



Original Research Article

A study on intra-operative and post-operative effects of dexmedetomidine on haemodynamic stress responses to surgeries

Viditha Korukonda¹, S Kaladhar^{2,*}¹Dept. of Anaesthesia, Kamineni Academy of Medical Sciences and Research Center, Hyderabad, Telangana, India²Dept. of Anaesthesia, Shadan Institute of Medical Sciences, Teaching Hospital and Research Center, Hyderabad, Telangana, India

ARTICLE INFO

Article history:

Received 18-03-2020

Accepted 15-05-2020

Available online 25-11-2020

Keywords:

Dexmedetomidine

Analgesia

Hemodynamic stress

Elective surgery

ABSTRACT

Introduction: Stress response usually involves hormonal and metabolic changes which follow injury or trauma. Many of the manoeuvres, such as laparoscopic surgeries, laryngoscopies, tracheal intubation and extubation involve sympathetic stimulation. Dexmedetomidine is a specific and short acting alpha-2 adrenoceptor agonist and a potent drug which decreases sympathetic tone, with attenuation of the neuroendocrine and hemodynamic responses to anaesthesia and surgery; reduces anaesthetic and opioid requirements; and causes sedation and analgesia.

Materials and Methods: 100 patients between the ages of 18-60 years, with ASA score of I and II and scheduled for surgery under general anaesthesia were included in the study and divided into 2 groups of 50 each. Group I was given saline solution as Placebo and Group II was given 100 µg/ml of Dexmedetomidine hydrochloride. The data collection was performed every 2 minutes during induction of anaesthesia and for 10 minutes after tracheal intubation. The need for post operative analgesia was decided according to the visual analogue scale.

Results: Dexmedetomidine reduced the heart rate significantly ($P < 0.05$) in comparison to the baseline values at 15 and 30 minutes, and compared to the control group. The heart rate values recorded after 15, 60, 120, 180 minutes, in PACU were significantly less in Dexmedetomidine group in comparison to control group.

Conclusion: The perioperative infusion of Dexmedetomidine appears to be effective to attenuate stress induced haemodynamic fluctuation, reduced Propofol requirements, decreased the intra and post-operative narcotic analgesic administration, produced perioperative sedation in patients.

© This is an open access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>) which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

1. Introduction

Stress response usually involves hormonal and metabolic changes which follow injury or trauma.¹ Its response to surgery is usually characterised by an increase in the secretion of the endocrinal system as well as the activation of immunological and sympathetic nervous system. There are continued efforts to attenuate the neuroendocrine, cardiovascular and inflammatory response to surgery in order to improve the effect on organ function.²

Many of the manoeuvres, such as laparoscopic surgeries, laryngoscopies, tracheal intubation and extubation involve sympathetic stimulation. The pneumoperitoneum and carbondioxide insufflation which are normally required in the laparoscopic surgeries result in increased plasma norepinephrine, epinephrine, and plasma renin activity.³ These changes further cause systemic and pulmonary vascular resistance, blood pressure and reduced cardiac output. Moreover, the reverse Trendelenberg position in surgery further causes reduction in the cardiac output. These hemodynamic changes may result in ischemia which is life threatening.⁴

* Corresponding author.

E-mail address: kaladhar_sheshala@yahoo.com (S. Kaladhar).

To prevent these sympathetic discharges and to provide haemodynamic stability, various opioids, beta blockers, benzodiazepines, calcium channel blockers and vasodilators are used.⁵ One of the most used analgesics is the alpha-2 adrenoceptors. One of the first alpha 2-adrenoceptor agonist to be synthesised was in the early 1960s, which had unexpected side effects with sedation and hours and symptoms of severe cardiovascular depression. Thus lead to the development of Clonidine in 1966 as a potent antihypertensive drug and also for the management of alcohol and drug withdrawal, for adjunctive medication in myocardial ischaemia, and for pain and intrathecal anaesthesia.⁶

Dexmedetomidine is a specific and short acting alpha-2 adrenoceptor agonist and a potent drug, at plasma concentrations less than 1.0 ng/ml it can produce profound physiological alterations. They decrease sympathetic tone, with attenuation of the neuroendocrine and hemodynamic responses to anaesthesia and surgery; reduce anaesthetic and opioid requirements; and cause sedation and analgesia. They also allow psychomotor function to be preserved while letting the patient rest comfortably, there by offering benefits in the prophylaxis and adjuvant treatment of perioperative myocardial ischemia.⁷ Its unique properties render it suitable for sedation and analgesia during the whole perioperative period. Its applications as a premedicant, as an anaesthetic adjunct for general and regional anaesthesia, and as a postoperative sedative and analgesic are similar to those of the benzodiazepines with more beneficial effects.⁸

Another advantage is that Dexmedetomidine has no respiratory depression effect; a feature that makes it suitable to be given even to an extubated or spontaneously breathing patients so it is safely and effectively used in ICU surgical patients prior to, during and after extubation.⁹

This study was therefore performed to evaluate the intra-operative, and post-operative haemodynamic stress responses in patients, when Dexmedetomidine is used as an anaesthetic adjunct.

2. Materials and Methods

This study was done by the Department of anaesthesiology at Kamineni academy of medical sciences and research centre for a period of Eighteen months after obtaining clearance from the Institutional Ethical Committee. 100 patients between the ages of 18-60 years, with ASA score of I and II and scheduled for surgery under general anaesthesia were included in the study. The nature of the study was explained in detail to the patients and relatives and informed consent was taken from them. For all these patients, the surgeries lasted for more than one hour. Patients below 18 years of age, those with morbid obesity, history of chronic pulmonary disease, chronic endocrinal disease, autoimmune disease and Raynaud's disease were excluded from the

study. Pregnant women were also excluded from the study.

The patients were randomly divided into 2 groups of 50 each. Group I was given saline solution as Placebo and Group II was given 100 µg/ml of Dexmedetomidine hydrochloride. The loading dose 1 µg/kg I.V infusion given over 10 minutes, and for maintenance 0.5 µg/kg/hour I.V. infusion was given. Similar method was followed with saline in the placebo group. All the patients received oral Alprazolam 0.5 mg, the night before operation. Intensity of pain was measured by Visual analogue scale (VAS).

Anaesthesia was induced with sleep dose of Propofol, Succinylcholine (1.5 mg/kg) given and endotracheal intubation was performed. Then Vecuronium(0.08 mg/kg) was given after partial resumption of muscle power. Anaesthesia was induced with sleep dose of Propofol, Succinylcholine (1.5 mg/kg) given and endotracheal intubation was performed. Then Vecuronium(0.08 mg/kg) was given after partial resumption of muscle power. The mean arterial blood pressure (MAP) and heart rate (HR) monitoring started 30 minutes before induction of anaesthesia; the data were collected and recorded every 15 minutes, and continued after the end of the surgery by 6 hours.

The data collection was performed every 2 minutes during induction of anaesthesia and for 10 minutes after tracheal intubation.

The need for post operative analgesia was decided according to the visual analogue scale (VAS).

3. Results

The age, weight and gender were similar in both the groups with no statistical differentiation.

The mean arterial blood pressure (MAP) and heart rate (HR) monitoring started 30 minutes before induction of anaesthesia; the data were collected and recorded every 15 minutes, and continued after the end of the surgery by 6 hours.

The data collection was performed every 2 minutes during induction of anaesthesia and for 10 minutes after tracheal intubation.

There was no significant difference between the two groups in baseline HR mean values. Before induction of anaesthesia, Dexmedetomidine decreased heart rate significantly compared to control group ($P < 0.05$) and baseline value ($P < 0.05$).

The heart rate increased in both groups after intubation, the increase was significant in the control group ($P < 0.05$) and is not significant in the Dexmedetomidine group ($P > 0.05$) compared to the baseline values, but the heart rate decreased significantly in the Dexmedetomidine group compared to the control group ($P < 0.05$).

During the course of surgery, Dexmedetomidine reduced the heart rate significantly ($P < 0.05$) in comparison to the baseline values at 15 and 30 minutes, and compared to the

Table 1: Demographic details of patients

Details	Group I Placebo Group	Group II Dexmedetomidine Group
Age (in years)	35	33
Gender (M/F)	22/28	19/31
Weight (in kgs)	55	56

Table 2: Comparison of heart rate (beats/min) between Group-1 and Group II at baseline, before induction, after intubation, during surgery and in the first 6 hours after end of surgery (in PACU)

Timing in minutes	Group 1 (control) Mean SD	Group II (Dexmedetomidine) Mean SD	p value
Base line	76.14 3.70	77.22 2.06	0.0809
Before induction	77.30 4.03	68.56 3.19	0.0001*
After intubation	77.24 3.15	68.98 4.14	0.0001*
2	85.50 4.60	78.04 2.29	0.0001*
4	81.04 4.29	77.94 2.10	0.0001*
15	77 1.04	75.78 3.45	0.0335*
30	77.24 3.54	75.90 3.31	0.0433*
45	76.68 1.86	77.22 3.24	0.3091
60	76.26 1.23	76.98 3.61	0.1843
75	75.94 2.03	76.82 3.73	0.0733
During Surgery	77.66 6.56	77.16 3.23	0.3150
105	77.64 6.07	76.92 3.61	0.2364
120	78.26 8.12	76.70 3.86	0.0412*
135	78.68 7.24	76.46 4.18	0.0317*
150	77.26 3.15	76.24 4.43	0.0939
165	77.58 6.08	76.46 4.18	0.1429
180	75.06 3.20	76.26 4.19	0.0554
1	86.5 3.00	74.52 1.94	0.0001*
15	77.52 6.10	69.92 1.31	0.0001*
60	77.3 3.31	68.04 0.97	0.0001*
In PACU	77.12 2.34	66.64 1.03	0.0001*
180	75.4 1.34	68.56 3.19	0.0001*
240	77.6 5.96	76.32 4.24	0.1056
300	75.16 2.41	76.28 4.23	0.0535
360	76.82 2.80	76.34 4.29	0.4251

*= significant difference compared to control group

control group at 15, 30, 120, 135 and 165 minutes, while in control group the heart rate increased significantly during surgery ($P<0.05$) in comparison to the baseline values at 120 and 135 minutes.

Dexmedetomidine reduced the hourly postoperative analgesia requirements in PACU to keep the VAS below 30 in the first 6 hours when compared to saline, this reduction was significant in 60, 120, 180 and 240 minutes ($P<0.05$) and it was not significant in the 300 and 360 minutes ($P>0.05$) (Table 5).

One minute after arrival of the patients to the Post Anaesthesia Care Unit (PACU) the values of heart rate recorded in the Dexmedetomidine group were significantly lower than values recorded in the control group ($P<0.05$) and baseline values. Rather it was significantly higher than baseline values in control group ($P<0.05$). The heart rate values recorded after 15, 60, 120, 180 minutes, in PACU were

significantly less in Dexmedetomidine group in comparison to control group ($P<0.05$) and to baseline values ($P<0.05$). After 240, 300, 360 minutes and in PACU there was no significant difference in the values of heart rate recorded in each group and its baseline values.

No electrocardiographic changes were noticed in the study patients other than sinus bradycardia, and the response to atropine was adequate (Table 2).

3.1. Mean arterial blood pressure

There was no significant difference between the baseline values in both groups. After administration of the study drug and before induction of anaesthesia the values of Mean Arterial Pressure (MAP) in Dexmedetomidine group were lower than the value in control group ($P>0.05$) and the baseline mean value ($P>0.05$) which was not significant.

Table 3: Comparison of mean arterial blood pressure (mm Hg) between Group-I and Group-II at the baseline, before induction, after intubation, during surgery and in the first 6 hours after end of surgery (in PACU)

Timing in minutes	Group I (control)		Group II (Dexmedetomidine)		p value
	Mean	SD	Mean	SD	
Base line	87.62	1.783	88.78	3.903	0.059
Before induction	88.14	1.807	87.66	2.767	0.307
1	87.26	1.759	89.38	4.218	0.0001*
After intubation	104.72	3.117	95.48	1.832	0.0001*
2	99.82	2.067	95.96	1.009	0.0001*
4	89.96	2.194	89.34	4.173	0.0001*
15	88.08	1.839	87.9	2.837	0.707
30	88.14	1.807	87.66	2.767	0.307
45	88.2	2.060	87.84	2.802	0.641
60	88.16	2.502	80.84	1.448	0.0001*
75	87.7	1.961	79.84	2.132	0.0001*
During Surgery	88.24	2.520	77.88	2.125	0.0001*
90	93.74	2.284	83.24	1.222	0.0001*
105	95.12	1.172	79.56	1.343	0.0001*
120	87.52	2.002	75	1.512	0.0001*
135	88.08	1.861	74.48	1.147	0.0001*
150	87.58	2.400	78	1.641	0.0001*
165	87.52	2.002	84.88	1.081	0.0001*
180	88.14	1.807	87.72	2.763	0.0001*
In PACU	88.06	1.695	89.3	4.032	0.0001*
1	86.96	2.857	87.8	2.814	0.0001*
15	87.6	2.020	89.34	4.173	0.0001*
60	87.52	2.002	87.68	2.917	0.0001*
120	88.08	1.839	87.72	2.763	0.445
180	88.14	1.807	87.84	2.802	0.526
240					
300					
360					

*= significant difference compared to control group.

Table 4: Sleep dose of Propofol (mg) and intraoperative Fentanyl (μg) used for each group. Values are mean (SD)

Timing	Group I (control)	Group II (Dexmedetomidine)	P value
Sleep dose of propofol (mg)	112.2(7.90)	92.04(2.84)	0.0001*
Intraoperative Fentanyl (μg)	105.4(9.08)	81.5(2.31)	0.0001*

* = significant difference compared to control group.

Table 5: Postoperative visual analogue score

Timing in minutes	Group I (control)	Group II (Dexmedetomidine)	P value
60	1.14(0.35)	0.42(0.50)	0.0001*
120	2.22(0.46)	1.14(0.35)	0.032*
180	3.2(0.45)	2.22(0.46)	0.0001*
240	4.14(0.45)	3.2(0.45)	0.0001*
300	4.66(0.77)	4.14(0.45)	0.058
360	5.68(0.62)	4.64(0.78)	0.061

* = significant difference compared to control group.

The blood pressure increased after endotracheal intubation in both groups, this increase was significant in control group ($P<0.05$) and in Dexmedetomidine group in comparison to the baseline values, however Dexmedetomidine attenuated this response compared to saline ($P<0.05$).

During the course of surgery Dexmedetomidine reduced the MAP significantly ($P<0.05$) compared to the baseline at 75, 90, 105, 135, 150, 165 and 180 minutes, and in comparison to control group ($P<0.05$) at 75, 90, 105, 120, 135, 150, 165 and 180 minutes. However, in control group the MAP increased significantly ($P<0.05$) during the course of surgery after 120 and 135 minutes in comparison to the baseline.

In PACU the MAP values recorded in Dexmedetomidine were lower than control group after 15, 60, 120, 180 and 240 minutes (Table 3).

3.2. Propofol and fentanyl requirements

Dexmedetomidine reduced the sleep dose of Propofol and intraoperative Fentanyl significantly when compared to control group ($P<0.05$) (Table 4).

4. Discussion

Dexmedetomidine is a novel lipophilic imidazole derivative with 100 times higher affinity for alpha-2- adrenoceptors compared to the prototype drug clonidine.¹⁰ This study was done to investigate the perioperative effect of Dexmedetomidine on stress response to surgeries. Heart rate and blood pressure measurement were taken as indicator for sympatho-adrenomedullary axis of stress response.

Surgical procedures, endotracheal intubation and anaesthesia are stressful to the patient and may induce potentially harmful reactions, such as increase in the secretion of catecholamines and other stress hormones, and increase in heart rate and blood pressure.¹¹ Patients with a history of hypertension or coronary artery disease are particularly prone to hyper-dynamic cardiovascular response to stressful events encountered during surgery. There is a clear relationship between surgical events known to produce intense sympathetic stimulation and perioperative myocardial ischemic episodes and post operative myocardial infarction.¹²

The hemodynamic effects of Dexmedetomidine is due to its central sympatholytic and peripheral vasoconstrictive effects.^{13–15} Its effect is dose dependent and a decrease in arterial blood pressure and heart rate is due to the decrease in serum norepinephrine concentrations. The receptors in the medullary vasomotor region are activated, thus reducing the norepinephrine turnover resulting in a decrease in the norepinephrine turnover and decrease in central sympathetic outflow. This suppresses the hemodynamic response to intubation and extubation, without any side effects.

In the present study, Dexmedetomidine caused variable degree of reduction in the heart rate and arterial blood pressure during surgery compared to the baseline values. This was corroborated by a study by Khare et al, who observed that due to laryngoscopy, endotracheal intubation, pneumoperitoneum and extubation, there was a significant rise of heart rate and arterial pressure in the placebo patients. However, in patients who were given Dexmedetomidine, bradycardia was not noted in any of the cases and they seem to be a significant hemodynamic stability among the patients.¹⁶ In contrast, in a study by Ohtani et al, sevoflurane had a shorter time of recovery than that of Dexmedetomidine, when given as an adjuvant to propofol.¹⁷ Similar results were observed by Aantaa et al who noticed that Dexmedetomidine attenuated the catecholamine response to anaesthesia and surgery and reduced the arterial blood pressure by 15–20% and heart rate by 10–15% during surgery.¹¹ Reduce.^{18,19} Dexmedetomidine has found to have reduced the requirements of opioids due to the hemodynamic stability.^{20–23}

5. Conclusion

In conclusion, the perioperative infusion of Dexmedetomidine appears to be effective to attenuate stress induced haemodynamic fluctuation, reduced Propofol requirements, decreased the intra and post-operative narcotic analgesic administration, produced perioperative sedation in patients who underwent elective surgeries when compared with placebo. These advantages provide a safe, effective, and attractive drug that may find a place in modern anaesthesia practice

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Desborough JP. The stress response to trauma and surgery. *Br J Anaesth.* 2000;85(1):109–17.
2. Kennedy BC, Hall GM. Neuroendocrine and inflammatory aspects of surgery. Do they affect outcome. *Acta Anaesthesiol Belg.* 1999;50:205–9.
3. Joris JL, Noirot DP, Legrand MJ, Jacquet NJ, Lamy ML. Hemodynamic Changes During Laparoscopic Cholecystectomy. *Anesth Analg.* 1993;76:1067–71.
4. Wilcox S, Vandam LD. Alas, Poor Trendelenburg and His Position! *Anesth Analg.* 1988;67:574–8.
5. Khan ZP, Munday IT, Jones RM, Thornton C, Mant TG, Amin D. Effects of dexmedetomidine on isoflurane requirements in healthy volunteers. I: Pharmacodynamic and pharmacokinetic interactions. *Br J Anaesth.* 1999;83(3):372–80.
6. Tamsen A, Gordh T. EPIDURAL CLONIDINE PRODUCES ANALGESIA. *Lancet.* 1984;324(8396):231–2.

7. Kamibayashi T, Maze M. Clinical Uses of α 2-Adrenergic Agonists. *Anesthesiol.* 2000;93(5):1345–9.
8. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: A Novel Sedative-Analgesic Agent. *Baylor Univ Med Center Proc.* 2001;14(1):13–27.
9. Khan ZP, Ferguson NC, Jones RM. Alpha 2 and imidazoline receptor agonists. Their pharmacology and therapeutic role. *Anaesth.* 1999;54:146–65.
10. Talke P, Li J, Jain U, Leung J, Drasner K, Hollenberg M, et al. Effects of Perioperative Dexmedetomidine Infusion in Patients Undergoing Vascular Surgery. *Anesthesiol.* 1995;82(3):620–33.
11. Aantaa R, Kanto J, Sheinin M, Kallio A, Scheinin H. Dexmedetomidine an alpha 2-adrenoceptor agonist, reduces anesthetic requirements for patients undergoing minor gynecologic surgery. *Anesthesiol.* 1990;73:230–5.
12. Slogoff S, Keats AS. Does Perioperative Myocardial Ischemia Lead to Postoperative Myocardial Infarction? *Anesthesiol.* 1985;62(2):107–14.
13. Talke P, Richardson CA, Scheinin M, Fisher DM. Postoperative pharmacokinetics and sympatholytic effects of dexmedetomidine. *Anesth Analg.* 1997;85:1136–42.
14. Talke P, Lobo E, Brown R. Systemically Administered α 2-Agonist-induced Peripheral Vasoconstriction in Humans. *Anesthesiol.* 2003;99(1):65–70.
15. Piascik MT, Soltis EE, Piascik MM, Macmillan LB. Alpha-adrenoceptors and vascular regulation: Molecular, pharmacologic and clinical correlates. *Pharmacol Ther.* 1996;72:215–41.
16. Khare A, Sharma SP, Deganwa ML, Sharma M, Gill N. Effects of dexmedetomidine on intraoperative hemodynamics and propofol requirement in patients undergoing laparoscopic cholecystectomy. *Anesth: Essays Res.* 2017;11(4):1040–5.
17. Ohtani N, Kida K, Shoji K, Yasui Y, Masaki E. Recovery Profiles from Dexmedetomidine as a General Anesthetic Adjuvant in Patients Undergoing Lower Abdominal Surgery. *Anesth Analg.* 2008;107(6):1871–4.
18. Afanador C, Marulanda L, Torres G, Marín A, Vidal C, Silva G. Effect of intraoperative use of dexmedetomidine on anesthetic requirements and time to tracheal extubation in elective adult heart surgery patients. A retrospective cohort study. *Internet J Anesthesiol.* 2009;22(2):1–9.
19. Bajwa SJS, Singh A, Singh G, Gupta S, Panda A, Kaur J, et al. Attenuation of pressor response and dose sparing of opioids and anaesthetics with pre-operative dexmedetomidine. *Indian J Anaesth.* 2012;56(2):123–8.
20. Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN, Ozcan B. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. *Can J Anesth.* 2006;53(7):646–52.
21. Tufanogullari B, White PF, Peixoto MP, Kianpour D, Lacour T, Griffin J, et al. Dexmedetomidine Infusion During Laparoscopic Bariatric Surgery: The Effect on Recovery Outcome Variables. *Anesth Analg.* 2008;106:1741–8.
22. Abdelmageed W, Shabana R, Nassar A, Elquesny K, Abushama H. Analgesic properties of a dexmedetomidine infusion after uvulopalatopharyngoplasty in patients with obstructive sleep apnea. *Saudi J Anaesth.* 2011;5(2):150–6.
23. Lin TF, Yeh YC, Lin FS, Wang YP, Lin CJ, Sun WZ, et al. Effect of combining dexmedetomidine and morphine for intravenous patient-controlled analgesia. *Br J Anaesth.* 2009;102(1):117–22.

Author biography

Viditha Korukonda, Assistant Professor

S Kaladhar, Assistant Professor

Cite this article: Korukonda V, Kaladhar S. A study on intra-operative and post-operative effects of dexmedetomidine on haemodynamic stress responses to surgeries. *Indian J Clin Anaesth* 2020;7(4):563-568.