists similar to clonidine. It shows a high ratio of specificity for the α_2-receptor (α_2/α_1 1600:1) compared with clonidine (α_2/α_1 200:1), making it a complete α_2-agonist. The α_2-agonists produce their sedative-hypnotic effects by an action on α_2-receptors in the locus ceruleus.[1] Dexmedetomidine has been found to exert its analgesic actions, both at the spinal and supraspinal levels.[2]

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Dexmedetomidine is used as a short-term (less than 24 hours) sedative, analgesic in the intensive care unit. Dexmedetomidine compared to clonidine is a much more selective α_2-adrenoceptor agonist, which might permit its application in relatively high doses for sedation and analgesia without the unwanted vascular effects from activation of α_1-receptors. In addition, it is a shorter acting drug than clonidine and has a reversal drug for its sedative effect, atipamezole. Dexmedetomidine offers a special type of sedation in which patients are readily arousable with preservation of respiratory function. Intraoperatively, it provides a stable haemodynamic profile by attenuating the stress response during surgery. It may offer protection from ischaemia due to attenuated neuroendocrine response in the perioperative period. These properties render dexmedetomidine suitable for sedation and analgesia during the whole perioperative period: as a premedication, as an adjunct to general and regional anaesthesia, and as postoperative sedative and analgesic.[3] Analgesic and sedative properties have been found when intrathecal, epidural or intravenous dexmedetomidine is used as an adjuvant.[4] It also produces good sedation levels in the patients that enable patient's cooperation and potentially better operating conditions without significant respiratory depression.[5] Atipamezol is a specific and selective α_2- receptor antagonist that rapidly and effectively reverses the sedative and cardiovascular effects of intravenous dexmedetomidine.[6]

This research work was designed to study the sedative and analgesic effect following the administration of intravenous dexmedetomidine as an adjuvant to intrathecal hyperbaric bupivacaine.

MATERIALS AND METHODS

The present study was conducted in a prospective double-blind randomized manner. Fifty patients of the American Society of Anesthesiologists (ASA) physical status I or II of either sex (20 – 50 years) presenting for inguinal hernia repair surgery were included in the study.

Patients having any contraindications to spinal anaesthesia (i.e. inability to maintain stillness during needle puncture, raised intracranial pressure, skin/soft tissue infection at the site of needle puncture, severe hypovolemia, coagulopathy, pre existing neurological disease), known allergy to study drug, heart block / dysrhythmia and patients on treatment with α-adrenergic antagonists were not included in the study.

All the patients were examined during the preoperative visit a day prior to surgery. Informed written consent was obtained from the patients. They were subjected to a detailed clinical history and a complete general physical examination. Routine investigations like haemoglobin (Hb), bleeding time (BT), clotting time (CT), complete urine examination and any other relevant investigation, if needed were carried out and recorded.

The patients were kept fasting for 6 hours prior to the scheduled time of surgery. They were pre-medicated with a tablet of alprazolam 0.25 mg orally the night before surgery. On arrival in the operating room, patients were preloaded with lactated Ringer's solution at 15 ml kg^{-1} and monitored for non-invasive blood pressure (NIBP), pulse oximetry (SpO_2) and electrocardiogram (ECG).

All patients received 2.5 ml of 0.5% hyperbaric bupivacaine intrathecally. Patients were randomly allocated on the basis of a sealed envelope technique to receive one of the following after subarachnoid block:

Group D (n=25) - Loading dose of 1 µg kg^{-1} dexmedetomidine over 10 minutes started 20 minutes after spinal block + maintenance dose of 0.4 µg kg^{-1} hr^{-1} dexmedetomidine till the end of surgery [50 ml syringe was prepared with dexmedetomidine (100 µg ml^{-1}) diluted in normal saline to a concentration of 4 µg ml^{-1}].

Group P (n=25) - same calculated volume of normal saline as loading dose over 10 minutes + maintenance till end of surgery.

After the administration of spinal block oxygen was administered via a face mask and highest sensory level, motor block, pulse rate, non-invasive blood pressure, respiratory rate and pulse oximetry were recorded.

Hypotension defined as a decrease in systolic blood pressure by more than 20% from baseline or less than 90 mm Hg was treated with incremental intravenous (IV) doses of ephedrine 3 mg along with rapid infusion of IV fluids as required. Bradycardia defined as heart rate (HR) less than 50 bpm was treated with IV atropine 0.6 mg. Sedation was assessed according to the Modified Wilson Sedation Scale.[7]

Sedation score

Score	Description
1	Oriented; eyes may be closed, but can respond to "Can you tell me your name?" "Can you tell me where you are right now?"
2	Drowsy; eyes may be closed, arousable only to command: "(name), please open your eyes."
3	Arousable to mild physical stimulation (ear lobe tug)
4	Unarousable to mild physical stimulation

Postoperative pain scores were recorded using the Visual Analog Scale (VAS) between 0 and 10 (0= no pain, 10= most severe pain) at every 30 minutes for 3 hours. Injection diclofenac 75 mg intramuscular was given as rescue analgesia when VAS ≥ 4. The patient was observed for 24 hours postoperatively for the need of analgesic requirement.

At the end of the study, the data, thus obtained was compiled and analyzed statistically using:

- Unpaired t-test for quantitative data.
- Chi-square test / Fisher's exact test for qualitative data.

The value of $p < 0.05$ was considered as statistically significant, $p < 0.01$ as highly significant and $p < 0.001$ as very highly significant for statistical analysis.

RESULTS

All the patients in both the study groups belonged to ASA status I. There were 21 male and 4 female patients in group D. There were 22 male and 3 female patients in group P. When compared statistically it was found to be comparable ($p = 0.269$). The age, weight, height and duration of surgery of patients in both the groups were also comparable [Table 1].

Table 1: Comparison of demographic parameters (Mean S.D.)

	GROUP D	GROUP P	p-value
Age (yrs)	34.32 ± 9.95	33.28 ± 9.89	0.301
Weight (kg)	66.00 ± 9.77	68.80 ± 9.18	0.072
Height (mt)	1.69 ± 0.06	1.71 ± 0.07	0.187
Duration of surgery (min)	46.87 ± 17.35	43.63 ± 13.56	0.150

The mean basal values of haemodynamic data for both the groups were statistically comparable. The number of patients who had hypotension and bradycardia was not significant between the two groups [(p= 0.138) and (p= 0.125) respectively]. The infusions were continued during episodes of hypotension and/or bradycardia and the severity of these effects did not warrant the stoppage of infusions at any point of time.

Patients in-group D had a significantly higher sedation score than those in group P (p< 0.001). Dexmedetomidine significantly reduced the requirement of diclofenac injection for pain relief in 24 hours postoperative period (p< 0.001) [Table 2]. No other complications like dizziness, fatigue, pruritus, tremors, headache etc. were observed in the two groups.

Table 2: Intra-operative parameters.

Parameter		Group D	Group P	p-value
Time of VAS ≥ 4 (min)		134.05 ± 28.68	97.00 ± 13.40	< 0.001
No. of patients having	Hypotension	5	3	0.138
	Bradycardia	4	3	0.125
Sedation score	1	0	25	
	2	6	0	
	3	18	0	
	4	1	0	
	Mean ± S.D.	2.76 ± 0.48	1.00 ± 0.00	< 0.001
No. of diclofenac injections	1	12	2	
	2	12	19	
	3	1	4	
	Mean ± S.D.	1.60 ± 0.61	2.08 ± 0.49	< 0.001

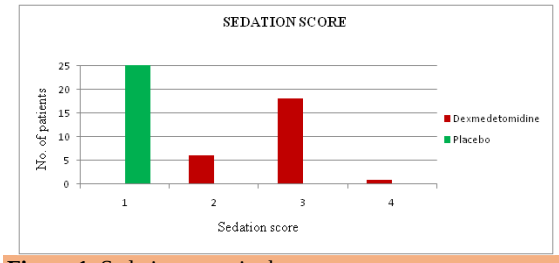

Figure 1: Sedation score in the two groups.

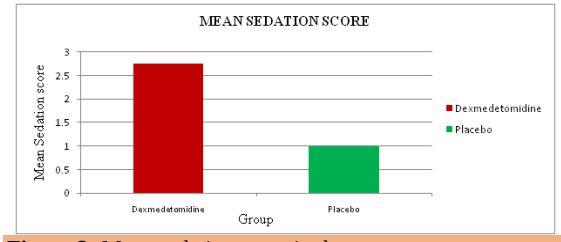

Figure 2: Mean sedation score in the two groups.

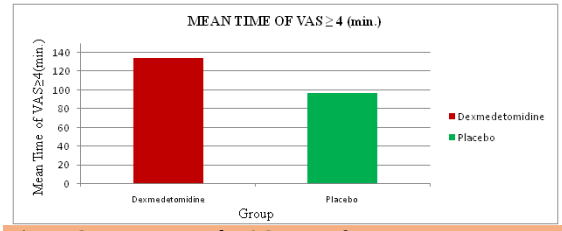

Figure 3: Mean time of VAS≥ 4 in the two groups.

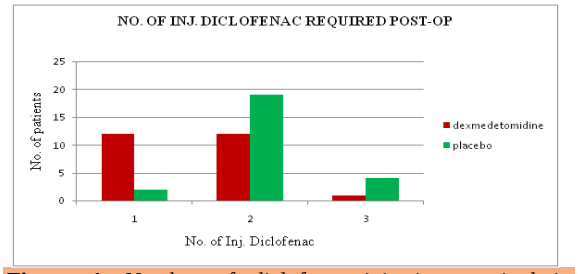

Figure 4: Number of diclofenac injection required in postoperative period in the two groups.

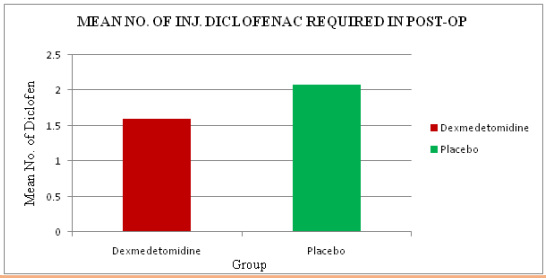

Figure 5: Mean number of diclofenac injection required in the two groups.

DISCUSSION

All patients in both the study groups belonged to ASA status I. The age, weight, height, gender distribution and duration of surgery of patients in both the groups were also comparable.

In our study, the time to VAS ≥ 4 was 134.05 ± 28.68 minutes in group D and 97.00 ± 13.40 minutes in group P which was very highly significant (p< 0.001). The number of injection diclofenac required for pain relief in 24 hours postoperative period was significantly less in group D as compared to group P (1.60 ± 0.61 vs 2.08 ± 0.49) (p< 0.001). Harsoor et al also noted that the duration of analgesia defined as time from administration of SAB until the first complaint of pain (VAS ≥ 3) was significantly prolonged in group D as compared to group C (222.8 ± 123.4 minutes vs 138.36± 21.62 minutes, p< 0.001) despite using a lower initial loading dose of 0.5 µg kg^{-1}. They explained this analgesic effect primarily due to inhibition of the locus ceruleus in the brain stem. In addition, dexmedetomidine infusion may result in increased activation of α_2-receptors in the spinal cord resulting in inhibition of nociceptive impulse transmission. This effect seems to be mediated through both pre-synaptic and the post synaptic α_2-receptors.[8] Whizar-Lugo et al in their study noted that the postoperative need for analgesics provided at VAS 4/10, was first given in the placebo group at 150 minutes, dexmedetomidine patients received their first analgesic dose at 220 minutes, and clonidine patients at 240 minutes after the end of surgery (dexmedetomidine vsplacebo 220 ± 30 minutes vs 150 ± 20 minutes, p< 0.05 and clonidine vsplacebo 240 ± 20 minutes vs150 ± 20 minutes, p< 0.05). No statistical differences were found between dexmedetomidine vs clonidine (p> 0.05). They explained that systemic or neuraxial injection of α_2-adrenergic agonists produces analgesia by acting at the spinal level, laminae VII and VIII of the ventral horns. The most accepted mechanism is the release of acetylcholine and nitric oxide. The locus ceruleus and the dorsal raphe nucleus are also important central neural structures where these drugs act producing sedation-analgesia.[9]

We found that none of the patients in group D had a sedation score of 1. Sedation score of 2 was noted in 6 patients and sedation score of 3 was noted in 18 patients in group D. One patient in group D also had a sedation score of 4. In group P all the patients were noted to have a sedation score of 1. The mean sedation score in group D was higher than in group P (2.76 ± 0.48 vs 1.00 ± 0.00) and was found to be very highly significant (p< 0.001). Harsoor et al noted that the mean intra-operative RSS in Group D was 2.34 ± 1.1 where as in Group C, it was 2.0 ± 0.0 (p= 0.034). However, RSS was comparable in both groups in the postoperative period. Dexmedetomidine produces sedation by its central effect and this seems to be dose dependent. Most of the patients receiving dexmedetomidine were sedated, but easily arousable. None of the patients had RSS greater than 3 at any point of observation highlighting the advantage of lower dose.[8] Our observations are consistent with their results.

Al-Mustafa et al also noted that the Ramsay sedation score (RSS) was 2 in all patients in group C, and ranged from 2 – 5 in group D, the maximum score was 5 in three patients, 4 in nineteen patients and 3 in one patient, and the maximum mean score of sedation (3.96 ± 0.55) was achieved 30 minutes after starting dexmedetomidine infusion. They explained that dexmedetomidine produces sedation and anxiolysis by binding to α_2-receptors in the locus ceruleus, which diminishes the release of norepinephrine and inhibits sympathetic activity, thus decreasing heart rate and blood pressure. [10]

Complications like dizziness, fatigue, pruritus, tremors, headache etc. were not observed in the two groups.

CONCLUSION

We conclude that loading dose of 1 µg kg^{-1} dexmedetomidine over 10 minutes started 20 minutes after spinal block followed by maintenance dose of 0.4 µg kg^{-1} hr^{-1} till the end of surgery resulted in significant prolongation of time to VAS ≥ 4 and a reduced postoperative analgesic requirement. Dexmedetomidine resulted in good sedation levels in all the patients without significant respiratory depression and complications.

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