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COMPARATIVE STUDY OF EFFECTS OF TWO DIFFERENT DOSES OF INTRAVENOUS DEXMEDETOMIDINE IN SPINE SURGERIES

KEYWORDS: Tympanoplasty, Canalplasty, middle ear, pure tone audiogram, hearing threshold.

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ABSTRACT

Background: *Present study was conducted to compare effectiveness of two doses of Dexmedetomidine to find the minimum dose of the drug required to achieve stable haemodynamic parameters with least side effects in spine surgery.*

Material and methods: *In this prospective randomized double blind study, two groups of 40 patients each received Dexmedetomidine intravenously. After bolus of 1 µg/kg over 10 minutes, Group A received Dexmedetomidine 0.4µg/kg/hr and Group B 0.2µg/kg/hr as maintenance infusion. Intra-operative monitoring of pulse rate, blood pressure, ECG and oxygen saturation was done. Extubation response, modified Aldrete's score, duration of extubation response, time to extubation and surgeon's satisfaction using bleeding score was noted . Data was analyzed using students't-test & chi square test.*

Results: *Demographic parameters were comparable in both the groups. Heart rate and blood pressure in both the groups were comparable at all times. The duration of extubation response was less in group A (3.28±0.89 min) than Group B (4.23±1.30 min; p=0.000). The difference in mean extubation time (min) in both the groups was statistically insignificant. (Group A: 19.62±6.44; Group B: 17.52±6.42; p=0.149). Modified Aldrete's score at 10th minute post-extubation showed earlier recovery in Group B (9.55±0.51) than Group A (8.42±0.50; p=0.001). Incidence of adverse cardiovascular events was low and comparable in both the groups. Quality of operative field was comparable in both the groups (bleeding score 2- in 85% and 82.5% patients, score 1 - 15% and 17.5% patients respectively, p = 0.762)*

Conclusion: *In spine surgery, dexmedetomidine when used as adjuvant to general anaesthesia in the dose of 0.2µg/kg/hr or 0.4µg/kg/hr provides intra-operative haemodynamic stability and improves quality of operative field with minimal side effects although dexmedetomidine 0.2µg/kg/hr provides earlier recovery than dexmedetomidine 0.4µg/kg/hr.*

Introduction

During spine surgery, induced hypotension is the preferred method to provide bloodless operative field which decreases risk of injury to major neurovascular structures and also operative time.[1] Surgeons prefer patients to be conscious and able to respond to commands immediately after surgery for early neurological assessment which plays a critical role in detection of new neurological deficits.[2,3] Dexmedetomidine, a new short acting, highly selective and potent 2-adrenergic agonist, can be used to produce induced hypotension. There are only few studies in literature using dexmedetomidine in spine surgeries where dexmedetomidine was compared with either placebo or drugs like nitroglycerine, esmolol, nimodipine, etc.[1,4,5,6] We did not find any study comparing effects of different doses of dexmedetomidine on quality of surgical field and recovery profile in addition to haemodynamic stability in spine surgery. We decided to study effects of two doses of dexmedetomidine (0.2 and 0.4mcg/kg/hr) after a bolus of 1mcg/kg in terms of haemodynamic stability, recovery profile and quality of operative field.

Material and methods

A prospective randomized double blind study was conducted after approval from the institutional ethical committee. ASA Grade 1 and 2 patients between age group 18-65 years undergoing elective spine surgeries were included in the study. Patients with significant cardiac disease, pregnancy or nursing mothers, morbid obesity (BMI>35), patients with bradycardia (HR <60/min.), uncontrolled hypertension (Systolic BP >160 mmHg &/ or Diastolic > 100 mmHg.) were excluded. Pre-operative baseline parameters like heart rate (HR), blood pressure (Systolic, Diastolic and mean) and oxygen saturation (SPO2) were recorded. Patients were preloaded with 5ml/kg of Ringer lactate. Dexmedetomidine (AlphadexTM, 2ml ampoule by Themis Medicare Limited) infusion @ 1µg/kg over 10 minutes was started. HR, BP, SPO2 and ECG changes were recorded during infusion. After loading dose, maintenance infusion was started.

A sample size of 20 patients per group was needed to detect an intergroup difference of at least 10% in blood pressure and HR with a power of 0.80 and of 0.05. We selected a sample size of 40 patients per group.

Patients were randomly divided using sealed envelop into two groups - each group containing 40 patients. Group A received dexmedetomidine 0.4µg/kg/hr and Group B received 0.2µg/kg/hr as maintenance. Dexmedetomidine solution was prepared in a 50 ml syringe in concentration of 4 µg/ml and 2µg/ml for Groups A & B respectively. For blinding, the person who prepared the drug and started the infusion was different from the one who made observations.

Patient was pre-medicated with IV Inj. Glycopyrrolate 0.003mg/kg and inj. Fentanyl 2µg/kg. Thiopentone in 50mg boluses was given till loss of eyelash reflex followed by Vecuronium 0.1mg/kg I.V. After ventilating the patient for 3minutes, intubation was done with appropriate size flexometallic endotracheal tube. Patient was given prone position. Anaesthesia was maintained with O2+N2O (50:50) & Sevoflurane (2%) using closed circuit at fresh gas flow rate of 2litres/minute. Inj. Fentanyl (0.5µg/kg every 1hr) + Vecuronium (0.025mg/kg I.V. every 20 minutes) was given. Intra-operative monitoring of HR, BP (Systolic, Diastolic, and Mean), ECG and SPO2 was done every 10minutes. Average hourly values of HR & BP (S, D, M) were calculated. Intra operative hypertension (MAP >90mmhg) was treated with increasing concentration of Sevoflurane to 4%, Inj. Propofol 20 mg I.V. and Inj. Labetalol 5 mg IV if required. Hypotension (MAP <65 mm Hg) was treated with fluid bolus and Inj. Mephentermine 6 mg IV if necessary. Tachycardia (HR >90bpm) was treated with increasing concentration of Sevoflurane to 4% & Inj. Metoprolol 2 mg I.V. Bradycardia (HR <50 bpm) was treated with Inj. Atropine 0.02 mg/Kg IV. Urine output was maintained > 1ml/kg/hr. Inj. Diclofenac 75mg IM & inj. Ondansetron 4mg I.V. was given 20 minutes prior to end of procedure. Dexmedetomidine drip was

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stopped 10minutes prior to skin closure. Sevoflurane was stopped after skin closure. Patient was reversed with Inj. Neostigmine 0.05 mg/kg & inj. Glycopyrolate 0.01mg/kg when spontaneous respiratory efforts were seen. All external stimuli to the patient were avoided except continual verbal requests to open the eyes & move the upper limbs. Extubation was performed when patient began breathing spontaneously and were able to respond to verbal request to move upper limb. Time for Extubation i.e. Time since discontinuation of Sevoflurane till patient's trachea was extubated was noted. After Extubation, monitoring of HR, BP and SPO2 was done at 1 minute and 5minute to note extubation response. Duration of Extubation Response i.e. the time taken for HR and BP to reach baseline value after extubation was noted. Modified Aldrete's score (Total score=10) was assessed at 10th, 20th and 30th minute after extubation.

Patient was shifted to ward, when aldrete score was ≥ 9 or after 30 minutes of Post anaesthesia care unit (PACU) stay whichever was later.

Surgeon's satisfaction about quality of surgical field was noted using bleeding score proposed by Fromme and colleagues. Complications like hypotension, hypertension and Bradycardia were noted if any.

Statistical Analysis:

For analysis of the data, SPSS (Statistical Software for social Sciences) software version 20 was used. Data was represented in form of mean & SD. Data was analyzed using t-test & chi square test. A "p" value < 0.05 was considered as statistically significant and < 0.01 as highly significant.

Results

There was no statistically significant difference in demographic parameters like age, weight and duration of surgery in both the groups as shown table 1.

Table 1 – Demographic data. Results are given as mean ± SD.

Parameters	Group A (n = 40)	Group B (n = 40)	P value
Age (in years)	43.22 ± 12.32	45.85 ± 12.30	P=0.343 NS
Weight (in Kilograms)	58.02 ± 10.01	57.32 ± 10.67	P=0.763 NS
Duration of surgery (in hours)	3.05 ± 0.78	3.15 ± 1.29	P=0.765 NS

NS = Not significant

Haemodynamic stability was well maintained throughout the intra operative period as shown in table 2.

Table 2 – Intra operative haemodynamic parameters. Results are expressed as mean ± S.D.

Time points	Group A				Group B			
	HR (/ min.)	BP (in mm of Hg)			HR (/ min.)	BP (in mm of Hg)		
		S	D	M		S	D	M
Baseline	78.77 ± 15.40	135.70 ± 17.65	79.95 ± 11.34	95.12 ± 10.48	76.92 ± 17.10	132.30 ± 18.59	78.45 ± 10.69	92.97 ± 11.05
Loading dose 5th minute	73.02 ± 13.43	135.00 ± 19.92	78.85 ± 12.56	94.45 ± 12.84	70.37 ± 17.27	137.35 ± 19.16	79.00 ± 9.43	94.30 ± 10.60
Loading dose 10th minute	67.35 ± 12.82	128.50 ± 17.84	74.65 ± 12.29	88.72 ± 11.99	66.80 ± 13.85	130.30 ± 21.54	75.82 ± 10.62	89.75 ± 11.90
Post Intubation 1 min	88.72 ± 12.50	145.00 ± 18.29	92.30 13.16	106.3 ± 13.76	84.42 ± 10.41	147.50 ± 20.59	90.65 ± 18.88	107.20 ± 12.64
Post Intubation 5 min	74.97 ± 9.83	111.85 ± 15.48	70.45 ± 9.70	82.10 ± 10.79	73.10 ± 10.64	109.45 ± 12.73	68.90 ± 9.56	79.42 ± 9.69
Intra-operative 1st hour	68.35 ± 10.29	98.125 ± 9.37	65.95 ± 7.14	74.22 ± 6.65	67.90 ± 11.58	95.70 ± 8.134	63.92 ± 8.69	72.61 ± 7.62
Intra-operative 2nd hour	64.51 ± 10.25	99.50 ± 7.56	63.62 ± 10.43	72.50 ± 13.66	63.12 ± 11.18	97.10 ± 10.52	68.15 ± 10.89	89.15 ± 14.55
Intra-operative 3rd hour	60.52 ± 9.71	98.92 ± 9.65	77.87 ± 9.13	82.58 ± 11.31	77.62 ± 11.25	100.65 ± 9.37	76.20 ± 8.88	87.15 ± 11.72
Post-extubation 1 min	84.00 ± 13.62	143.67 ± 20.18	87.12 ± 13.57	102.27 ± 13.97	87.55 ± 17.37	144.92 ± 19.76	91.65 ± 13.09	107.0 ± 13.45
Post-extubation 5 min.	74.22 ± 13.32	122.80 ± 14.32	74.82 ± 10.57	87.20 ± 9.85	73.77 ± 14.07	123.92 ± 16.05	75.75 ± 8.88	89.17 ± 9.27

P > 0.05 for all the parameters.

The haemodynamic variables i.e. heart rate and BP (Systolic, Diastolic and mean) in both the groups were comparable at all time points with p value > 0.05. The duration of extubation response was less in group A, the difference being statistically significant. (Group A:- 3.28±0.89 min; Group B:- 4.23±1.30 min; p=0.000).(Table 3)

Table 3 – Duration of extubation response. Results are expressed as mean ± SD.

Parameter	Group A	Group B	P value
Duration of extubation response(min)	3.28±0.89	4.23±1.30	P = 0.000 HS

HS = statistically highly significant P < 0.01

Recovery was earlier in group B.(Table 4)

Table 4 – Recovery parameters. Results are expressed as mean ± SD.

Parameters	Group A (n = 40)	Group B (n = 40)	P value
Time for extubation (in minutes)	19.62 ± 6.44	17.52 ±6.42	P=0.149 NS
Duration of extubation response (in minutes)	3.28 ± 0.89	4.23 ±1.30	P=0.000 HS
Aldrete score at 10th minute	8.42 ± 0.50	9.55 ± 0.51	P=0.001 HS
Aldrete score at 20th minute	10 ± 0.00	10 ± 0.00	---

NS = Not significant, HS = highly significant

The difference in mean extubation time (min) in both the groups was statistically insignificant. (Group A: 19.62±6.44; Group B: 17.52±6.42; p=0.149). There was a statistically significant difference in Aldrete's score obtained at 10th minute post-extubation. (Group A:- 8.42±0.50; Group B:- 9.55±0.51; p=0.001). Modified Aldrete's score of 10 was obtained at 20th minute post-extubation in both the groups.

Incidence of adverse cardiovascular events i.e. hypotension, hypertension and Bradycardia was very low in both the groups, the difference being statistically not significant. (Table 5)

Table 5 – Incidence of adverse cardiovascular effects

Sideeffect	Group-A(n=40)	Group-B(n=40)	P-value
Hypotension	00 (0%)	01 (2.5%)	P = 0.314 NS
Hypertension	00 (0%)	01 (2.5%)	P = 0.314 NS
Bradycardia	02 (5%)	01 (2.5%)	P = 0.556 NS

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NS = not significant

In our study, 85% patients in Group A had bleeding score 2 and 15% patients had score 1. In Group B, 82.5% patients had score2 and 17.5% patients had score 1, the difference being statistically insignificant (p = 0.762) (Table 6)

Table 6 – Comparison of Bleeding score

Bleeding Score	Group A		Group B		P value
	No.	Percentage	No.	Percentage	
1	06	15%	07	17.5%	0.0762 NS
2	34	85%	33	82.5%	
Total	40	100%	40	100%	

NS = Not significant

Discussion

Surgeons demand controlled hypotension for spine surgery. Direct acting vasodilators (sodium nitroprusside, nitroglycerine), ganglion-blocking agents, beta adrenergic blockers (esmolol), calcium channel blockers (nicardipine), 2 agonists (Clonidine, dexmedetomidine), volatile agents and magnesium sulphate provide hypotension. The side effects of these agents may be tachyphylaxis, cyanide toxicity, cerebral vasodilatation, Bradycardia, conduction delay, reflex tachycardia and rebound hypertension.[7,8] Increasing depth of anaesthesia by volatile agents can lead to delayed recovery.[1] Easy arousability after Dexmedetomidine is advantageous in performing early motor testing in spine surgeries for detection of new neurological deficits.[2]

Majority studies on spine surgery have used Dexmedetomidine infusion of 0.4-0.7 μg/kg/hr titrated to maintain a MAP between 65 to 70 mmHg.2,4,26 We chose 0.2 μg/kg/hr (lowest recommended dose) and 0.4 μg/kg/hr (most commonly used dose) as constant infusion throughout the intra-operative period.

Demographic parameters like age, weight and duration of surgery were comparable in our two groups. Both the groups received same loading dose of dexmedetomidine 1 μg/kg for 10 minutes followed by maintenance infusion. Haemodynamic parameters at the end of loading dose were comparable in both the groups.

The maintenance dose of dexmedetomidine was kept constant at 0.2 μg/kg/hr or 0.4 μg/kg/hr throughout the intra-operative period. MAP was chosen as a parameter to quantify hypotension as it is a true measure of tissue perfusion.[8] We targeted to maintain MAP above 65 mm of Hg as perfusion to vital organs is well maintained with least probability of spinal cord ischaemia.[] We found intra-operative average MAP in both the groups comparable. MAP in 1st hour was (Group A; 74.22±6.65; Group B; 72.61±7.62 p=0.320), in 2nd hour (Group A:- 72.50±13.66; Group B:- 89.15±14.55 p=0.242), in 3rd hour (Group A: 82.58±11.31; Group B:- 87.15±11.72 p=0.301). As we maintained constant infusion rate of dexmedetomidine, our values of mean MAP were slightly higher than other studies where they maintained MAP within a narrow range of 65 -70 mm of Hg by titrating Dexmedetomidine infusion from 0.2 – 0.7 μg/kg/hr.

As primary outcome of our study was to test intra operative haemodynamic stability, we monitored systolic and diastolic B.P. in addition to MAP. There was no statistically significant difference in intra-operative hourly average systolic blood pressure between the two groups. Average systolic BP in 1st hour was (Group A: 98.125±9.37; Group B: 95.70±8.134; p=0.220), in 2nd hour (Group A: 99.50±7.56; Group B: 97.10±10.52; p=0.134) and in 3rd hour (Group A: 98.92±9.65; Group B: 100.65±9.37; p=0.242). In a study conducted by Bekker A et al[7] using dexmedetomidine in a dose of 1 g/kg followed by 0.5 g/kg/hr in patients undergoing craniotomy, intra-op average systolic BP in Dex group was 102.2±9.4 which corresponds to our values.

There was no statistically significant difference in intra-operative hourly average diastolic blood pressure between the two groups. Average diastolic BP in 1st hour was (Group A: 65.95±7.14; Group B: 63.92±8.69; p=0.259), in 2nd hour (Group A: 63.62±10.43; Group B: 68.15±10.89; p=0.243) and in 3rd hour (Group A: 77.87±9.13; Group B: 76.20±8.88; p=0.124).

Intra operative heart rate was comparable between the groups. Intra-op mean heart rate in 1st hour was (Group A:- 68.35±10.29; Group B:- 67.90±11.58; p=0.855), in 2nd hour (Group A:- 64.51±10.25; Group B:- 63.12±11.18; p=0.213) and in 3rd hour (Group A:- 60.52±9.71; Group B:- 77.62±11.25; p=0.242).

Ozkose Z et al[9] in their study using dexmedetomidine (1 μg/kg followed by 0.2 μg/kg/hr) for surgery in prone position and Jamaliya R H et al[8] in a study using dexmedetomidine (0.2-0.7μg /kg/hr) in posterior fixation surgery following traumatic spine injury found that heart rate remained stable throughout surgery in dexmedetomidine group. Bekker A et al[7] observed that heart rate remained within targeted range (dex group 67.9 ±1.7). Our results are similar with these reports.

We assessed extubation response i.e. increase in heart rate and blood pressure by more than 20% from the baseline. Increase in mean heart rate from baseline in Group A was 8.97% whereas in Group B it was 11.40% at post-extubation 1minute. In Group A the increase from baseline in mean SBP, DBP and MAP was 7%, 10.84% and 9.77% respectively at 1min post extubation where as the values for same parameters in Group B were 8.89%, 14.93% and 12.76% respectively. This increase is less than 20% suggesting insignificant extubation response. Values of Heart rate and blood pressure reached baseline within 5minutes in both the groups. The haemodynamic variables in two groups were comparable at all time points with $p > 0.05$.

This result in our study corresponds to results obtained by various authors. Jamaliya RH et al[8] found that dexmedetomidine maintained haemodynamic stability at the time of extubation with HR=92.5 ± 11.8076 bpm and MAP=89.33 ± 8.08941 mmHg. In a study by Tanskanen PE et al[3] the values for maximum increase in SBP and HR at 1 min post extubation in Dex 0.2 and 0.4 mcg/kg/hr groups were12 (19) and 6 (19) respectively. The mean increase in systolic BP was smallest in Dex-0.4 group with no significant difference between the groups in heart rate at extubation. We found a similar mean increase in heart and systolic BP immediately post-extubation in both the groups with the increase being lesser in Group A (Dex-0.4).

We found a statistically significant difference in duration of extubation response between the two groups. (Group A:- 3.28±0.89mins; Group B:- 4.23±1.30 mins; p=0.000). This may be due to higher dose of dexmedetomidine used in group A causing blunting of sympatho-adrenal response due to dose dependent decrease in release of norepinephrine. Many studies using dexmedetomidine have compared the haemodynamics at extubation with the baseline values and found that dexmedetomidine helps in attenuating the extubation response but none of them have measured the duration of extubation response.[3,8,10,11] 4,5,19,29,30

We used the time to extubation and modified Aldrete's score to study recovery. In our study, difference between Mean extubation time (min) in both the groups was statistically insignificant. (Group A: 19.62±6.44; Group B: 17.52±6.42; p=0.149).

Mohamed H S et al (2) comparing dexmedetomidine (0.4-0.8 mcg/kg/hr) and nimodipine in spine surgery found extubation time in Dex group as 8.9±1.8. Ozkose Z et al[9] in their study observed extubation time in Dex group (0.2 mcg/kg/hr) as 3.9±1.5 min. Ibraheim OA et al[6] compared Esmolol and dexmedetomidine (0.4-0.7 mcg/kg/hr) in patients undergoing scoliosis repair. They used total intravenous anaesthesia with Propofol and Fentanyl along with

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study drugs in intra operative period. Their extubation time in Dex group was 27.2 ± 13.4 min.

This wide variability in extubation time from 3.9±1.5 min to 27.2±13.4 min might be because of different dose of dexmedetomidine, different extubation criteria or use of additional drugs and advanced monitoring (like BIS) in intra-operative period in these studies.

In our study, Modified Aldrete's score of 10 was obtained at 20th minute post-extubation in both the groups. However there was a statistically significant difference in the score obtained at 10th minute post-extubation. (Group A:- 8.42±0.50; Group B:- 9.55±0.51; p=0.001). Various studies have used modified Aldrete's score to study recovery of patients in PACU. Mohamed H S et al[1] found time for total recovery from anaesthesia using dexmedetomidine (1mcg/kg followed by 0.4-0.8mcg/kg/hr) as 7.6±2.1 min. The time to reach the score of 9 in their study was shorter than our study, since they used TOF =0.9 as criteria for extubation which ensured complete recovery from neuromuscular blockade. Modified Aldrete's score at 10th minute post-extubation observed by Ozkose Z et al[9] in Dex group (9.2±2.1) was comparable to the score in Group B (9.5±0.5) at 10th minute in our study as same dose of dexmedetomidine was used in both the studies. Patel C R et al[12] in their study observed that at 30 minutes post extubation the modified Aldrete's score in Dex group was 8.06 ± 0.64. Their low score may be due to higher dose of dexmedetomidine (0.2-0.8 mcg/kg/hr).

In our study, 2/40 patients in group A and 1/40 patient in group B had an episode of bradycardia during intra-operative period requiring single bolus dose of inj. Atropine 0.6mg I.V. 1/40 patients in group B had an episode of hypotension during intraoperative period which was treated with I.V fluids followed by two doses of Inj. Mephentermine 3 mg I.V. This hypotension was due to major vascular bleed which was immediately controlled. 1/40 patient in group B had an episode of hypertension probably due to light plane of anaesthesia which was treated with increasing concentration of Sevoflurane to 4% and two boluses of inj. Propofol 20mg I.V. None of the patient had any haemodynamic complication in the PACU. Jamaliya R H et al[8] found that 3/20 patients in Dex group had episode of bradycardia and none had severe hypotension. Patel C R et al[12] using Dex (1mcg/kg followed by 0.2-0.8mcg/kg/hr) observed that 2/30 patients had bradycardia within 10 minutes post extubation. The higher incidence of bradycardia in these studies may be due to the use of higher dose of dexmedetomidine. Ozkose Z et al[9] observed that none of the patients' required ephedrine for treating hypotension and 4/20 patients in Dex group required atropine for treating bradycardia in the intra-operative period. The reason for difference in incidence of bradycardia was not clear.

We documented surgeon's satisfaction regarding quality of operative field using Fromme and colleagues' bleeding scoring system from 0 to 5.[10] In Group A 85% patients had score 2 and 15% patients had score 1. In Group B 82.5% patients had score2 and 17.5% patients had score 1, the difference being statistically insignificant. Surgeons were highly satisfied with the operative field. Aboushanab O H et al[10] in their study using magnesium sulphate and dexmedetomidine (1mcg/kg followed by 0.4-0.8mcg/kg/hr) during middle ear surgery, assessed the quality of the surgical field using same scale. Surgical field quality score was 2.4(1-4) in Dex group which was similar to our result. Majority of studies on spine surgery have estimated the amount of blood loss instead of using subjective scale for assessing quality of surgical field.[1,4,6,8] In our study we initially included different types of spine surgeries ranging from laminectomy (minimal blood loss) to spine stabilization surgeries (more blood loss) due to availability of limited number of patients. It would have been difficult for us to assess whether decrease in blood loss was due to effect of Dexmedetomidine. Hence instead of comparing the amount of blood loss we used subjective scoring system to assess quality of operative field although in the end we could study sufficient number of patients undergoing spine surgeries with minimum blood loss.

Conclusion

The present study demonstrated that, in spine surgery dexmedetomidine when used as adjuvant to general anaesthesia in the dose of 0.2μg/kg/hr or 0.4μg/kg/hr provides intra-operative haemodynamic stability and improves quality of operative field with minimal side effects although dexmedetomidine 0.2μg/kg/hr has better recovery profile than dexmedetomidine in dose of 0.4μg/kg/hr.

Limitations of the study

As we did not measure plasma concentration of dexmedetomidine which may vary due to difference in the ability to metabolize the drug, it is possible that patients might have received either higher or lower effective doses. A study using titrated dose of dexmedetomidine to achieve constant plasma concentration may demonstrate better haemodynamic stability with shorter awakening time.

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