



## Effects of Premedication with Dexmedetomidine on Perioperative Hemodynamics and Anesthetic Requirements during Elective General Abdominal Surgeries

Authors

\*Nuzhat Ul Islam<sup>1</sup>, Rukhsana Najeeb<sup>2</sup>, Masarat Ara<sup>3</sup>, M Ahsan Wani<sup>4</sup>, M Ommid<sup>5</sup>

<sup>1,3</sup>Resident, Department of Anesthesiology & Critical Care, Govt. Medical College, Srinagar, India

<sup>2</sup>Professor Department of Anesthesiology & Critical Care, Govt. Medical College, Srinagar, India

<sup>4</sup>Sr. Resident, Bone & joint, Govt. Medical College, Srinagar, India

<sup>5</sup>Assistant professor Department of Anesthesiology & Critical Care, Govt. Medical College, Srinagar, India

Corresponding Author

**Dr Nuzhat Ul Islam**

Resident, Department of Anesthesiology & Critical Care, Govt. Medical College, Srinagar, India

Email: [drehsanwani@gmail.com](mailto:drehsanwani@gmail.com), Mobile No: +91-9796599959

### Abstract

**Background and Aims:** *Effective use of sedative-hypnotic and analgesic agents is an integral part of providing patient comfort and safety for patients during general anaesthesia. The present study was carried out to evaluate the effects of premedication with dexmedetomidine on perioperative haemodynamic and dose requirement of propofol and fentanyl during laryngoscopy and tracheal intubation.*

**Methods:** *100 patients belonging to ASA class I and ASA class II of either sex, in the age group of 20-55 years were divided into two groups, Group 1 and Group 2 with 50 patients in each group. Group 1 received 100ml of Normal saline over a period of 10 minutes and 1µg/kg of fentanyl 3 minutes before induction of general anaesthesia. Group 2 received 1µg/kg of dexmedetomidine in 100 ml of normal saline over a period of 10 minutes and 1µg/kg of fentanyl 3 minutes before induction of general anaesthesia.*

**Results:** *The demographic profile was comparable. The pressor response to laryngoscopy, intubation, surgery and extubation were effectively decreased by dexmedetomidine, and were highly significant on comparison ( $P < 0.001$ ). The mean dose of fentanyl and propofol were also decreased significantly by the administration of dexmedetomidine. The total dose requirement of fentanyl and propofol was decreased by 33.58% and 43.01% in Group 2 as compared to Group 1 and the difference was statistically significant.*

**Conclusions:** *Dexmedetomidine is an effective drug when used as an adjunct to general anaesthesia for attenuation of pressor response. It not only decreased the magnitude of stress response to intubation, surgery and extubation but also decreased the dose of propofol and opioids in achieving adequate anaesthesia and analgesia respectively.*

**Keywords:** *Dexmedetomidine, fentanyl, heart rate, propofol, mean arterial pressure, entropy, pressor response.*

## Introduction

Induction of anesthesia and tracheal intubation may induce profound alteration in the hemodynamic state of the patient subsequent to both the effects of anesthetic drug administered perioperatively, and the adrenergic state of the patient.<sup>1</sup>

The perioperative period is characterized by increased sympathetic activity, leading to stress-induced tachycardia and hypertension. Laryngoscopy and Endotracheal intubation are an integral part of anesthesiologist's contribution to patient care and are regarded as one of the core skills of anaesthesiologist. Laryngoscopy and endotracheal intubation are the fundamental components of airway management. Laryngoscopy itself is a noxious and an invasive stimulus during endotracheal intubation<sup>2</sup>. Manipulation of the respiratory tract during laryngoscopy and endotracheal intubation are associated with hemodynamic and cardiovascular response consisting of increased circulating catecholamines, heart rate, blood pressure, myocardial oxygen demand, tachycardia and dysrhythmias<sup>3</sup>.

Most anaesthesiologists agree that a skilled anaesthesiologist applies only a small force to the patient's larynx when using a laryngoscope and that reducing the force on the larynx might prevent excessive hemodynamic response to endotracheal intubation<sup>4</sup>. These changes can result in potentially harmful effects thereby increasing morbidity and mortality especially in susceptible patients. Many studies have been conducted for prevention of these effects due to stress response to laryngoscopy and endotracheal intubation by many techniques and pharmacological agents.

Many studies have concentrated on attenuation of the stress response to laryngoscopy and endotracheal intubation and a number of pharmacological measures and techniques have been used to attenuate the hemodynamic stress response to laryngoscopy and endotracheal intubation. No single drug or technique is completely satisfactory and without side effects.

Among the various pharmacological agents for attenuation of the stress response to laryngoscopy and endotracheal intubation are inhalational anaesthetic agents (increasing the depth of anaesthesia)<sup>5</sup>,  $\alpha$ -adrenergic blockers like phentolamine,  $\beta$ -adrenergic blockers like acebutol, labetalol and propranolol<sup>6</sup>, directly acting vasodilators like sodium nitroprusside and nitroglycerine, low doses of opioids like morphine, fentanyl, alfentanyl and sufentanyl<sup>7</sup>, topical administration of local anaesthetics<sup>8</sup>.

Minimizing the duration of laryngoscopy and endotracheal intubation was found effective in minimizing the stress response to laryngoscopy and endotracheal intubation<sup>9</sup>.

Calcium channel blockers like nicardipine, verapamil, and diltiazem have also been found to suppress the stress response<sup>10</sup>.

All the above pharmacological agents have been used for attenuation of the stress response to laryngoscopy and endotracheal intubation but most of them are not without side effects resulting in their limited use for this purpose.

Clonidine and other  $\alpha$ -2 adrenoceptor agonists like Dexmedetomidine have recently been used effectively to suppress the stress response to laryngoscopy and endotracheal intubation with minimal side effects. Dexmedetomidine not only has been shown to suppress stress response to laryngoscopy and endotracheal intubation but at the same time resulted in decreased requirements of IV anaesthetic agents like propofol for induction of general anaesthesia<sup>11</sup>.

Drugs acting as agonists at alpha 2 ( $\alpha$ 2) adrenoceptors may enhance anesthesia by producing dose related sedation, anxiolysis, decreased upper airway secretions, perioperative hemodynamic stability and analgesia. There is substantial evidence that the alpha 2 – agonists also exert anesthetic sparing effect mediated in part through a decrease in central noradrenergic activity, but mainly through a direct effect on central  $\alpha$ <sub>2</sub>-adrenoceptors in the locus coeruleus, a predominant noradrenergic nucleus of brainstem, which is an important modulator of vigilance and

other sites. The  $\alpha_2$  agonists also have activity at the imidazoline receptors involved in central blood pressure control.<sup>12</sup>

Dexmedetomidine, a highly selective, and potent  $\alpha_2$  adrenoceptor agonist possessing hypnotic, sedative, anxiolytic, sympatholytic and analgesic properties without producing significant respiratory depression. In recent studies dexmedetomidine has been shown to have clinically significant effects on anaesthetic requirements, hemodynamic response induced by anesthesia and surgery in patients.<sup>13</sup>

Dexmedetomidine has a complex vasodilative and vasoconstrictive hemodynamic effects specific to its activation of pre- and post-synaptic alpha 2 – receptors.

These effects are dose-dependent and biphasic: Vasodilation at lower dosages, vasoconstriction at higher dosages and an initial short-term increase in blood pressure (BP) followed by a longer lasting reduction in BP and heart rate (HR)<sup>14</sup>.

It has been observed that an intraoperative infusion of dexmedetomidine combined with inhalational anesthetics provided satisfactory intraoperative conditions without adverse hemodynamic effects and decreases emergence agitation in children.<sup>15</sup> Dexmedetomidine has been increasingly used as a sedative for monitored anaesthesia care (MAC) because of its analgesic properties, “cooperative sedation” and lack of respiratory depression. It has also been explored as a non-invasive pre medication through intra-nasal route.<sup>16</sup>

## Methods

The present study was conducted at the SMHS Hospital which is one of the associated hospitals of Government Medical College Srinagar. After obtaining approval from hospital ethical committee, a written informed consent was taken from the patients for participation in the study.

This was a prospective observational study in tertiary care hospital conducted over a period of 1 ½ years.

Hundred patients of either sex in the age group of 20-55 years, belonging to ASA class I and II scheduled for elective general abdominal surgeries of the duration of 1-2 hrs were elected for this study.

Patients selected for the surgery were admitted at least 24 hours prior to surgery. Preanaesthetic check up was done at this stage. A thorough history including history of any comorbid disease, preanaesthetic exposure, medications, allergy to any drug and personal habits was elicited.

General physical examination as well as systemic examination of cardiovascular system, respiratory system, and central nervous system was performed. Airway assessment was also done to predict any difficult intubation.

All routine investigations like Haemoglobin (Hb), platelet count, BT/CT (Bleeding time/Clotting time), CBC (Complete Blood Count), KFT (Kidney Function Test), blood glucose (F/R), chest X-ray (PA view) and ECG (Electrocardiogram) were checked. The patients were advised to remain fasting according to latest ASA guidelines.

Patients undergoing surgery were divided into two equal groups of 50 patients each and were allocated to one of the two groups:

1. Group 1 – Isoflurane – Opioid – Saline infusion
2. Group 2 – Isoflurane – Opioid – Dexmedetomidine infusion

On arrival in the operating room, the patient's baseline heart rate, blood pressure and SPO<sub>2</sub>, mean arterial blood pressure (MAP) were recorded by connecting the patient to multi-channel monitor after 5 minutes of settling in the operative room. Entropy electrodes were connected to patient's forehead.

Two 18G intravenous cannula were inserted for drug and continuous fluid infusion. All the patients were given an infusion of 500ml of Ringer's lactate solution. In Group 1 all the patients received 100ml of normal saline over a period of 10 minutes preoperatively and injection fentanyl 1 $\mu$ g/kg 3 minutes before induction of

anaesthesia. All the patients in group 2 received injection dexmedetomidine in a dose of 1µg/kg in 100ml of normal saline over a period of 10 minutes preoperatively and injection fentanyl 1µg/kg 3 minutes before induction of anaesthesia. All the patients were premedicated with injection pantaprazole.

Patients were preoxygenated for 3 min and then a dose of injection propofol sufficient to abolish verbal response was injected followed by injection Atracurium 0.5mg/kg to facilitate laryngoscopy and tracheal intubation. The patient's lungs were ventilated by facemask for at least 3 minutes using 100% O<sub>2</sub>.

Laryngoscopy was performed with Macintosh laryngoscope and trachea was intubated with appropriate size endotracheal tube. With a strict and vigil monitoring of haemodynamics at regular intervals of 1 minute, 3 minutes and 5 minutes and thereafter were observed continuously but recorded at 30 minutes interval till completion of surgery. During surgery, anaesthesia was maintained with isoflurane and 66% nitrous oxide in oxygen. Entropy was maintained between (40-60) by adjustment in the inspiratory concentration of isoflurane by increment or decrement values of 0.2%, as also judged by the increase or decrease in heart rate and MAP of 20% from the baseline values. An additional 0.5µg/kg dose of fentanyl was repeated whenever the inspiratory

concentration of inhalational anaesthetic reached 1%. and Entropy reached 60.

At the end of surgical procedure the neuromuscular blockade was antagonized with injection Neostigmine 0.05mg/kg and injection Glycopyrrolate 0.01mg/kg intravenously. Patients were extubated when respiratory effort was deemed sufficient and patients were able to obey simple commands.

### Statistical Analysis

Statistical Package for Social Sciences (SPSS - version 20.0) and Microsoft Excel software's were used to carry out the statistical analysis of data. Descriptive Statistics of data including the means and standard deviations for numerical variables and the percentages of different categories for categorical variables was obtained. Student's independent t-test was employed for inter group analysis of data. Intra group analysis was carried out with the help of Paired t-test. Chi-square test or Fisher's exact test, whichever appropriate, was used for comparison of categorical variables. Graphically the data was presented by bar and line diagrams. A P-value of less than 0.05 was considered statistically significant.

### Results

There was no significant difference with respect to age, sex, weight, ASA physical status, duration of surgery and anaesthesia time [Table 1].

Variable	Group 1 (n=50)	Group 2 (n=50)	P-value
Age	37.3±9.78	39.8±9.73	0.211*
Weight	61.1±6.57	59.6±5.11	0.194*
Gender (M/F)	27/23	32/18	0.309*
ASA (I/II)	41/9	39/11	0.617*
Duration of surgery	94.3±18.77	91.4±15.34	0.406*
Duration of anaesthesia	106.1±18.65	103.2±14.65	0.402*

ASA American society of Anaesthesiology, SD standard deviation, \* Level of significance.

**Table: 2** Dose of propofol and fentanyl

Variable	Group 1	Group 2	P-value
Propofol	129.5±12.38	73.8±6.82	<0.001*
Fentanyl	2.68±0.94	1.78±0.69	

SD standard deviation, \* Level of significance

Propofol and fentanyl dose requirement in Group 1 was  $129.5 \pm 12.38$  mg,  $2.68 \pm 0.94$  and in Group 2 was  $73.8 \pm 6.82$ mg,  $1.78 \pm 0.69$  and reduction in dose in group 2 was 43.01%, 33.58% and the difference was statistically significant ( $p \leq 0.001$ ).table:2.

Study groups were comparable with respect to baseline heart rate with no statistical difference.

There was statistically significant difference at 10min after infusion of study drug and after induction of anesthesia, after intubation 1, 3, 5 mins after intubation, after reversal of neuromuscular blockade, at extubation and 1 min after extubation. ( $p \leq 0.001$ ).fig 1

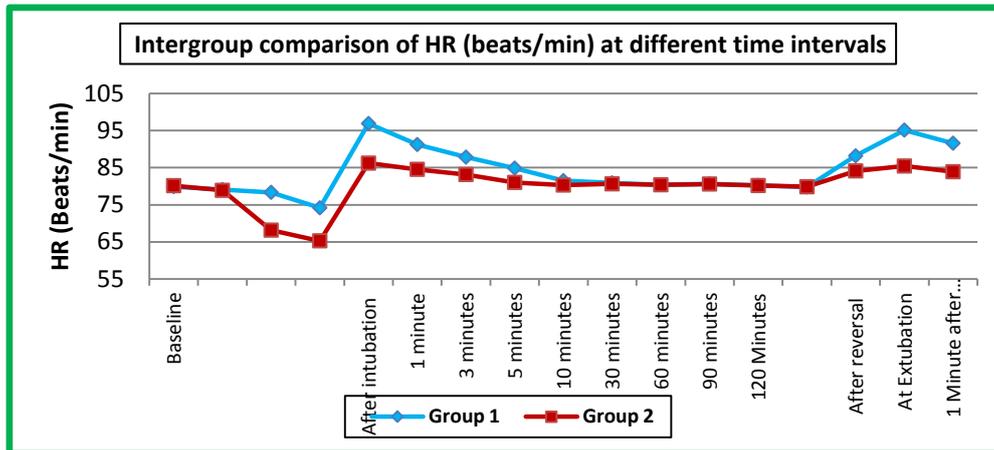


Fig.1

Study groups were comparable with respect to baseline SBP ( $p=0.464$  no statistical difference). There was statistically significant difference at 10min after infusion of study drug ( $p= 0.018$ ) and

after induction of anesthesia, after intubation 1, 3, 5 mins after intubation, after reversal of neuromuscular blockade, at extubation and 1 min after extubation. ( $p \leq 0.001$ ).fig.2.

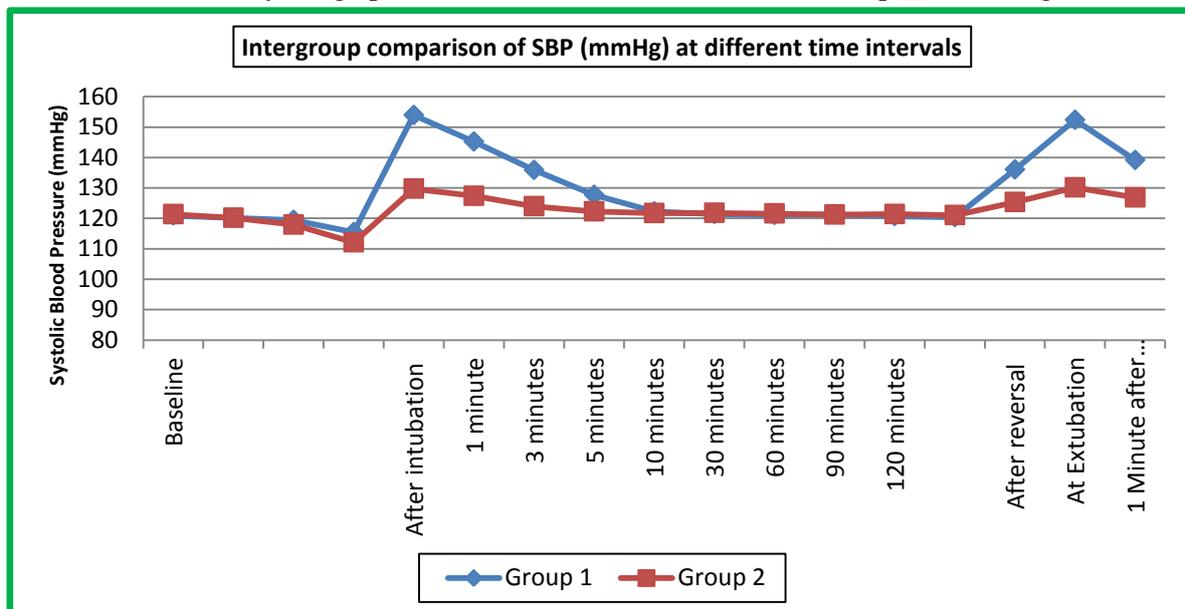


Fig.2

Groups were comparable regarding DBP values ( $p = 0.312$ ). There was statistically significant difference in DBP values at 10 mins after infusion of study drug ( $p = 0.015$ ), after induction of

anesthesia ( $p = 0.002$ ), after intubation, 1, 3, 5 mins after intubation, after reversal of neuromuscular blockade, at extubation and 1 min after extubation ( $p \leq 0.001$ ). Fig.3.

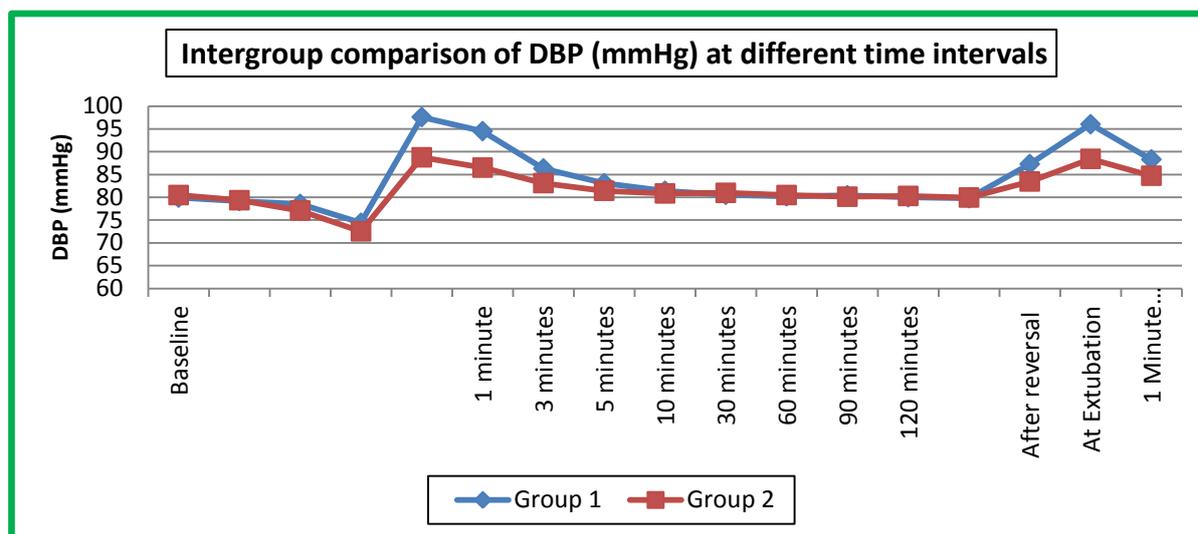


Fig.3

### Discussion

Dexmedetomidine is a highly selective  $\alpha_2$  agonist that has been shown to have sedative, analgesic, and anaesthetic sparing effects. The analgesic, sedation, anxiolytic, sympatholytic and blunting of exaggerated hemodynamic responses are being extensively studied and are mainly mediated by activation of  $\alpha_2$  receptors located in postsynaptic terminals in the central nervous system, which causes decreased neuronal activity and augmentation of the vagal activity<sup>17</sup>.

Mean duration of laryngoscopy in the two groups was less than 15 secs. Mean duration of laryngoscopy in Group 1 was  $14.3 \pm 1.90$  seconds and in Group 2 was  $13.6 \pm 1.88$  seconds and the difference was statistically insignificant ( $p=0.075$ ). Robert K Stolting et al<sup>18</sup> noted that the best way to prevent laryngoscopic response was to minimize the duration of laryngoscopy and intubation. He noted that if laryngoscopy and intubation were performed within 15 secs, the haemodynamic changes seem to be minimal. Hence, in our study the duration of laryngoscopy was restricted as much as possible and all the laryngoscopy and intubations were performed by an expert anesthesiologist.

The dosage of general anaesthetic for the induction of anaesthesia decreases significantly after premedication with dexmedetomidine, as was also evident from the decreased requirement

of propofol in group 2. The mean dose requirement of propofol in Group 1 was 129.5mg and in Group 2 was 73.8mg. The mean dose of propofol needed for induction was reduced significantly by 43.01% in the patients receiving dexmedetomidine. This finding was consistent with the study done by Suvadeep Sen et al<sup>19</sup>, who studied the effect of dexmedetomidine infusion on propofol requirement for maintenance of optimum depth of anaesthesia during elective spine surgery and concluded that requirement of propofol at induction and during maintenance was lessened by 48.08% and 61.87% respectively and dose was calculated maintaining bispectral index between 40 and 60 ( $p<0.05$ ).

In the present study, the dose of  $1\mu\text{g}/\text{kg}$  of dexmedetomidine attenuated but did not completely obtund the hemodynamic responses to laryngoscopy, tracheal intubation and extubation. We used dexmedetomidine in a pre-operative infusion dose of  $1\mu\text{g}/\text{kg}$  over a period of 10 minutes and observed moderate reduction in the HR, BP, DBP, and MAP at the end of 10 minute of infusion of dexmedetomidine to the extent 10-18% from the baseline values, and the findings are very much similar to the observations of other studies and can be explained on the basis of markedly decreased CNS sympathetic activity.

SJS Bajwa et al<sup>20</sup> who studied the Attenuation of pressor response and dose sparing of opioids and

anaesthetics with pre-operative dexmedetomidine and concluded that there was a moderate reduction of MAP and HR to the extent of 10-15% from the baseline value after the infusion of study drug.

Subsequently HR started settling down and almost approached to baseline in group 2 ( $p \leq 0.001$ ) at 5 minutes but was still high in group 1 ( $p \leq 0.001$ ) even at 5 minutes suggesting that dexmedetomidine was successful in attenuating the increase in HR following laryngoscopy and endotracheal intubation. These results are consistent with the study done by SJS Bajwa et al<sup>20</sup>.

Siddareddigari Velayudhu Reddy et al<sup>21</sup> studied Dexmedetomidine versus esmolol to attenuate the hemodynamic response to laryngoscopy and tracheal intubation: A randomized double-blind clinical study and concluded that both the drugs attenuated the pressor response. Of the two drugs administered, dexmedetomidine 1 $\mu$ g/kg provides a consistent, reliable and effective attenuation of pressor response compared to esmolol 2.0 mg/kg ( $p < 0.001$ ).

Munise Yildiz et al<sup>22</sup> studied the Effect of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation and concluded that preoperative administration of dexmedetomidine resulted in blunted haemodynamic responses during laryngoscopy, there was an increase in both heart rate and blood pressure in both groups dexmedetomidine and placebo group but response was less in dexmedetomidine group ( $p < 0.05$ ) and reduced opioid and anaesthetic requirements.

Thereafter till completion of surgery, no statistically significant difference was noted in these respective parameters HR, SBP, DBP and MAP ( $p \geq 0.05$ ). These findings are inconsistent with the study done by SJS Bajwa et al<sup>20</sup> who studied the attenuation of pressor response and dose sparing of opioids and anaesthetics with preoperative dexmedetomidine.

After reversal of anaesthesia MAP increased in Group 1 by 10.62%, at extubation by 22.65% and 1 minute after extubation 12.44% ( $p \leq 0.001$ ). In Group 2, after reversal MAP increased by 3.5%, at

extubation 8.7% and 1 minute after extubation 4.9% ( $p \leq 0.001$ ). Between the two groups dexmedetomidine showed attenuation of extubation response of MAP. These findings are in consistent with the study done by Guler G et al<sup>23</sup> who studied that single-dose dexmedetomidine attenuates airway and circulatory reflexes during extubation and concluded that HR, SBP, DBP increased at extubation in both the groups ( $p < 0.05$ ), but the increase was less significant with dexmedetomidine.

### Conclusion

Dexmedetomidine is an effective drug when used as an adjunct to general anaesthesia for attenuation of pressor response. It not only decreased the magnitude of stress response to intubation, surgery and extubation but also decreased the dose of propofol and opioids in achieving adequate anaesthesia and analgesia respectively.

### References

1. Iannuzzi E, Iannuzzi M, Cirillo V, et al. Peri-intubation cardiovascular response during low dose remifentanyl or sufentanyl administration in association with propofol TCI. A double blind comparison. *Minerva Anestesiologica*; 2004 Mar, 70(30); 109-15.
2. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. *Br J Anaesth* 1987; 59:295-9
3. Seyed Mojtaba Marashi et. al. Attenuation of hemodynamic responses following laryngoscopy and tracheal intubation: Comparative assessment of Clonidine and Gabapentin premedication. *M.E.J. Anesth* 2009; 20(2).
4. Bucx MJ, Snijders CJ, van Geel RT, et al. Forces acting on the maxillary incisor teeth during laryngoscopy using the

- Macintosh laryngoscope. *Anaesthesia* 1994; 49: 1064–70.
5. Bedford RF and Lt Marshal K. Cardiovascular responses to endotracheal intubation during four anaesthetic techniques. *Acta Anaesthesiologica Scandinavia*. 1984; 28: 563-566.
  6. Chandrashekara PM and King R. Attenuation of cardiovascular responses to endotracheal intubation. *Indian Journal of Anaesthesia*. 1984; 32(5): 358-367.
  7. Kay B, Nolan D, Mayall R, Healy TEJ. The effects of sufentanil on the cardiovascular response to tracheal intubation. *Anaesthesia*. 1987; 42: 382-386.
  8. Mounir-Abou-Madi, Hugo Keszler and Odile Yacoub. A method for prevention of cardiovascular responses to laryngoscopy and intubation. *Canadian Anaesthetic Society Journal*. 1975; 22(3): 316-329.
  9. Kimura A et al .Use of fiberoptic stylet scope reduces the hemodynamic response to intubation in normotensive and hypertensive patients. *Can J Anaes* 2001; 48: 919-23.
  10. Yoshitaka Fujii MD, Yuhji Saitoh MD, Shinji Takahashi MD, Hidenori Toyooka MD. Diltiazem-lidocaine combination for the attenuation of cardiovascular responses to tracheal intubation in hypertensive patients. *Canadian Journal of Anaesthesia*. 1998; 45: 935-937.
  11. Hayashi Y, Maze M. Alpha<sub>2</sub> adrenoceptor agonists and anaesthesia. *Br J Anaesth* 1993; 71: 108-180.
  12. Segal IS, Vickery RG, Walton JK, Doze VA, Maze M. Dexmedetomidine diminishes halothane anesthetic requirements in rats through a postsynaptic alpha<sub>2</sub> – adrenergic receptor. *Anesthesiology* 1988; 69: 818-23.
  13. Aho M, Lehtinen AM, Erkola O, Kallio A, Korttila K. The effect of intravenously administered dexmedetomidine on perioperative hemodynamics and isoflurane requirements in patients undergoing abdominal hysterectomy. *Anesthesiology* 1991; 74: 997-1002.
  14. Aantaa R, Kanto J, Scheinin M et al. Dexmedetomidine, an  $\alpha_2$  adrenoceptor agonist, reduces anesthetic requirements for patients undergoing minor gynecologic surgery. *Anesthesiology* 1990; 73: 230-235.
  15. Patel A, Davidson M, Tran MC, Quraishi H. Dexmedetomidine infusion for analgesia and prevention of emergence agitation in children with obstructive sleep apnea syndrome undergoing tonsillectomy and adenoidectomy. *Anesth Analg* 2010; 111: 1004-10.
  16. Vivian M, Micheal G, Theresa W, Man K, Libby H. A double-blind, cross over assessment of the sedative and analgesic effects of intranasal dexmedetomidine. *Anesth Analg* 2007; 105: 374-80.
  17. Hall JE, Uhrich TD, Barney JA, Arain SA, Ebert TJ. Sedative, amnestic and analgesic properties of small dose dexmedetomidine infusions. *Anesth Analg* 2000; 90: 699-705.
  18. Stoelting RK. Circulating responses to laryngoscopy and intubation with or without prior oropharyngeal viscous lignocaine. *Anaesthesia Analgesia*. 1977; 56: 618-21.93
  19. Suvadeep Sen, Jananti Chakraborti, Sankari Santra et al. The effect of dexmedetomidine infusion on propofol requirement for maintenance of optimum depth of anaesthesia during elective spine surgery. *Indian Journal of Anesthesia* Aug. 2013; Vol. 57, Issue 4.
  20. SJS Bajwa, Jasbir Kaur, Amarjit Singh, SS Parmer, Gurpreet Singh, Ashish Kulshreshtha, Sachin Gupta, Veenita Sharma, Aparajita Panda. Attenuation of pressure response and dose sparing of Opiodes and anesthetics with preoperative

- dexmedetomidine. *Indian J Anaesth.* 2012 Mar-Apr; 56(2): 123–128.
21. Siddareddigari velayudha Reddy, Donthu Balaji, Shaikh Nawaz Ahmad. Dexmedetomidine versus esmolol to attenuate the hemodynamic response to laryngoscopy and tracheal intubation: A randomized double- blind clinical study. *International Journal of Applied and Basic Medical Reseach*, Jul-Dec 2014; Vol.4, Issue 2.
  22. Yildiz Munise, Tavlan Aybars, Tuncer Sema, Reisli Ruhiye et al. Effects of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation: perioperative haemodynamics and anaesthetic requirements. *Drugs in R&D* 2006; 7(1): 43-52.
  23. Guler G, Akin Z, Tosun E, Eskitascoglu, Mizrak A, Boyaci A. Single-dose dexmedetomidine attenuates airway and circulatory reflexes during extubation. *Acta Anaesthesiol Scand* 2005; 49: 1088-91.