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Comparison of Intravenous Dexmedetomidine Alone and in Combination with Midazolam as Premedication in Patients Receiving Spinal Anaesthesia

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Abstract

Study Objective: To compare intravenous dexmedetomidine in combination with midazolam and dexmedetomidineas premedication in patients receiving spinal anaesthesia. *Design:* Prospective randomized controlled double blind study. *Methodology:* 60 patients belonging to ASA physical status I and II scheduled for surgery under spinal anaesthesia were randomly selected for the study and were randomly divided into two groups of 30 each. Group DM patients received intravenous dexmedetomidine 1 µg/kg in combination with midazolam 0.025 mg/kg (bolus) and group D patients received intravenous dexmedetomidine1 µg/kg (bolus) as premedication before receiving 3 ml (15 mg) of intrathecal hyperbaric bupivacaine (spinal anaesthesia). Hemodynamic changes, to note down the level of sedation, additional analgesic requirements preoperatively, and complication if any were studied. *Results:* Ramsay sedation score was statistically significant in the dexmedetomidine in combination with midazolam group (DM) for 20 minutes in comparison with Dexmedetomidine (D) group, and there after the sedation scores were similar in both the groups (sedation score of 2-3) without any respiratory depression. The time request for analgesia, hemodynamic parameters and side effects were similar in either of the groups. *Conclusion:* Intravenous bolus of dexmedetomidine (D) is sufficient to provide adequate sedation with good hemodynamic stability and without respiratory depression in patients who receive spinalanesthesia.

Keywords: Intravenous; Dexmedetomidine; Midazolam; Hyperbaric bupivacaine; Intrathecal; Ramsay sedation score; and Spinalanesthesia.

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Introduction

Spinal anesthesia may be defined as the interruption of conduction of nerve impluses by injecting an anesthestic into subarachnoid space that reduces sensitivity to pain without loss of conscious. Procedures below the level T10 can be performed under spinal anesthesia. Spinal anesthesia(subarachnoid block) has least failure rates, easy to administer and cost effective. It also has the advantage of being free from the risk of intubation and pulmonary aspiration. However, the patient's anxiety presents as disadvantage of spinal anesthesia [1,2,3], which is more common

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among younger patients, women, and people with negative experience of anesthesia or fear of death [1,2,3]. Anxiolytics will be benifical for the patients [1,2].

High catecholamine levels increase arterial blood pressure, heart rate, and oxygen consumption [2]. Various agents such as phenothiazine, benzodiazepines, barbiturates, opioids are anxiolytics and provide sedation. Commonly used drug is midazolam which is a benzodiazepine, as it is a water soluble agent, its onset time is much faster then other benzodiazepines, and it has a relatively short elimination half-life (2-4 h) [1]. Its sedative effect is shown in many studies [4]. Dexmedetomidine is a selective, specific, and highly potent apla-2 adrenoreceptor agonist (1620:1 α_2 to α_1) is also used for permedication [5,10,11] due to its sedative and analgesic effect. The analgesic effect is due to the activation of the alpha2- adrenergic receptors [3,5]. Dexmedetomidine decreases the stress response; in turn reduce the heart rate and blood pressure by decreasing the catecholamine secretion. It doesn't cause respiratory depression in comparison with benzodiazepines and opioids [4,5,6]. Various studies have shown the sedative and analgesic effect of dexmedetomidine on acute postoperative pain after major surgical procedures [2,3,5,7]. Midazolam is the most popular anxiolytic and hypnotic agent used in surgical and non-surgical settings. Therefore, midazolam is preferred drug. However, intravenous midazolam should be used in tittered doses to achieve and maintain the desired sedative level as well as to minimize side effects due to over-dosage [1,12].

In view of these facts, this study was planned to analyze the effects of intravenous dexmedetomidine in combination with midazolam (DM) and intravenous dexmedetomidine (D), on duration of sedation and the intraoperative hemodynamic profile when given intravenously in patients receiving intrathecal bupivacaine (spinal anaesthesia).

Aims and Objectives

To analyze the difference between intravenous dexmedetomidine 1 µg/kg in combination with midazolam 0.025 mg/kg and intravenous dexmedetomidine 1 µg/kg when given as premedication in patients receiving intrathecal hyperbaric bupivacaine 3 ml (15 mg).

1. To compare level of sedation.
2. Assess the hemodynamic stability.
3. Additional analgesic requirements post operatively.
4. Complications if any.

Materials and Methods

This study was conducted on patients undergoing elective surgery under spinal anaesthesia for a period of 18 months. Written inform content was obtained after explaining the patients the procedure.

Inclusion Criteria

1. Patients under ASA grade 1 & 2.
2. Patients undergoing elective surgeries.
3. Patients giving valid consent.
4. Patients aged between 18 yrs to 55 yrs.

Exclusion Criteria

1. Patient refusal.
2. Patients with ASA grade 3 & 4.
3. Patients posted emergency surgery.
4. Patients on any opioids or any sedative medication in the week prior to the surgery.
5. Patient with history of alcohol or drug abuse.
6. Patients who are allergic to any of the test drugs.
7. Contraindication to spinal anesthesia (example; coagulation profile derangement, infection at local site, preexisting neurological defects.

Study Design

Pre anesthetic evaluation was done the day prior to surgery. Nil per oral guidelines were followed prior to the day of surgery and patient had received proton pump inhibitor as premedication, no anxiolytics were given. With the consent of the patients, the study was conducted. 60 patients (of either sex) were randomly divided into two groups, DM group and D group.

According to ASA standard monitoring. Patients peripheral oxygen saturation, blood pressure (systolic, diastolic, mean arterial pressure), electrocardiogram were monitored including Ramsay sedation scoring, and basal values were noted. The study drugs were premixed to a total volume of 10 ml in a 10 ml syringe and were administered intravenously over a 10 minutes period as a single dose (bolus). 5 minutes after receiving

the premedication, the patient was placed in lateral position and dural puncture was performed at L3-L4 interspace using standard mid line approach with a 23G Quincke needle. Hyperbaric bupivacaine 0.5% 3 ml (15 mg) was injected intrathecally. All the parameter of sedation and anxiety and the vital signs in this study was done by the same observer to minimize inter observer variation.

Parameters Evaluated

1. Level of Sedation was assessed using Ramsay Sedation Score

1. Patient anxious and agitated.
2. Patient cooperative, oriented and tranquil.
3. Patient responds to commands.
4. Patient has a brisk response to a light glabellar tap or loud auditory stimulus.
5. Patient asleep, sluggish response to light glabellar tap or loud auditory stimulus.
6. Patient does not respond to painful stimulus.

The score were revaluated during the surgery and post operatively up to 120 minutes.

2. Hemodynamic Assessment

Systolic, diastolic, mean arterial blood pressure, heart rate, oxygen saturation, end tidal carbon dioxide concentration were recorded before premedication, 2 minutes after end of premedication, immediately before and after dural puncture and every 15 minutes for 120 minutes after spinal anesthesia.

Hypotension was considered when mean arterial pressure decreases to less than 20% from baseline. They were treated with intravenous sympathomimetic drug (Ephedrine).

Bradycardia (heart rate less than 60 beats/min or 20% the base line) was treated with intravenous atropine in boluses of 0.6 mg.

3. Severity of pain by visual analogue scale postoperatively

The intensity of pain was assessed using a 10-cm visual analog scale (VAS; 0: no pain and 10: worst imaginable pain). The number that correlates with the position on the VAS the patient pointed to, was noted. The time for the first request for postoperative analgesia and the number of patients who required supplemental analgesia was also recorded. All patients were observed during the postoperative period for 2 hours and later 6th hourly to know the duration, quality and intensity of pain.

4. Complications

Complications in relation to respiratory or cardiovascular problem, nausea vomiting and headache were noted down.

Statistical Methodology

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 17.0 statistical Analysis Software. The values were represented in Number (%), Mean, and Standard Deviation. Level of significance: "p" is level of significance.

Results

With an objective to analyze the sedative effects of intravenous dexmedetomidine 1 µg/kg in combination with midazolam 0.025 mg/kg and

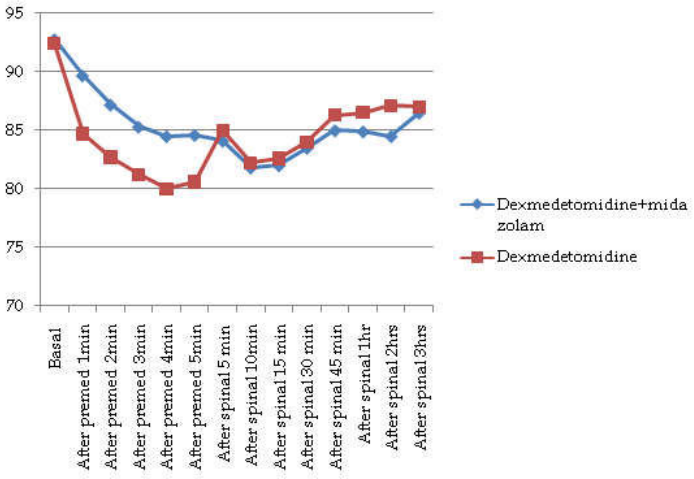

Chart 1:

dexmedetomidine 1 µg/kg as premedication in patients receiving spinal anesthesia. A total of 60 patients were enrolled in this study and were randomly distributed into two equal groups, comprising of 30 patients each. Group DM comprised of 30 patients who were given dexmedetomidine in combination with midazolam, while Group D comprised of 30 patients who were given intravenous dexmedetomidine as premedication.

Haemodynamically in both the groups patients were stable through out the procedure, nil statistical signifiance.

There is no statistical difference in the mean SpO_2 recording among two groups of patients except in the 30th min (p value 0.023) and in the 45th min (p value 0.014) of the DM group.

Group DM showed higher Ramsay Sedation Score than Group D, which is statistically significant at 10th, 15th and 30th minute (p 0.016, p 0.031, p 0.007 respectively). Ramsay Sedation Score in group DM than group D was not statistically significant at 5, 45, 60, 120 and 180 minutes.

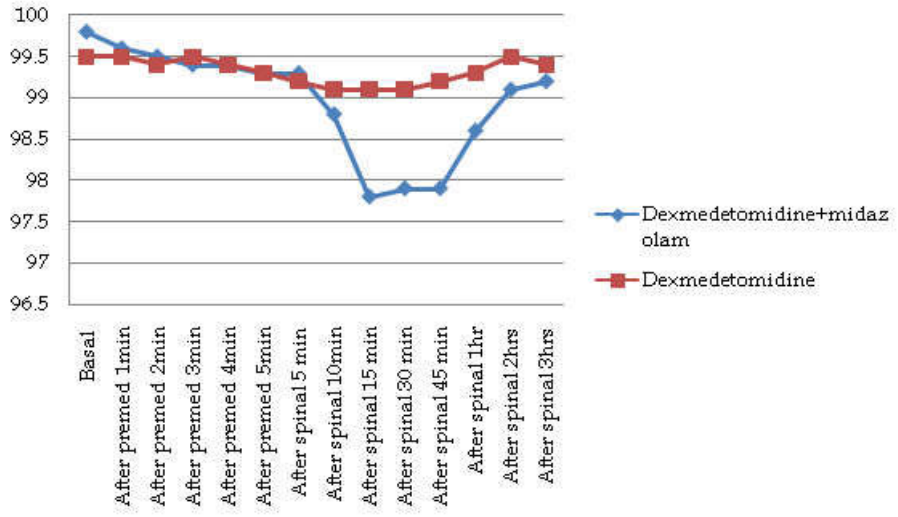

Chart 2: line graph showing SpO_2

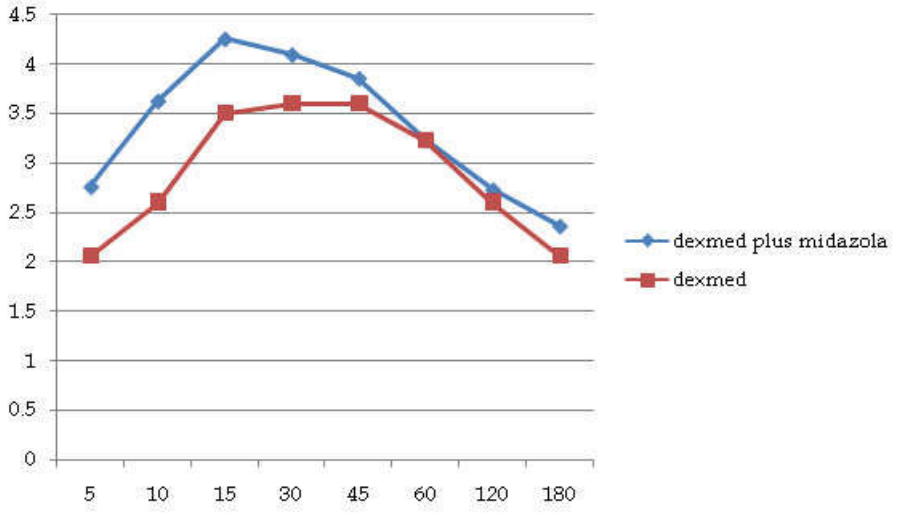

Chart 3: Line graph showing level of sedation.

Discussion

Procedures below the level of T10 may be performed under spinal anesthesia (subarachnoid block). Spinal anaesthesia is the most preferred anesthesia because of its least failure rates, easy to administer and cost effective. It also has the advantage of being free from the risk of intubation and pulmonary aspiration.

Patient undergoing spinal anesthesia will be anxious, more common among younger patients, women, and people with negative experience of anesthesia or fear of death [1,2,3]. High catecholamine levels increase arterial blood pressure, heart rate, and oxygen consumption [2,16]. Anxiolytic will be benifical for the patient [1,2,3]. Various agents such as phenothiazines, benzodiazepines, barbiturates, opioids are anxiolytics and provide sedation. Commonly used drug is midazolam with rapid onset and short acting. Its sedative effect is shown in many studies [4].

The present study was planned with an objective to analyze the sedative effects of intravenous dexmedetomidine 1 µg/kg (iv bolus) in combination with midazolam 0.025 mg/kg (iv bolus) and dexmedetomidine 1 µg/kg (iv bolus) as premedication in patients receiving intrathecal hyperbaric bupivacaine. Both the groups did not have statistically significant differences in their demographic data.

Variable	DM group	D group	p value
Age	36.8 ± 15.5	36.5 ± 14.0	0.615
Height	167.13 ± 11.00	165.87 ± 11.00	0.423
Weight	59.7 ± 15	59.1 ± 15.80	0.268
BMI	21.29 ± 3	21.34 ± 2.5	0.405
ASA I/II	22/08	22/08	0.432

Gertler *et al.* [5], Bloor BC *et al.* [8], Dyck JB *et al.* [9], Hall JE *et al.* [11], in their studies have shown that after administration of a intravenous bolus of 1 µg/kg dexmedetomidine, initially resulted in a transient increase of the blood pressure and a reflex decrease in heart rate, especially in younger, healthy patients. Dexmedetomidine does not appear to have a direct effect on heart [7]. A biphasic cardiovascular response is noted after the administration of dexmedetomidine [4,7,8,10]. The initial reaction can be explained by the peripheral α_{2B} –adrenoceptor stimulation of vascular smooth muscle and can be attenuated by slow infusion over 10 or more minutes. Another possible explanation for subsequent heart rate decrease is the stimulation of the presynaptic α2-adrenoceptor, leading to a decreased norepinephrine release [9]. In the present study group there was nil statistical significance changes in the heart rate. (DM group patients had a basal mean heart rate of 83.9 ± 6.5 & after premedication 74.4 ± 7.6. D group patients had a basal heart rate of 84.5 ± 6.5, after premedication 70.3 ± 5.9).

Linag *et al.* [17] study 8 of 63 patients had respiratory depression which appears to be a CNS mediated effect [1]. Hall JE *et al.* [11], Bhana *et al.* [16], Venn *et al.* [17], al in their study they have shown that dexmedetomidine does not cause any respiratory depression. There was a nil statistical significane fall in the SpO_2 in either of the group except at 30th min (p value 0.023) and 45th min (p value 0.014) in DM group as compared to D group, probably due to the synergistic action. Respiratory rate were similar in the groups. With nil statistical significance.

In the present study, Ramsay sedation score was statistically significant in the DM group at the 10th min (p value 0.016), 15th min (p value 0.031), and 30th min (p value 0.007) probably due the synergistic effect. Eren *et al.* [19], in their study have shown that rapid and short acting midazolam [1] showed initial high Ramsay sedation score. Midazolam in doses of 1mg to 2.5mg iv the onset of action is 30 to 60 seconds, with a peak effect in 3 to 5 mins and duration of sedation 15 to 80 minutes [1].

Non of the patients required rescue analgesia. Postoperative request for first analgesia in either of the groups was almost the same.The incidences of side effects in both the groups were statistically insignificant. Three patients had nausea and vomiting (PONV). One patient of each in either group had headache. Two patients in either group had bradycardia similar to Eren et al study.

Conclusion

In conclusion, intravenous bolus supplementation of dexmedetomidine during subarachnoid block produces satisfactory arousal sedation with good hemodynamic stability and without causing respiratory depression. Addition of intravenous midazolam to dexmedetomidine may be beneficial for patients who are highly anxious and who require deeper sedation.

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