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Research Article

Comparative Evaluation of Two Different Doses of Dexmedetomidine for Intra Operative Moderate Sedation During Spinal Anesthesia

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ABSTRACT

Background: Intravenous (IV) sedation is often used to relieve anxiety or stress during surgery under regional anesthesia. Subarachnoid block is a widely followed regional anaesthesia technique, especially in lower abdominal and lower limb surgeries. Intense sensory and motor block, continuous supine position and the inability to move the body also brings a feeling of discomfort and phobia in many patients. Sedation has been shown to increase patient satisfaction during regional anaesthesia. Dexmedetomidine is well suited for conscious sedation as patient can be quickly aroused and oriented on demand. Aim of this study was to compare infusion doses of 0.3µg/kg/hr and 0.5µg/kg/hr, after loading dose of 1µg/kg of injection (inj).dexmedetomidine in order to obtain a better regimen for patients undergoing procedures under spinal anaesthesia in terms of sedation and hemodynamic stability.
Objective: To compare efficacy of dexmedetomidine for intraoperative sedation and hemodynamic stability at doses of 0.3µg/kg/hr and 0.5µg/kg/hr after loading dose of 1 µg/kg in patients operated under spinal anaesthesia.
Methods: Adult 80 Patients were randomly divided into two groups, (Group D-0.3) and (Group D-0.5). They were given spinal anaesthesia with 0.5% hyperbaric bupivacaine and initial dose of inj.dexmedetomidine 1 µg/kg was infused over 10 minutes. Group D-0.3 received maintenance dose of inj.dexmedetomidine of 0.3µg/kg/hr and Group D-0.5 received maintenance dose of 0.5µg/kg/hr. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate (RR), spO2 and sedation using observer's assessment of alertness/sedation (OASS) were recorded at baseline, after loading dose, before spinal anesthesia, after spinal anesthesia at every 5 minutes upto 30 minutes, followed by every 15 minutes till the end of surgery and every 5 minutes upto 15 minutes after surgery. Data were compared using chi-square and unpaired t test.
Results: The mean age for Group D-0.3 is 43.9+11 and for Group D-0.5 is 35.3+20. There is no statistically significant difference in demographic profile between two groups. It was also observed that there is no statistically significant difference in HR, SBP, DBP, MAP, RR and SpO2 in all point of time ($p>0.05$). According to sedation score in group D-0.3 72% patients were sleeping comfortably but easily arousable and 8% patients were in deep sleep, while in group D-0.5 70% were sleeping comfortably but easily arousable and 15% in deep sleep.
Conclusion: After a loading dose of 1 µg/kg intravenously, an iv infusion of dexmedetomidine at a lower rate, i.e. 0.3µg/kg/hr is equally effective in providing sedation for patients undergoing surgeries under spinal anesthesia as 0.5µg/kg/hr.

The authors declare no conflicts of interest.

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Introduction

Intravenous (IV) sedation is often used to relieve anxiety or stress during surgery under regional anesthesia. Subarachnoid block is a widely followed regional anaesthesia technique, especially in lower abdominal and lower limb surgeries [1]. Intense sensory and motor block, continuous supine position and the inability to move the body also brings a feeling of discomfort and phobia in many patients. Sedation has been shown to increase patient satisfaction during regional anaesthesia [2]. Moderate sedation requires no intervention to maintain a patent airway and cardiovascular stability. Regional anaesthesia definitely has an advantage of conscious, spontaneously breathing patient, who can maintain a patent airway during the surgical procedure. Many drugs such as midazolam, propofol, midazolam-remifentanil combination, Clonidine and dexmedetomidine have been studied to achieve goals of adequate sedation for patients under spinal anaesthesia but with midazolam respiratory depression was a major concern, with propofol hemodynamic instability and respiratory depression were the adverse effects to be managed and higher incidence of bradycardia with Clonidine was a major drawback [3-6].

It was found that dexmedetomidine has property of analgesia, sympatholysis and flexibility to titrate sedation without causing major respiratory depression. It is well suited for conscious sedation as patient can be quickly aroused and oriented on demand [7]. Intravenous administration of dexmedetomidine prolonged the duration of spinal anaesthesia by inducing sedation and increasing post-operative analgesia with minimal effect on cardiovascular and respiratory systems. This advantage of dexmedetomidine was used as a strong base to study the effects of dexmedetomidine by administrating it intravenously in association with the spinal anaesthesia [8]. Dexmedetomidine is also associated with adverse effects. Literature survey reveals that a dose of 1mcg/kg, 0.5 mcg/kg and 0.6mcg/kg were found adequate for levels of sedation, but incidence of bradycardia/hypotension was significant with them [9-10]. Similar observation was also seen while comparing 0.2mcg/kg/hr versus 0.6mcg/kg/hr maintenance infusions [11]. Hence the prime objective of this study was to use a lower dose of dexmedetomidine which provides a desirable levels of sedation. The present study aims to compare infusion doses of 0.3µg/kg/hr and 0.5µg/kg/hr, after loading dose of 1µg/kg, in order to obtain a better regimen for patients undergoing procedures under spinal anesthesia in terms of sedation and hemodynamic stability.

Methods

The research study was approved by the Institutional ethical and scientific committee. Written informed consent was obtained from all the patients. All the information collected was strictly used for the study purpose only and confidentiality was strictly maintained.

The study design was prospective, randomised, double blind. Purposive sampling method, which is a nonprobability sampling technique was used considering the patient inflow rate in the institute during the study duration of 11 months.

A total sample size of 80 patients who were admitted in GMERS civil hospital, Gandhinagar for elective surgical procedure under spinal anaesthesia with inclusion criteria of age between 18 to 80 years, weighing between 30 to 80 kilograms (kgs), both male and female, ASA grade 1 and 2 were asked for the consent and included in this study. Exclusion criteria were age less than 18 years and more than 80 years, weight less than 30 kgs and more than 80 kgs, ASA grade 3 and 4, patients allergic to any drugs, any contraindication to spinal anesthesia, patients with poorly controlled hypertension, neuromuscular diseases, haematological diseases and severe hepatic or renal derangement.

Patients were randomly allocated into two groups, Group D-0.3 (n=40) and Group D-0.5 (n=40). Randomisation was done by coin toss for each patient. The study drug was prepared by anesthesia resident/faculty who was not directly involved in the study. The patient and the observer remained blinded to the study drug.

Detailed preoperative history was taken. Thorough systemic examination was done and any spinal deformity was ruled out. Patients were investigated for complete blood count, blood sugar, renal function test, serum electrolytes, serum bilirubin, chest X-ray and ECG. Procedure was explained to the patients and written informed consent was taken. Nil per oral for minimum 6 hours was advised prior to schedule time of surgery. Inside the operation theatre intravenous line of 18 or 20 gauge was secured and each patient was preloaded with 10-15 ml/kg of ringer lactate solution before procedure. Pulse oximeter, non-invasive blood pressure and ECG monitors were applied and baseline readings were taken. Total loading dose of 1 µg/kg of injection (inj).dexmedetomidine was calculated and diluted in normal saline to make total volume of 10 ml, which was infused at rate of 1ml/min over 10 minutes before spinal anesthesia. Total maintenance dose of inj.dexmedetomidine for 1 hour was calculated according to individual group and diluted in normal saline to make total volume of 30 ml. This was infused at a rate of 0.5 ml/min over 1 hour. If surgery continued after first hour, then infusion was prepared in the same manner for second hour and infused in same manner. Under all aseptic precaution spinal anaesthesia was performed in sitting position at L2-L3 or L3-L4 intervertebral space with 23G quincke spinal needle. Inj.bupivacaine 0.5% hyperbaric,

3 ml was injected slowly. After completion of subarachnoid block, patients were immediately turned to supine position and time of subarachnoid injection was noted.

Inj.dexmedetomidine iv infusion of 0.3mcg/kg/hr was started in patients included in Group D-0.3 and 0.5mcg/kg/hr was started in patients included in Group D-0.5. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate (RR), spO2 and sedation using OASS were recorded baseline before loading dose of inj.dexmedetomidine, at every 5 minute till first 30 minutes, followed by every 15 minutes till the end of the surgery and postoperatively every 5 minutes for 15 minutes. Infusion of maintenance dose of inj.dexmedetomidine was stopped 10minutes before completion of the surgery. Sedation was assessed with OASS – Observer's assessment of alertness/sedation [3].

5 Responds readily to name spoken in normal tone

4 Lethargic responses to name spoken in normal tone

3 Responds only after name is called loudly and/or repeatedly

2 Responds only after mild prodding or shaking

1 Does not respond to noxious stimuli

The onset of sedation was taken as time taken to reach OASS scale of 3. The infusion of inj. dexmedetomidine continued at a constant rate throughout the procedure and was not altered till a sedation scale of 3.

For Statistical analysis collected data was entered in the excel data sheet and data analysis was done with the help of epi Info.7.2 software. Data were compiled using Microsoft excel and were statistically described in terms of mean + standard deviation (SD) or frequencies (number of cases) and percentage accordingly. For comparing categorical data Chi square test was performed. Unpaired t test was used to compare two population means. P value < 0.05 was considered statistically significant.

Results

(Table 1) shows demographic characteristics. There was statistically insignificant difference between two groups with regards to age, sex, height, weight and ASA grade (P >0.05).

(Figure 1) shows comparison of HR between two groups. There was a decrease in HR in both groups but it was statistically insignificant (P value > 0.05).

(Figure 2,3,4) shows comparison of SBP, DBP and MAP. There was a decrease in SBP, DBP and MAP in both groups, although there was no statistically significant difference in both groups (P>0.05).

(Table 2) shows comparison of respiratory rate and spO2 between two groups. There was no statistical significance found between respiratory rate and spO2 in both groups intraoperatively (P>0.05).

(Figure 5) and (Table 3) shows sedation score. In group D-0.3 72% patients were sleeping comfortably but easily arousable and 8% patients were in deep sleep. While in group D-0.5 70% were sleeping comfortably but easily arousable and 15% in deep sleep.

There were intraoperative incidences of bradycardia in 1 (2.5%) patients in group D-0.3 and in 3 (7.5%) patients in group D-0.5 and hypotension in 2 (5%) patients in group D-0.3 and 4 (10%) patients in group D-0.5. There was no postoperative incidence of bradycardia or hypotension. There were also no complications of nausea/vomiting, respiratory depression or shivering.

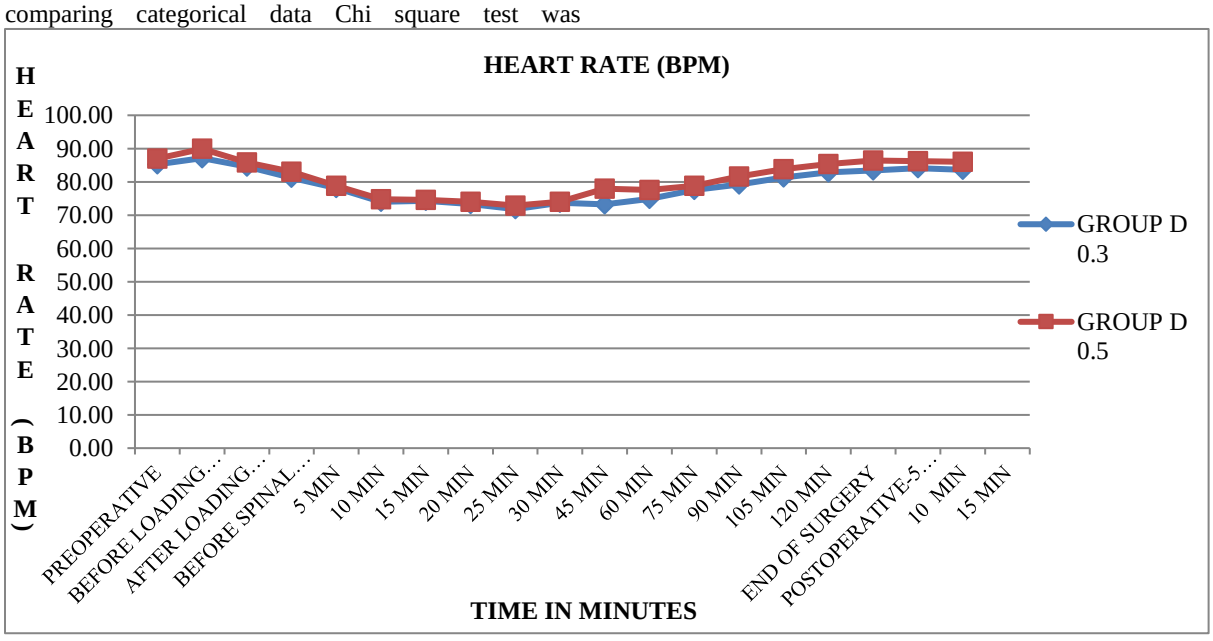

Figure 1- Comparison of heart rate (Mean ± SD)

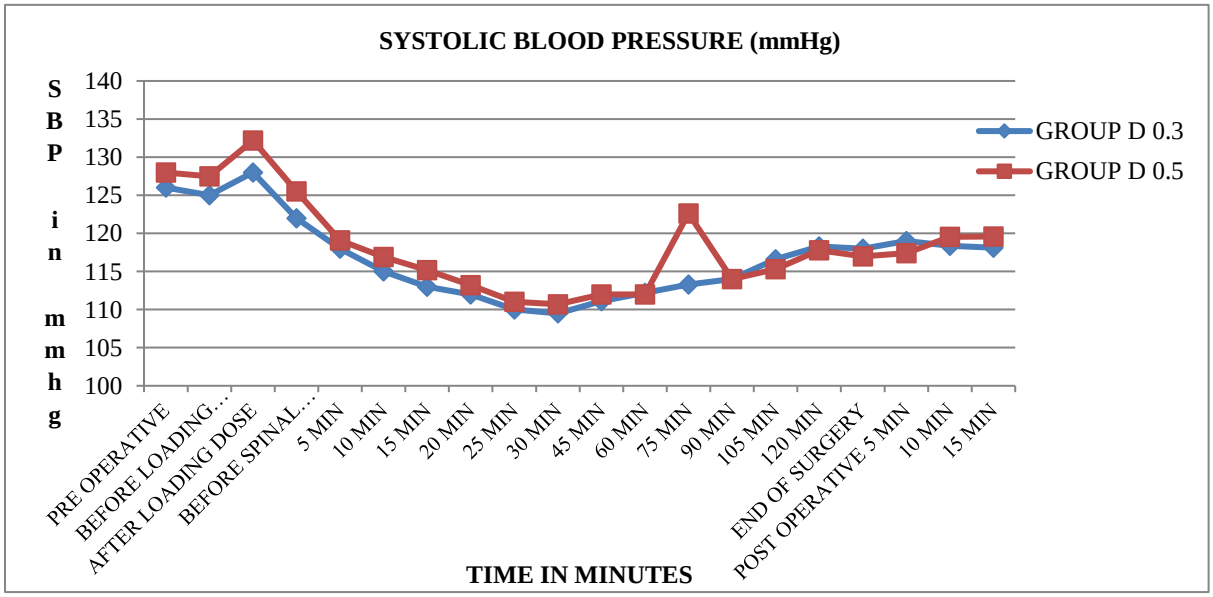

Figure 2- Comparison of systolic blood pressure (Mean ± SD)

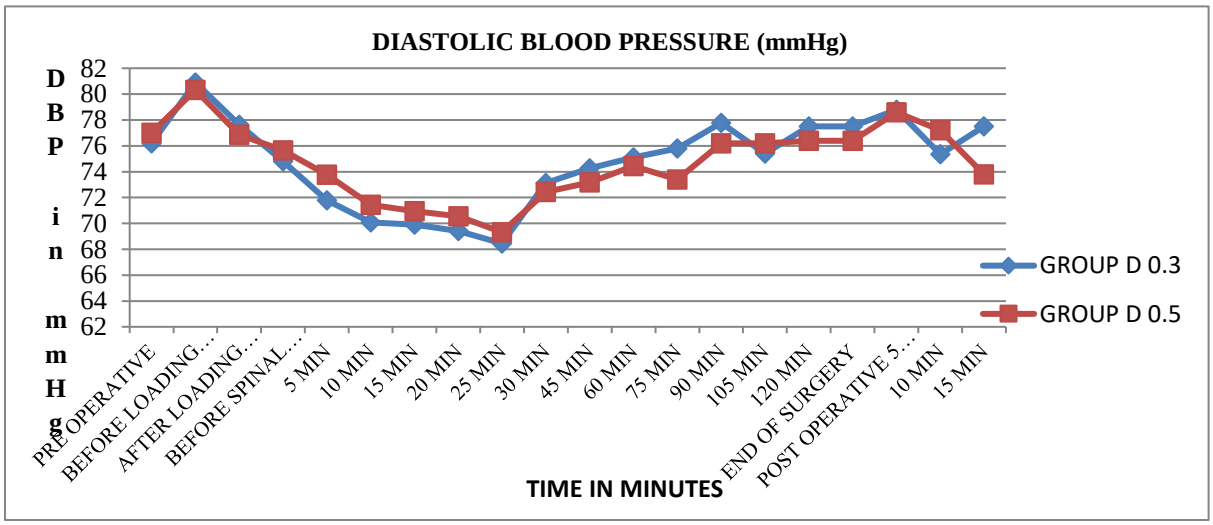

Figure 3- Comparison of diastolic blood pressure (Mean ± SD)

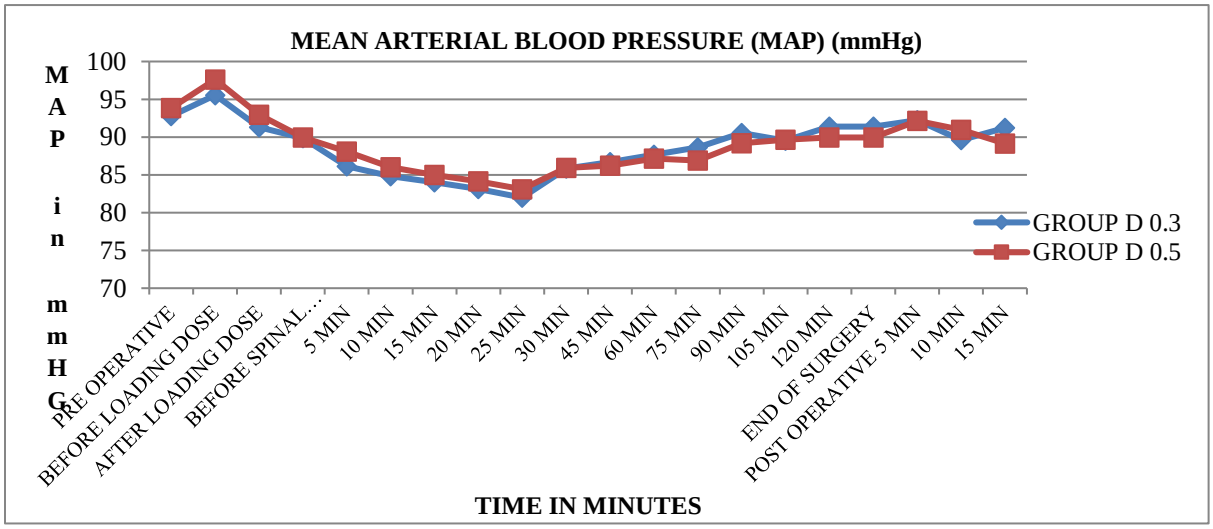

Figure 4- Comparison of mean arterial blood pressure (Mean ± SD)

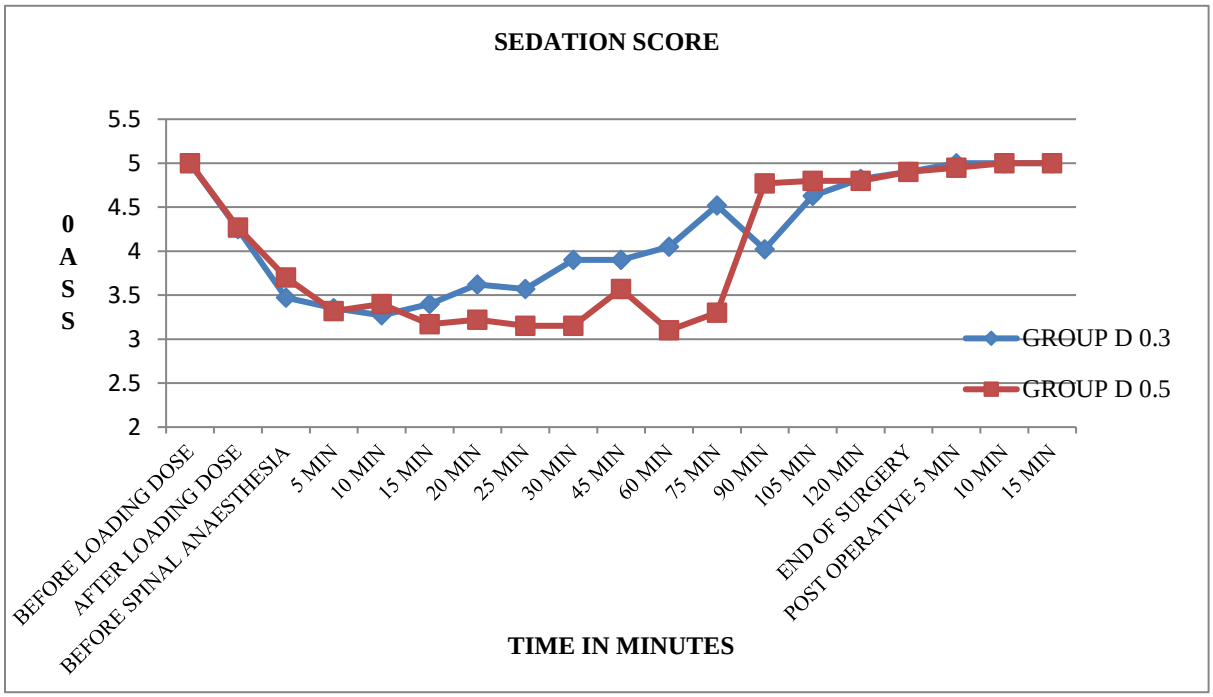

Figure 5- Comparison of sedation score

Table 1- Demographic characteristics

		Group D-0.3	Group D-0.5	P value
No. of patient		40	40	>0.05
Age (years) (mean ± SD)		43.9 + 11	35.3 + 20	>0.05
Height (in cm) (mean ± SD)		158.2 + 2.34	157.7 + 4.24	>0.05
Weight (in kg) (mean ± SD)		57.62 + 2.5	57.27 + 1.42	>0.05
Sex (M:F)		19:21	20:20	>0.05
ASA	Grade-I	18	19	>0.05
	Grade- II	22	21	>0.05

Table 2- Comparison of respiratory rate and spO2 (Mean ± SD)

Parameters	Group D-0.3 (mean ± SD)	Group D-0.5 (mean ± SD)	P value
Respiratory rate/minute	14.7 + 0.54	14.4 + 0.82	P>0.05
SpO2 (%)	98.9 + 0.1	99.0	P>0.05

Table 3- Sedation score (according to OASS)

Sedation score	No. (%) of patients	
	Group D-0.3	Group D-0.5
5	0	0
4	8 (20%)	6 (15%)
3	29 (72%)	28 (70%)
2	3 (8%)	6 (15%)
1	0	0

Discussion

Hwoe-Gyoeng et al (2013) [4] conducted a study to find optimal dose of dexmedetomidine for sedation during spinal anesthesia. They recruited 180 patients between age 20 to 70 years. After spinal anesthesia, a loading dose of dexmedetomidine (1 μg/kg) was administered for 10 min, followed by the maintenance infusion of the following: Group A (n = 33; normal saline), Group B (n=35; dexmedetomidine 0.2 μg/kg/hr), and Group C (n=39; dexmedetomidine 0.4 μg/kg/hr). They reported no significant difference between the mean arterial pressure between these three groups. Sang Hi et al (2014) [15] conducted a similar study in which they observed that the

heart rate in both DMT (dexmedetomidine) groups dropped by 8-9 beats per minute. However between the two DMT groups there was no significant difference regarding the heart rate and other hemodynamic values. These findings are similar to the results of our study. In our study though there was no statistically significant difference of sedation score between the two groups but group D showed consistent lower sedation score between 15 minutes to 75 minutes. (figure 5) Mean arterial pressure and heart rate dropped in both the study groups but there was no statistically significant difference between both the groups. It is likely that the frequency of hypotension does not increase when a low dose of dexmedetomidine is administered with spinal anesthesia.

Belleville JP (1992) [12] evaluated four dose levels of dexmedetomidine (0.25, 0.5, 1.0 and 2.0 μg/kg iv over 2 min) in 37 healthy male volunteers in double blind, placebo controlled experiment. Dexmedetomidine is a highly selective centrally acting alpha2-adrenergic agonist thought to provide significant sedation without appreciable respiratory effects. Measurements of sedation, arterial blood gases, resting ventilation, hypercapnic ventilatory response and metabolic rate (O2 consumption and CO2 production) were performed at baseline, 10 min after dexmedetomidine infusion, and thereafter at the end of each subsequent 45min period. No respiratory depression was found in any of the groups. In present study, we did not compare arterial blood gases, resting ventilation, hypercapnic ventilatory response and metabolic rate but compared two different doses of dexmedetomidine for intra operative and postoperative hemodynamic parameters and moderate sedation during spinal anaesthesia and found no statistically significant difference. (figure 5) No other complications like respiratory depression, nausea, vomiting or urinary retention were observed.

Hong et al (2012) [13] studied the effects of intravenous dexmedetomidine in doses of 1.0 μg/kg (Group DMT) or normal saline (Group control) on low dose bupivacaine (1.2 ml) spinal anaesthesia in elderly patients. Bradycardia was more profound in group DMT than in control group (24.0% vs. 3.8%). In our study, age in group D-0.3 was 43.9+11 (mean ± SD) and in group D-0.5 was 35.3+20. The loading dose was also 1 μg/kg but there was no profound bradycardia. This might be due to slow intravenous injection of diluted dexmedetomidine over 10 minutes.

Mi Hyeon Lee et al (2014) [14] tried to find out appropriate amounts of single dose dexmedetomidine in the absence of maintenance infusion to prolong the duration of spinal anesthesia in a clinical setting in three groups receiving normal saline (control group, n=20) or 0.5 or 1.0 μg/kg dexmedetomidine (D-0.5 group, n=20; D-1, n=20) iv prior to spinal anesthesia. In their study, dexmedetomidine provided sufficient sedation (83.6 ± 40.4 vs 89.9 ± 42.7 min), and the duration did not differ between the two dexmedetomidine (D-0.5 and D-1) groups. However, there were no patients with oxygen desaturation in dexmedetomidine groups. The incidences of hypotension and bradycardia showed no differences among the three groups. In our study we also used maintenance infusion after loading dose of dexmedetomidine and we used OASS score for sedation and both the groups provided sufficient sedation with no statistically significant difference. (figure 5) There were no incidence of respiratory depression and statistically insignificant difference in the incidence of bradycardia (2.5% in group D-0.3 vs 7.5% in group D-0.5) and hypotension (5% in group D-0.3 vs 10% in group D-0.5).

Singh DR et al (2017) [15] did a similar study in the group of 60 patients (two groups of 30 each) to receive dexmedetomidine in a loading dose of 1 μg/kg in both groups followed by continuous infusion of 0.3 μg/kg/h in Group D-0.3 and 0.5 μg/kg/h in Group D -0.5 and observed that trends in heart rate exhibited a decrease in both the dexmedetomidine groups, although there was no statistically significant difference found between the two groups. Median observer assessment sedation score (OASS) ranged between four and three at all times during dexmedetomidine infusion in Group D-0.3 and between three and two in Group D-0.5. In our study we had sample size of 80 with 40 in each group with similar loading and infusion doses of dexmedetomidine. There was decrease in heart rate in both the groups with no statistically significant difference. Median OASS ranged between three and four in both the groups. (Table 3) Current findings are similar to above study.

Gaye Aydin et al (2018) [16] evaluated the effects of intravenous infusion of inj.dexmedetomidine during spinal anaesthesia with that of saline infusion. Group I received iv dexmedetomidine infusion at a rate of 0.2 μg/kg/hr. Control patients in Group II received iv saline infusion at a rate of 0.5 mg/kg/hr. Dexmedetomidine infusion had a hemodynamic depressant effect intraoperatively. It had no significant effect on peripheral oxygen saturation and respiratory rate. In our study we used dexmedetomidine infusion at the rates of 0.5 μg/kg/hr and 0.3 μg/kg/hr without saline control group. All hemodynamic parameters decreased in both the groups but there was no statistically significant difference. There was also no statistically significant difference in peripheral oxygen saturation and respiratory rate in both the groups.

Benefit of this study is that it can guide physicians to use lower dose of dexmedetomidine to achieve same level of sedation with same hemodynamic stability.

Limitations of this study are that further studies will be required using these dose regimens on children, elderly, obese, pregnant patients and patients with comorbidities. Secondly, this study did not look into effects of dexmedetomidine on onset and regression of motor and sensory effects of spinal anesthesia.

Conclusion

In this study, both the dose regimens of inj.dexmedetomidine provided satisfactory sedation levels for patients under spinal anesthesia. Hemodynamic stability was also comparable for both groups. Side effects noted were bradycardia and hypotension which was statistically insignificant in both groups. Thus, we conclude that after a loading dose of 1 µg/kg intravenously, an intravenous infusion of dexmedetomidine at a lower rate of 0.3 µg/kg/hr is equally effective as infusion at a higher rate of 0.5 µg/kg/hr in providing sedation for patients undergoing surgeries under spinal anesthesia.

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