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To Study the Efficacy and Heamodynamic Response to Dexmedetomidine as Hypotensive Agent in Elective Spine Surgeries

Smruti Govekar[1], VRR Chari[2], Amey Sable[3], Ashwini Khamborkar[4]

[1,3,4]Third Year Resident [2]Professor, Department of Anesthesiology, Dr. D.Y. Patil Medical College, Hospital & Research Centre, Dr. D.Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra 4011018 India.

Abstract

Background: Spine surgeries require reduced intraoperative blood pressures to make better visualization of surgical site. Deliberate hypotension or controlled hypotension have been preferred technique used for many surgical procedures to attain clear surgical fields. *Aim:* The aim of our study is to evaluate the efficacy and hemodynamic response to IV Dexmedetomidine and placebo [Normal saline] as hypotensive agent in elective spine surgeries. *Methods:* Sixty patients between age group of 18–60 years were selected who were posted for elective spine surgeries. They were divided into two groups of 30 each i.e. Dexmedetomidine Group and Normal Saline Group and were be given their respective drug. Group D: Inj. Dexmedetomidine 100 mcg [diluted in 50 ml of 0.9% Normal saline]. Group N: 50 ml of 0.9% of normal saline. Patients in the D Group received 1 mcg/kg infusion (diluted in 50 ml of 0.9% normal saline) over a period of 10 min prior to premedication. After induction of anesthesia, patients in the D Group received a continuous infusion of Dexmedetomidine at 0.2 mcg/kg/h, whereas patients in the N Group received infusion of Normal saline at same dose as dexmedetomidine. The hemodynamic parameters Pulse Rate (PR), Systolic Blood Pressure, Diastolic Blood Pressure and Mean Arterial Blood Pressure (SBP, DBP, MAP), Respiratory Rate (RR), SpO_2 were studied in all the groups at baseline, after giving drug, after intubation, 15 minutes, 30 minutes and 45 minutes, 60 minutes, 75 minutes, 90 minutes, 105 minutes, 120 minutes, after stopping drug and after extubation. Postoperative sedation score was also measured. Patient were shifted to postanesthesia care unit and monitored for hemodynamic parameters, Ramsay sedation score and adverse effects if any. The statistical analysis was done based on Student's *t*-test for continuous variables and Chi-square test for categorical variables. Final interpretation will be based on *Z*-test with 95% level of significance. *Results:* Patients in D Group achieved desired MAP as compared to normal saline (placebo) group with good control over heart rate. With no significant difference in postoperative sedation score was found in patients with Dexmedetomidine group as compared to normal saline (placebo). *Conclusion:* Dexmedetomidine is an effective drug for achieving controlled hypotension and thus, can be used as hypotensive agent in spine surgery to maintain clear surgical field.

Keywords: Hypotension; Deliberate hypotension; Dexmedetomidine; Spine surgery; Surgical field.

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Corresponding Author: VRR Chari, Professor, Department of Anesthesiology, Dr. D.Y. Patil Medical College, Hospital & Research Centre, Dr.D.Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra 4011018 India.
E-mail: smrutigovekar114@gmail.com

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Introducton

Spine surgeries for traumatic spine fractures or tumors or other etiologies were known to cause tremendous blood loss during surgery. This resulted in severe complications to deal with intraoperative as well as postoperative. It also made surgical field visualization difficult. "Controlled hypotension or deliberate hypotension" is a commonly used technique to limit blood loss and improve visualization of the operative field during surgery. This involves reducing arterial pressure MAP to 65 mm Hg reversibly according to various literature and maintain the same throughout the surgery.[1,2] It reduces intraoperative blood loss which will facilitate good surgical field exposure also resulting in faster surgeries ultimately reducing intraoperative and postoperative need of blood transfusions. There are various anecdotal reports to describe this technique and have been published since the 1970s[3,4] Various types of trials have been undertaken mainly prospective type to demonstrate the efficacy of deliberate hypotension, which were aimed to decrease the blood loss and transfusion necessity during major spine or neurological surgery.[5,6] Dexmedetomidine is a potent and highly selective α2-adrenergic agonist, with a differential affinity for the α_2 : α_1 receptors in a ratio 1,620:1. It is a sedative, analgesic, and possesses anesthetic sparing effect and sympatholytic properties too. The central and peripheral sympatholytic action of Dexmedetomidine by binding to α2 adrenergic receptors brings about dose-dependent decrease in Mean Arterial Blood Pressure (MAP), Heart Rate (HR), cardiac output, and norepinephrine release.[7] In this study, the efficacy and hemodynamic response of Dexmedetomidine would be studied as hypotensive agent in elective spinal surgeries.

Materials and Methods

After approval from the hospital ethical committee and informed written consent, this study was carried out in Department of Anesthesiology, DY Patil Hospital and Research Centre, Pune. It was conducted in 60 adult patients belonging to American Association of Anesthesiologists (ASA) Grade I/II in age Group of 18–60 years of age and posted for elective spine surgery under General Anesthesia.

Patients who were unwilling, or with respiratory of cardiac dysfunction or with renal or liver impairement were not included in the study. Also, patients with any coagulopathy, heart rate < 65 beats/min prior to surgery or having known drug allergy were excluded from the study.

After detailed preanesthetic evaluation, routine and specific investigation, each patient was informed regarding nature, purpose of the study. Preoperative adequate fasting hours (6–8 hrs) were confirmed. The patients were randomized into two groups using the equal group random allocation method, that is, D and N Groups. The anesthesiologist loading the drugs and administering the premedication was different than the one conducting the case and managing patients in postanesthesia care unit. Thus, both the anesthesiologists were blinded to the assignment.

Patients were prepared by securing 20 gauge Intravenous (IV) cannula, applying basic monitoring like plethysmography, standard 5-lead Electrocardiography (ECG), noninvasive blood pressure. Patients in the D Group received 1 µg/kg infusion (diluted in 50 ml of 0.9% normal saline) over a period of 10 min prior to premedication. While patients on N Group received normal saline in the rate similar to Group D.

After premedication with injection ondansetron 4 mg IV, injection glycopyrrolate 0.2 mg IV, injection midazolam 0.05 mg/kg and injection fentanyl 2 µg/kg in both the groups, anesthesia induction was done with injection propofol 2 mg/kg. Tracheal intubation was facilitated by injection vecuronium bromide 0.1 mg/kg. The patients was then positioned prone on a Relton's frame. Necessary precautions were taken to protect pressure points and avoid nerve injury and limb ischemia. Patients in the D Group received a continuous infusion of Dexmdetomidine at 0.2 mcg/kg/h, whereas patients in the N Group received continous infusion of Normal saline at 0.2 mcg/kg/hr, similar to D Group.

Throughout the surgery heart rate, blood pressure [S.B.P, D.B.P., Mean B.P], Oxygen saturation, $EtCO_2$, Postoperative sedation, Urine output, Blood loss, Temperature were continulusly monitored.

The above parameters were measured at the following time points:

Baseline (Tb), at the start of the hypotensive agent - (Ts), immediately after intubation - (Ti), after 15 minutes (T15), after 30 minutes (T30), after 45 minutes (T45), after 60 minutes (T60), after 75 minutes (T75), after 90 minute (T90), after 105 minutes (T105), after 120 minutes after induction (T120), at the point of stoppage of administration of hypotensive agent (Tt) and at extubation (Te).

Target MAP was taken as 65–85 mm Hg and target HR was taken as more than 60 beats per minute.

Modified Ramsay sedation scale was used measure postoperative sedation.

Modified Ramsay sedation scale

Score	Characteristics
1	agitated, restless
2	cooperative, tranquil
3	responds to verbal commands while sleeping
4	brisk response to glabellar tap or loud noise while sleeping
5	Sluggish response glabellar tap or loud noise while sleeping
6	No sluggish response to glabellar tap or loud noise while sleeping

Adequate data was collected, compiled and tabulated in stipulated time. The statistical analysis was done based on Student's *t*-test for continous variables and Chi-square test for categorical variables. Final interpretation were done based on *Z*-test with 95% level of significance.

Results

The present study was conducted on 60 adult patients.

The demographic profile was comparable in both the study groups as given in Table I. The two groups were similar in age, weight, sex and ASA status.

Table 1: Demographic profile

	Dexmedetomidine	Normal saline	*p* - value
Age (in years)	34.63 ± 10.555	36.43 ± 10.464	5.10
Sex (male/ female)	16/14	18/12	0.79
Weight (kgs)	57.60 ± 7.295	54.27 ± 5.477	0.062
ASA Grade I/II	18/12	19/11	0.791

As shown in Fig. 1. All the patients in D Group achieved target MAP and maintained it throughout the surgery. 30 minutes after induction MAP was significantly low in Group D (86.73 ± 3.12 mm Hg) as compared to Group N (97.20 ± 2.49 mm Hg). It was also observed that mean Heart rate in Group D was sigmificantly lower than Group N (Fig. 2).

Table 2: Mean Arterial Blood Pressure distribution between Dexmedetomidine Group and the Normal Saline Group

Mean Arterial Blood Pressure (mm Hg)	Group	Mean	SD	*t* - test	*p* - value
Baseline	Dexmedetomidine	97.47	4.46	-1.73	0.08
	Normal saline	98.56	2.92		
After giving drug	Dexmedetomidine	97.09	3.58	-1.76	0.08
	Normal saline	98.13	2.70		
After intubation	Dexmedetomidine	99.42	3.58	-1.74	0.08
	Normal saline	100.87	2.70		
After 15 mins	Dexmedetomidine	96.64	2.40	-2.10	0.04
	Normal saline	97.84	2.64		
After 30 mins	Dexmedetomidine	86.73	3.12	-14.33	<0.001
	Normal saline	97.20	2.49		
After 45 mins	Dexmedetomidine	81.71	3.31	-20.89	<0.001
	Normal saline	96.76	2.10		
After 60 mins	Dexmedetomidine	77.56	3.63	-25.02	<0.001
	Normal saline	96.56	2.38		
After 75 mins	Dexmedetomidine	76.82	4.79	-20.19	<0.001
	Normal saline	96.73	2.10		
After 90 mins	Dexmedetomidine	76.42	5.19	-19.27	<0.001
	Normal saline	96.56	2.38		
After 105 mins	Dexmedetomidine Ondansetron	75.58	5.07	-20.31	<0.001
	Normal saline	96.42	2.41		
After 120 mins	Dexmedetomidine	75.31	5.30	-19.86	<0.001
	Normal Saline	96.44	2.42		
After stopping drug	Dexmedetomidine	75.40	5.10	-20.39	<0.001
	Normal Saline	96.44	2.42		
After extubation	Dexmedetomidine	97.16	3.23	-1.634	0.108
	Normal Saline	98.42	2.73		

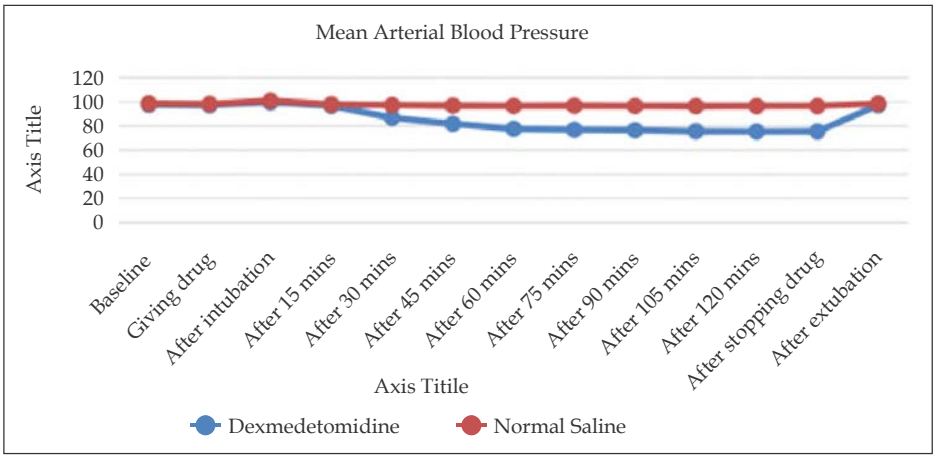

Fig. 1: Line diagram showing MAP in both the study groups

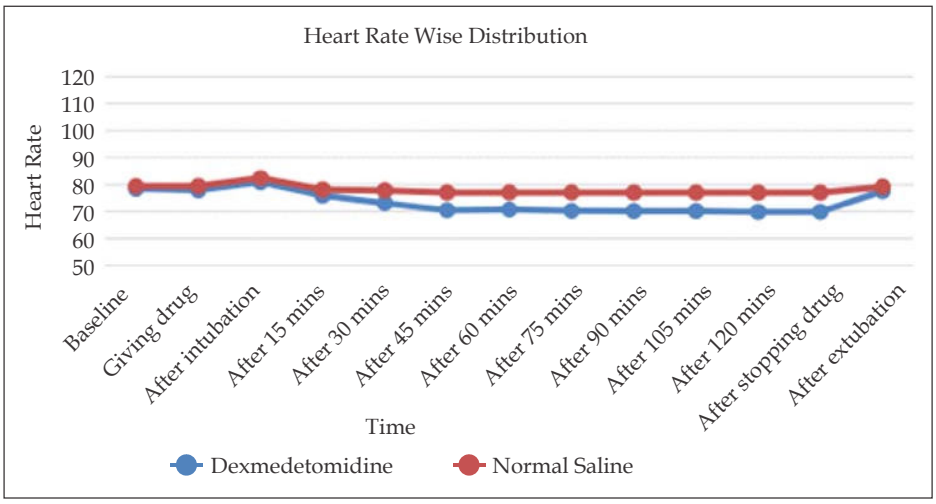

Fig. 2: Line diagram showing Heart rate in both the study groups

Table 3: Heart rate wise distribution between Dexmedetomidine group and the Normal Saline group

Heart Rate (beats/min)	Group	Mean	SD	*t* - test	*p* - value
Baseline	Dexmedetomidine	78.53	2.403	-1.407	0.165
	Normal Saline	79.47	2.726		
After giving drug	Dexmedetomidine	78.00	2.407	-2.209	0.312
	Normal Saline	79.47	2.726		
After intubation	Dexmedetomidine	81.00	2.407	-2.209	0.080
	Normal Saline	82.47	2.726		
After 15 mins	Dexmedetomidine	76.00	3.201	-2.111	0.39
	Normal Saline	78.20	2.644		
After 30 mins	Dexmedetomidine	73.20	3.263	-5.966	<0.001
	Normal Saline	77.87	2.776		
After 45 mins	Dexmedetomidine	70.73	4.653	-6.140	<0.001
	Normal Saline	77.13	3.309		
After 60 mins	Dexmedetomidine	70.73	4.653	-6.065	<0.001
	Normal Saline	77.13	3.309		
After 75mins	Dexmedetomidine	70.27	5.245	-6.026	<0.001
	Normal Saline	77.13	3.309		

(Contd.)

Heart Rate (beats/min)	Group	Mean	SD	*t* - test	*p* - value
After 90 mins	Dexmedetomidine	70.20	5.391	-6.026	<0.001
	Normal Saline	77.07	3.269		
After 105 mins	Dexmedetomidine	70.20	5.345	-5.952	<0.001
	Normal saline	77.07	3.269		
After 120 mins	Dexmedetomidine	69.87	5.823	0.852	<0.001
	Normal Saline	77.07	3.269		
After stopping drug	Dexmedetomidine	69.90	5.391	-6.026	<0.001
	Normal Saline	77.07	3.269		
After extubation	Dexmedetomidine	77.70	2.562	-2.260	0.28
	Normal Saline	79.27	2.803		

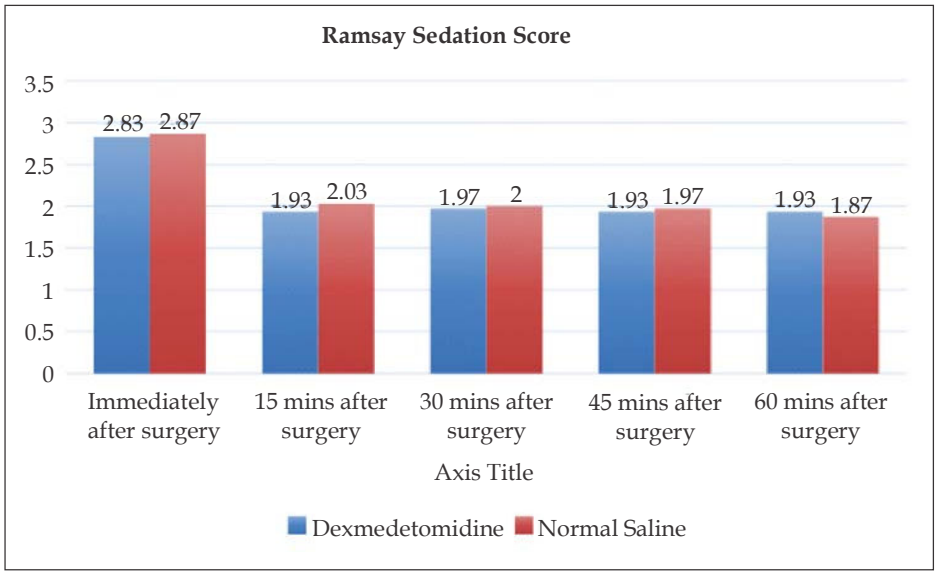

Fig. 3: Bar diagram showing Ramsay Sedation Score

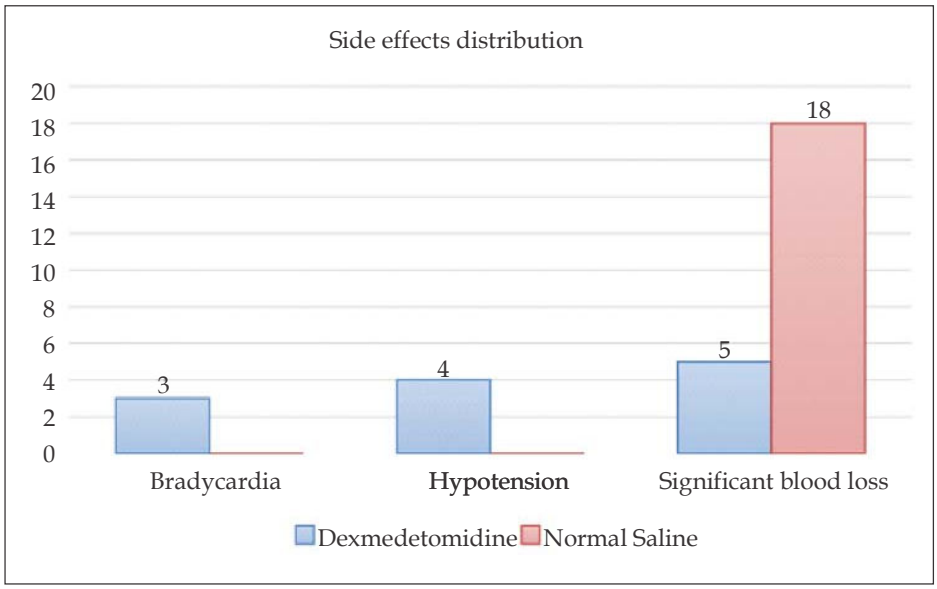

Fig. 4: Bar diagram showing distributon of side-effects between both the study groups

Table 4: Mean Ramsay Sedation Score distribution between Dexmedetomidine Group and the Normal Saline Group

Ramsay Sedation Score	Dexmedetomidine		Normal Saline		*t*-test	*p* - value
	Mean	SD	Mean	SD		
Immediately after surgery	2.83	0.461	2.87	0.507	-0.266	0.791
15 mins after surgery	1.93	0.254	2.03	0.183	-1.752	0.085
30 mins after surgery	1.97	0.183	2.00	0.263	-0.571	0.570
45 mins after surgery	1.93	0.254	1.97	0.183	-0.584	0.561
60 mins after surgery	1.93	0.254	1.87	0.346	0.851	0.398

The maximum decrease in heart rate in Group D was at 120 minutes (with mean 69.87 ± 5.823 beats/min). However, there was no significant changes in heart rate in Group N at start immediately after intubation and remained the same throughout the surgical duration. Clinically and statistically, there was no significant difference in the Ramsay Sedation Score (RSS) in the two groups, Fig. 2. As far as adverse events are concerned 3 patients with Dexmedetomidine had bradycardia which was treated with anticholinergics like Inj. Atopine or Inj. Glycopyrrolate. 4 patients in Dexmedetomidine Group had hypotension which was treated with vassopressors. In Normal Saline Group pateints there were no side effects like bradycardia or hypotension as seen in Dexmedetomidine Group (Fig. 3).

However, significant blood loss was seen in 18 patients with Normal Saline Group as compared to Dexmedetomidine where it was in only 5 patients (Fig. 4).

Disscusion

Anesthesia techniques for spine surgery is challenging to anesthesiologist. Many of the patients are of chronic pain complaints, of which mostly are of geriatric age group. These patients mostly have comorbidities with or with autonomic impairement. The main concerns during surgery which are challenging is to maintain hemodynamic stability without causing the intraoperative patient awareness to the surgery. This means keeping the plane of anesthesia deep enough yet no hemodynamic parameters to be affected.

This type of surgeries are often related to blood loss and large fluctuation in blood pressure during its course both intraoperative and postoperative. The main aim of anesthesiologist should be to maintain the blood pressure keeping in mind the blood less surgical site with adequate perfusion of end organs.

This practice of hypotensive anesthesia is being widely used for various types of surgeries using different anesthetic agents and drugs. As far as spine surgeries are concerned , various agents have been used till date. It includes drugs like propofol, esmolol, clonidine, inhalationals like isoflurane and sevoflurane etc. Alpha 2 adrenergic agonist are now-a-days being used and investigated in anesthetic practice as far as their sympatholytic, hemodynamic stabilizing, analgesic properties.

This study was done primarily, to compare the efficacy and hemodynamic response to intravenous Dexmedetomidine and placebo (Normal Saline) used as hypotensive agent in elective spine surgeries. Secondarily, to compare the sedation postoperatively in both the groups. And to study the side effects if any in both the groups. We choose mean arterial pressure as an important parameter to estimate the amount of hypotension. As MAP is a best indicator that reflects us the amount tissue perfusion. Baseline mean arterial pressure in both our study groups were comparable.

However, it was found that there was fall in mean arterial pressure at 30 minutes in dexmedetomidine group and continue to decrease throughout the surgery. The maximum decrease in MAP was seen after stopping drug in Dexmedetomidine Group (75.40 ± 5.10 mm Hg). For our study, we had considered lower-limit of MAP as 65 mm Hg. But it was observed that MAP did not fall below 65 mm Hg in any of the patients in our study group. For normal saline group there was no fall in mean arterial pressure throughout the surgery. There was increase in MAP in both the study groups at extubation. Similar observation was found in a study conducted by Ramila H Jamaliya et al. (2014).[8] they found that MAP was decreased from baseline values in dexmedetomidine group after induction, and remain low throughout the surgery and increased at the time of extubation. This finding is similar to our findings.

One more study, done by, Shams T, et al. (2013)[9] states that if dexmedetomidine infusion has been started 10 mins prior to surgery in dose of 1 mcg/kg/hr there is significant decrease in MAP and mean heart rate throughout the surgery. In our study, we also have similar finding with same loading dose of dexmedetomidine. These effects of dexmedetomidine are mainly due to its sympatholytic action on alpha-2 adrenergic

receptors present in blood vessels.

In our study, there was significant decrease in heart rate at 15 mins onwards in Group D with mean 76 ± 3.201 mm Hg SD and that persisted throughout the surgery and increased after extubation. The maximum decrease in heart rate in Group D was at 120 minutes with mean 69.87 ± 5.823 mm Hg. While there was no significant variation in heart rate from baseline in Group N from start of surgery and it remained same throughout the course of surgery.

In a study, by Sukhminder Bajwa et al (2016)[10], compared nitroglycerin, esmolol and dexmedetomidine as hypotensive agents in middle ear surgeries. They found that there was significant decrease in mean heart rate after giving the loading dose of the drug. They also found that heart rate increased after extubation . The mean heart rate remained low significantly through out the surgery compared to nitroglycerin and esmolol. They also stated that the cause of lower heart rate with dexmedetomidine is due to its sympatholytic properties.

This findings are similar to the findings found in our study. In our study, we used Ramsay Sedation Score to evaluate the postoperative sedation of patients from the study drugs used and compare the level of sedation in both the study groups. And we found that, there was no significant difference in both the study group for postoperative sedation using Ramsay Sedation Score**.** This findings are similar to the findings in a study conducted by Neamat I. Abel Rahman (2014)[11] where they found no significant difference in extubation or post operative sedation in dexmedetomidine group compared to placebo (normal saline). The limitations to our study was relatively small sample size, BIS monitoring or arterial line monitoring could not be done due lack of resources.

Conclusion

Thus, we conclude that, Dexmedetomidine in 1 mcg/kg loading dose given 10 minutes prior to induction and a continuous infusion at 0.2 mcg/kg/h intraoperatively maintains target mean arterial pressure and target heart rate to during the surgery. Dexmedetomidine thus helps in producing "deliberate or controlled" hypotension in spine surgeries. This helps in reducing the bloodloss during the surgery and helps in maintaining bloodless surgical site.

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