ISSN 2515-8260 Volume 09, Issue 02, 2022

Dexmedetomidine in prevention of myoclonus: Side effects and haemodynamic study

[1]Dr. Mohamed Faizuddin, [2]Dr. Lokesh SB, [3]Dr. Geetha M

[1]Assistant Professor, Department of Anesthesia, Kanachur Institute of Medical Sciences, Mangalore, Karnataka, India
[2]Senior Resident, Department of Anesthesia, ESIC Medical College PGIMSR and Model Hospital, Rajajinagar, Bangalore, Karnataka, India
[3]Junior Resident, Department of Anesthesia, ESIC Medical College PGIMSR and Model Hospital, Rajajinagar, Bangalore, Karnataka, India

Corresponding Author:
Dr. Geetha M

Abstract

Dexmedetomidine the S-enantiomer of medetomidine a highly sedative and potent α2-adrenergic agonists has a potentially useful role as a sedative agent. In healthy volunteers dexmedetomidine increases sedation, analgesia and amnesia and decreases heart rate, cardiac output and circulating catecholamine in a dose dependent fashion. Anaesthesia workstation was checked. Appropriate size endotracheal tubes, working laryngoscope with medium and large sized blades, stylet and working suction apparatus were kept ready before the induction of general anaesthesia. Emergency drug tray consisting of atropine, adrenaline and mephentermine were also kept ready for any eventuality. Post extubation Ramsay sedation score was significantly higher in group D compared to group S at 30^{th}, 60^{th} and 90^{th} minute with p value = 0.001, 0.001 and 0.051 respectively. However no patients in group D required intervention for sedation and were easily arousable. There was no statistically significance between the groups immediately after extubation and at 120^{th} minute postoperatively. 3 patients in group D (8.57%) and 3 patients in group S (8.57%) had vomiting immediately following extubation which was statistically not significant (p = 0.721). 1 patients in group D (2.86%) and 2 patients in group S (5.71%) had vomiting after 30 minutes of extubation which was statistically not significant (p = 0.555).

Keywords: Dexmedetomidine, myoclonus, haemodynamic study

Introduction

α-2 agonists are assuming greater importance as anaesthetic adjuvants and analgesics. Their primary effect is sympatholysis. They reduce peripheral norepinephrine release by stimulation of prejunctional inhibitory α-2 adrenoceptor. They inhibit central neural transmission in the dorsal horn by presynaptic and postsynaptic mechanisms and also have direct sympatholytic effect on spinal preganglionic sympathetic neurons [1].

Although experience with α2-agonists as sole anaesthetic is limited, these drugs reduce anaesthetic requirement and provide a more stable cardiovascular course, presumably because of their sympatholytic effect and the need for lower dose of cardio active anaesthetics [2].

Dexmedetomidine a selective α2-adrenoceptor has a 1600:1 preference for α2 receptors compared to α1 receptors. This drug was introduced into clinical practice as an adjunct to

ISSN 2515-8260 Volume 09, Issue 02, 2022

regional, local and general anaesthetics. Additionally a met analysis of the perioperative use of clonidine, dexmedetomidine and mivazerol indicated a decrease in MI and perioperative mortality in patients undergoing vascular surgery [3].
Dexmedetomidine the S-enantiomer of medetomidine a highly sedative and potent α2-adrenergic agonists has a potentially useful role as a sedative agent. In healthy volunteers dexmedetomidine increases sedation, analgesia and amnesia and decreases heart rate, cardiac output and circulating catecholamine in a dose dependent fashion. The purported MAC-reducing sedative and analgesic effects demonstrated in preclinical and voluntary studies have largely been borne out in clinical practice. Although dexmedetomidine infusions attenuate haemodynamic liability of induction, maintenance and emergence, the dose of other anaesthetics must be carefully reduced because requirement for other anaesthetics may decrease. The impact of α2-induced sedation on respiratory function combined with short duration of action of dexmedetomidine led to several reports of use of dexmedetomidine in awake fibreoptic intubation. Dexmedetomidine infusions have been used for perioperative management of obese patients with obstructive sleep apnoea to minimize narcotic needs while providing adequate analgesia [4].

Methodology

Anaesthesia workstation was checked. Appropriate size endotracheal tubes, working laryngoscope with medium and large sized blades, stylet and working suction apparatus were kept ready before the induction of general anaesthesia. Emergency drug tray consisting of atropine, adrenaline and mephentermine were also kept ready for any eventuality.
After obtaining informed written consent from the patients, participation consent and surgeon's consent, the patients were randomly divided into two groups.
Group D: Dexmedetomidine (n = 35).
Group S: Saline (n = 35).

Patients on arriving to operation theatre, IV cannulation was done with 18 G cannula and ringer lactate was connected. Patients were connected to monitors such as ECG, noninvasive blood pressure, pulse oximetry and entropy. The patients were premedicated with IV 50 mg of Inj. ranitidine and 0.2 mg of Inj. glycopyrrolate. The study drug syringes were prepared by an anesthetist not involved in the observation. Patients in group D received 0.5 μg/kg of Inj. dexmedetomidine in 10 ml saline and group S received 10 ml of Saline over a period of 10 minutes. Oxygen supplementation through mask was given during this period. Ramsay Sedation Score was noted at baseline, 5^{th} and 10^{th} minute during infusion (annexure 3). Etomidate 0.3 mg/kg was administered over 30 seconds and pain related with injection was evaluated; 0: no pain, 1: mild pain, 2: moderate pain, 3: severe pain (annexure 4). Also myoclonus was observed for two minutes following etomidate induction and graded; 0: no myoclonus, 1: mild myoclonus, 2: moderate myoclonus, 3: severe myoclonus (annexure 5). Two minutes after etomidate injection, Inj. midazolam 0.02 mg/kg, Inj. fentanyl 2 μg/kg and Inj. Atracurium 0.5 mg/kg was administered. After three minutes, patients were intubated with appropriate sized cuffed oral endotracheal tube. Anaesthesia was maintained according to institutional protocol with N_2O + O_2 +sevoflurane. Hypotension, defined as more than 20% decrease in mean arterial pressure, was treated with fluid boluses and injection ephedrine 6 mg IV. Bradycardia, defined as heart rate less than 50 beats/min, was treated with injection atropine 0.6 mg IV. At the end of surgery, residual paralysis was reversed with 0.05 mg/kg of Inj. neostigmine and 0.01 mg/kg of Inj. glycopyrrolate. At the time of extubation, recovery profile was noted (the time between cut off of inhalational agent to the opening of eyes) and extubation time (the time between cut off of inhalational agent to removal of endotracheal tube) was recorded. Ramsay sedation score after extubation was recorded.

ISSN 2515-8260 Volume 09, Issue 02, 2022

Parameters observed

1. The heart rate, peripheral oxygen saturation (SpO_2), systolic, diastolic and mean blood pressure measurements, ET CO_2 before pretreatment, every 2 minutes during pretreatment, every minute for 10 minutes after etomidate and at 5 minutes interval after that till the end of the surgery.
2. Ramsay sedation score at the baseline, after administering study drug and after extubation, Myoclonus grading, Pain grading, Time to extubation and eye opening.
3. Postoperative RSS, RR, nausea and vomiting every $^1/_2$ an hour for 2 hour.

Results

Table 1: Gender distribution of patients studied.

Gender	Group D		Group S	
	No	%	No	%
Female	29	82.86	28	80
Male	6	17.14	7	20
Total	35	100.0	35	100.0

70 patients of either sex had participated in the study. The gender distribution was comparable among the groups.

The heart rate was significantly lower in group D compared to group S from 6th minute of starting dexmedetomidine infusion and then throughout intraoperative period ($p < 0.05$). However no patients in group D required treatment for bradycardia.

Intra group analysis using paired t test revealed significant decrease in HR with dexmedetomidine infusion compared to baseline values. However HR maintained > 50 beats/min throughout the procedure and no patients required treatment for bradycardia. In group S there was no reduction in HR following saline infusion.

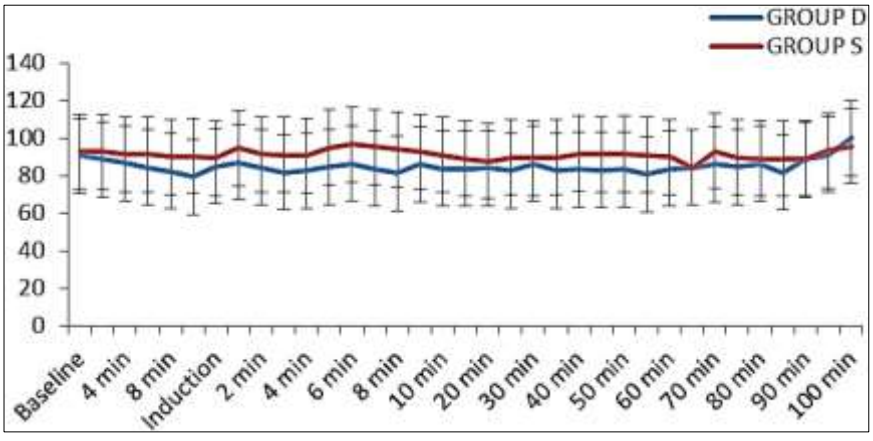

Fig 1: Comparison of Heart rate (bpm) in two groups studied.

The systolic blood pressure during study drug infusion was comparable in both the groups.

There was a significant decrease in SBP in group D compared to group S from 7th minute to 10th minute and then from 55th minute to 75th minute following etomidate induction ($p < 0.05$).

Intra group analysis using paired t test revealed significant decrease in SBP with dexmedetomidine infusion compared to baseline values whereas in group S there was no significant reduction in SBP following saline infusion. But there was significant decrease in SBP in both the groups following etomidate induction.

ISSN 2515-8260 Volume 09, Issue 02, 2022

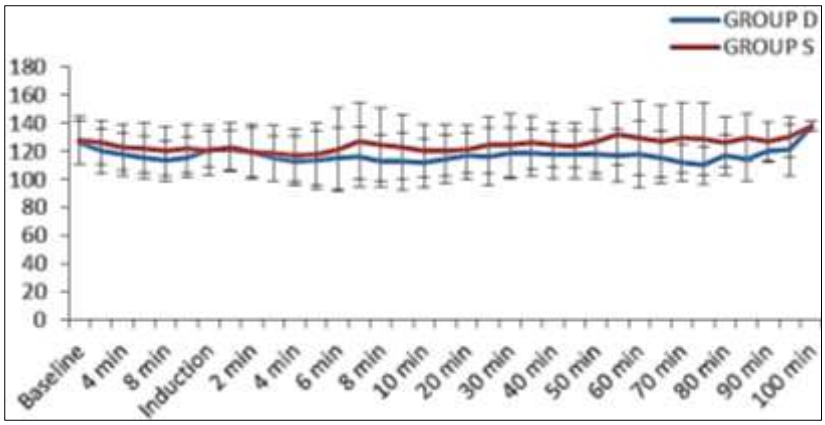

Fig 2: Comparison of SBP (mm Hg) in two groups studied.

The diastolic blood pressure during study drug infusion was comparable between the two groups.

There was a significant decrease in DBP in group D compared to group S from 7th minute to 10th minute and then from 45th minute to 70th minute following etomidate induction ($p < 0.05$).

Intra group analysis using paired t test revealed significant decrease in DBP with dexmedetomidine infusion compared to baseline values whereas in group S there was no significant reduction in DBP following saline infusion. But there was significant decrease in DBP in both the groups following etomidate induction.

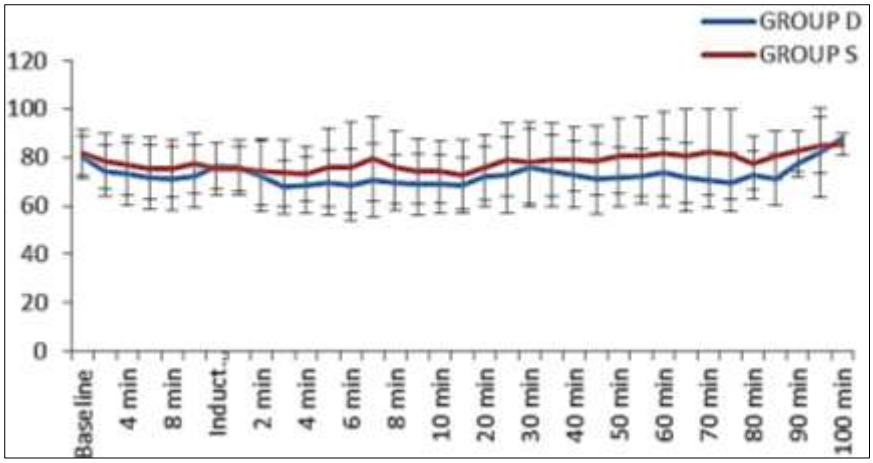

Fig 3: Comparison of DBP (mm Hg) in two groups studied.

The mean arterial pressure during study drug infusion was comparable between the two groups.

There was a significant decrease in MAP in group D compared to group S from 7th minute of etomidate induction until 10th minute ($p < 0.05$).

Intra group analysis using paired t test revealed significant decrease in MAP with dexmedetomidine infusion compared to baseline values whereas in group S there was no significant reduction in MAP following saline infusion. But there was significant decrease in MAP in both the groups following etomidate induction. However decrease of MAP was within 20% of baseline values throughout the procedure and no patients required treatment for hypotension.

ISSN 2515-8260 Volume 09, Issue 02, 2022

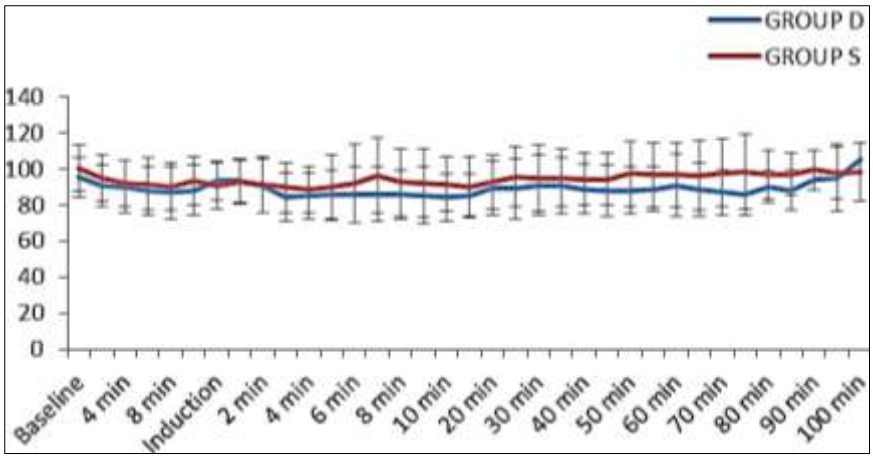

Fig 4: Comparison of MAP (mm Hg) in two groups studied.

End tidal CO_2 was comparable between the studied groups during study drug infusion and intra operatively.

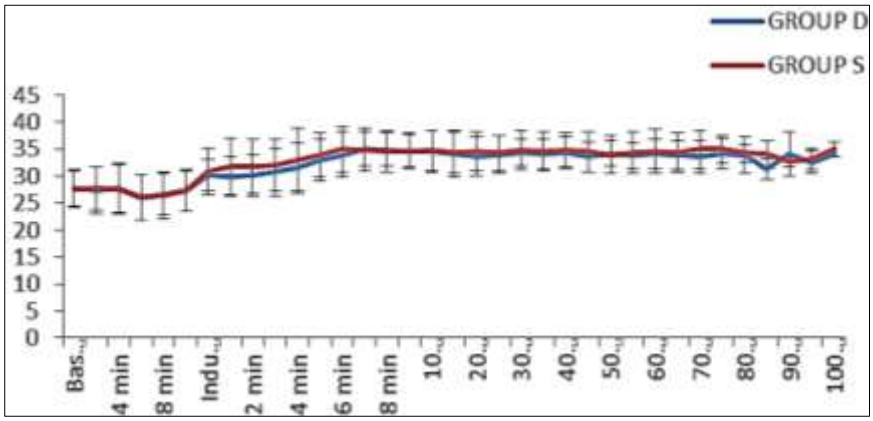

Fig 5: Comparison of $ETCO_2$ in two groups studied.

Table 2: Ramsay sedation score during study drug infusion.

RSS		Group D	Group S	P value by χ2 test
Baseline	1	6 (17.14%)	2 (5.71%)	0.133
	2	29 (82.85%)	33 (94.28%)	
	3	0 (0%)	0 (0%)	
	4	0 (0%)	0 (0%)	
	5	0 (0%)	0 (0%)	
	6	0 (0%)	0 (0%)	
5 min	1	0 (0%)	0 (0%)	0.151
	2	33 (94.28%)	35 (100%)	
	3	2 (5.71%)	0 (0%)	
	4	0 (0%)	0 (0%)	
	5	0 (0%)	0 (0%)	
	6	0 (0%)	0 (0%)	
10 min	1	0 (0%)	0 (0%)	0.001**
	2	24 (68.57%)	35 (100%)	
	3	10 (28.57%)	0 (0%)	
	4	1 (2.85%)	0 (0%)	
	5	0 (0%)	0 (0%)	
	6	0 (0%)	0 (0%)	

ISSN 2515-8260 Volume 09, Issue 02, 2022

Most of the patients were cooperative, oriented, tranquil (82.85% in group D and 94.28% in group S) before starting the study drug infusion. Ramsay sedation score was comparable between group D and group S at the baseline (p = 0.133) and at 5th minute of the study drug infusion (p=0.151). Ramsay sedation score at 10th minute of study drug infusion was significantly higher in group D than group S (p = 0.001). 10 patients in group D (28.57%) were drowsy; responsive to verbal commands (RSS-3) and 1 patient in group D (2.85%) was asleep, responsive to light stimulation (RSS-4). However no patients required intervention for sedation during study drug infusion and were arousable.

Table 3: Post extubation Ramsay sedation score.

RSS		Group D	Group S	P value by χ2 test
0 min	1	0 (0%)	0 (0%)	0.316
	2	0 (0%)	1 (2.86%)	
	3	19 (54.29%)	23 (65.71%)	
	4	16 (45.71%)	11 (31.43%)	
	5	0 (0%)	0 (0%)	
	6	0 (0%)	0 (0%)	
30 min	1	0 (0%)	0 (0%)	0.001**
	2	1 (2.86%)	13 (37.14%)	
	3	31 (88.57%)	21 (60%)	
	4	3 (8.57%)	1 (2.86%)	
	5	0 (0%)	0 (0%)	
	6	0 (0%)	0 (0%)	
60 min	1	0 (0%)	0 (0%)	0.001**
	2	7 (20%)	21 (60%)	
	3	28 (80%)	14 (40%)	
	4	0 (0%)	0 (0%)	
	5	0 (0%)	0 (0%)	
	6	0 (0%)	0 (0%)	
90 min	1	0 (0%)	0 (0%)	0.051+
	2	17 (48.57%)	25 (71.43%)	
	3	18 (51.43%)	10 (28.57%)	
	4	0 (0%)	0 (0%)	
	5	0 (0%)	0 (0%)	
	6	0 (0%)	0 (0%)	
120 min	1	0 (0%)	0 (0%)	0.759
	2	29 (82.86%)	28 (80%)	
	3	6 (17.14%)	7 (20%)	
	4	0 (0%)	0 (0%)	
	5	0 (0%)	0 (0%)	
	6	0 (0%)	0 (0%)	

Post extubation Ramsay sedation score was significantly higher in group D compared to group S at 30th, 60th and 90th minute with p value = 0.001, 0.001 and 0.051 respectively. However no patients in group D required intervention for sedation and were easily arousable. There was no statistically significance between the groups immediately after extubation and at 120th minute postoperatively.

Table 4: Nausea in two groups of patients studied.

Nausea		Group D	Group S	P value by χ2 test
0 min	0	27 (77.14%)	27 (77.14%)	0.232
	1	5 (14.29%)	2 (5.71%)	

ISSN 2515-8260 Volume 09, Issue 02, 2022

	2	0 (0%)	3 (8.57%)	
	3	3 (8.57%)	3 (8.57%)	
30 min	0	32 (91.43%)	28 (80%)	0.423
	1	2 (5.71%)	3 (8.57%)	
	2	0 (0%)	2 (5.71%)	
	3	1 (2.86%)	2 (5.71%)	
60 min	0	32 (91.43%)	30 (85.71%)	0.786
	1	1 (2.86%)	3 (8.57%)	
	2	1 (2.86%)	1 (2.86%)	
	3	1 (2.86%)	1 (2.86%)	
90 min	0	33 (94.29%)	32 (91.43%)	0.389
	1	1 (2.86%)	1 (2.86%)	
	2	0 (0%)	2 (5.71%)	
	3	1 (2.86%)	0 (0%)	
120 min	0	34 (97.14%)	35 (100%)	0.314
	3	1 (2.86%)	0 (0%)	

8 patients in group D (22.86%) and 8 patients in group S (22.86%) had nausea immediately following extubation which was statistically not significant (p = 0.232). 3 patients in group D (8.57%) and 7 patients in group S (20%) had nausea after 30 minutes of extubation which was statistically not significant (p = 0.423).
3 patients in group D (8.57%) and 5 patients in group S (14.29%) had nausea after 60 minutes of extubation which was statistically not significant (p = 0.786).
2 patients in group D (5.71%) and 3 patients in group S (8.57%) had nausea after 90 minutes of extubation which was statistically not significant (p = 0.423).
1 patient in group D (2.86%) and no patients in group S had nausea after 2 hours of extubation which was statistically not significant (p = 0.314).

Table 5: Vomiting in two groups of patients studied.

Vomiting		Group D	Group S	P value by $\chi 2$ test
0 min	0	32 (91.43%)	32 (91.43%)	0.721
	1	1 (2.86%)	2 (5.71%)	
	2	1 (2.86%)	0 (0%)	
	3	1 (2.86%)	1 (2.86%)	
30 min	0	34 (97.14%)	33 (94.29%)	0.555
	1	0 (0%)	0 (0%)	
	2	0 (0%)	0 (0%)	
	3	1 (2.86%)	2 (5.71%)	
60 min	0	33 (94.29%)	34 (97.14%)	0.602
	1	1 (2.86%)	1 (2.86%)	
	2	0 (0%)	0 (0%)	
	3	1 (2.86%)	0 (0%)	
90 min	0	34 (97.14%)	34 (97.14%)	0.368
	1	0 (0%)	1 (2.86%)	
	2	0 (0%)	0 (0%)	
	3	1 (2.86%)	0 (0%)	
120 min	0	34 (97.14%)	35 (100%)	0.314
	1	0 (0%)	0 (0%)	
	2	0 (0%)	0 (0%)	
	3	1 (2.86%)	0 (0%)	

3 patients in group D (8.57%) and 3 patients in group S (8.57%) had vomiting immediately following extubation which was statistically not significant (p = 0.721). 1 patients in group D

(2.86%) and 2 patients in group S (5.71%) had vomiting after 30 minutes of extubation which was statistically not significant (p = 0.555).
2 patients in group D (5.71%) and 1 patients in group S (2.86%) had vomiting after 60 minutes of extubation which was statistically not significant (p = 0.602).
1 patients in group D (2.86%) and 1 patients in group S (2.86%) had vomiting after 90 minutes of extubation which was statistically not significant (p = 0.368).
1 patient in group D (2.86%) and no patients in group S had vomiting after 2 hours of extubation which was statistically not significant (p = 0.314).

Discussion

Salman N *et al*. reported that 0.5 μg/kg dexmedetomidine could be used for pretreatment with etomidate without significant cardiovascular side effects, especially in patients with low cardiac reserve [5].
Sema Aktolga *et al*. in their study compared the haemodynamic effects of midazolam 0.5 mg/kg and dexmedetomidine 1 μg/kg following etomidate induction. It was noted that the systolic, diastolic arterial blood pressure and the heart rate were similar among midazolam and dexmedetomidine groups at all the observation times [6].
Mizrak *et al*. in their study compared the haemodynamic effects of 0.5 μg/kg dexmedetomidine and 1 mg/kg thiopental. In dexmedetomidine group, MAP decreased significantly from the baseline value at 5 min after the induction of anaesthesia ($p < 0.05$). The HR of patients in dexmedetomidine group was significantly higher than the thiopental and saline group at baseline, 0 and 5 min after the induction of anaesthesia ($p < 0.05$) [7].
H.F. Luan *et al*. in their study compared two doses of dexmedetomidine, 0.5 (group II) and 1.0 μg/kg (group III) with saline group (group I) and found that the incidence of severe sinus bradycardia was significantly increased in group III compared with group I ($P < 0.05$). But there was no significant difference in heart rate in groups I and II. Low blood pressure had an incidence of 6.7%, 10% and 13.3% in groups I, II and II respectively and there were no significant differences among the 3 groups [8].
In the present study, the haemodynamic findings were consistent with the above studies. There was significant decrease in heart rate in patients receiving dexmedetomidine from 6th minute of starting infusion and throughout the intraoperative period, compared to saline group ($p < 0.05$). However there was no incidence of bradycardia (< 50 beats/min) and no patients required treatment for the same. The systolic, diastolic and mean arterial pressures were comparable to saline group during the period of dexmedetomidine infusion but showed significant decrease during intraoperative period ($p < 0.05$). Intragroup analysis showed significant fall in SBP, DBP, MAP compared to baseline in dexmedetomidine group during pretreatment and in both the groups following etomidate induction; however decrease of MAP was within 20% of baseline values throughout the procedure and no patients required treatment for hypotension.
Salman N *et al*. in their study compared dexmedetomidine 0.5 μg/kg and midazolam 0.25 mg/kg and observed that sedation scores were lower in dexmedetomidine group ($p< 0.05$) compared to midazolam group [5]. In a study conducted by Sema Aktolga *et al*. pretreatment with midazolam 0.5 mg/kg and dexmedetomidine 1 μg/kg caused significant differences in the incidence of respiratory depression, the incidence and severity of sedation in midazolam group compared to dexmedetomidine group ($p < 0.05$) [6]. These authors assessed the sedation based on a scale between 0 and 3 as 0 = none, 1= mild (responsive to patient's name spoken in normal voice), 2= moderate (responsive to name spoken loudly) and 3 =severe (responsive to a painful stimulus).
In the present study, Ramsay sedation score was used for assessment of sedation. Ramsay sedation score was comparable between the studied groups at the baseline (p = 0.133) and at 5th minute of the study drug infusion (p = 0.151) but was significantly higher at the end of

dexmedetomidine infusion (p = 0.001). We also assessed sedation scores following extubation which was not done by the other authors. Post extubation sedation scores were comparable between the studied groups' immediately after extubation and at 120th minute following extubation (p > 0.05). It was significantly higher in group D compared to group S at 30th, 60th and 90th minute with p = 0.001, 0.001 and 0.051 respectively. However no patients in group D required intervention for sedation and were easily arousable during dexmedetomidine infusion as well as following extubation. Also the recovery profile, time to extubation, respiratory rate after extubation, 30th, 60th, 90th and 120th minute postoperatively were comparable between the two studied groups.

Mizrak *et al*. in their study did not find any statistically significant difference between the incidences of nausea and vomiting among the groups.[7] in our study, the findings were consistent with the above study. The incidence of nausea and vomiting after extubation, 30th, 60th, 90th and 120th minute postoperatively was comparable between group D and group S (p > 0.05).

None of the patients experienced hypotension, bradycardia, hypertension, arrhythmia or other side effect of the drug during the study.

The findings of the present study are limited, to some extent, by the relatively small sample size of 70 patients. A larger sample would provide more reliable observation and evaluation. Similar studies are required, utilizing larger patients group, to strengthen the findings of the present study.

Conclusion

Haemodynamic parameters such as HR, SBP, DBP, and MAP were significantly lower in group D compared to group S during pretreatment and intraoperatively but decrease of MAP was within 20% of baseline values throughout the procedure.

References

1. Ellison SH. Current thinking in hand scrubs and skin preparations. Journal of Nursing. 1960;1:43.
2. Jean Davies, Babb JR, Ayliffe GAJ, Wilkins MD. Disinfection of the skin of the abdomen. British Journal of Surgery. 1978;65:855-8.
3. Hugo WB, Longworth AR. Some aspects of the mode of action of chlorhexidine. Brit J Pharm Pharmacop. 1964;16:658.
4. Brown TR, Clarence E Ehrlich, Frederick B Stehman, Alan M Golichowski, James A Madura, Harold EE. A clinical evaluation of chlorhexidine gluconate spray as compared with iodophor scrub for preoperative skin preparation. Surgery, Gynecology and Obstetrics. 1984;158(4):363.
5. Pearson RD, Valenti WM, Steigbigel RT. Clostridium perfringens wound infections associated with elastic bandages. JAMA. 1980;244:1128-30.
6. Richet HM, Craven PC, Brown JM, Lasker BA, Cox CD, McNeil MM, *et al*. A cluster of Rhodococcus (Gordona) bronchialis sternal-wound infections after coronary-artery bypass surgery. N Engl J Med. 1991;324:104-9.
7. Wenger PN, Brown JM, McNeil MM, Jarvis WR. Nocardia farcinica sternotomy site infections in patients following open heart surgery. J Infect Dis 1998;178:1539-43.
8. Lowry PW, Blankenship RJ, Gridley W, Troup NJ, Tompkins LS. A cluster of Legionella sternal-wound infections due to postoperative topical exposure to contaminated tap water. N Engl J Med. 1991;324:109-13.