



Anaesthesiology

COMPARATIVE EVALUATION OF INTRAVENOUS DEXMEDETOMIDINE AND INTRAVENOUS FENTANYL TO ATTENUATE PRESSOR RESPONSE DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

Tripti Nagdev*

Senior Resident Department of Anaesthesiology, Dr. D. Y. Patil Medical College, Dr. D. Y. Patil Vidyapeeth (DPU), Pune *Corresponding Author

Smita Joshi

Professor Department of Anaesthesiology Dr. D. Y. Patil Medical College, Dr. D. Y. Patil Vidyapeeth (DPU), Pune

ABSTRACT **Introduction:** Laryngoscopy and Endotracheal Intubation is the gold standard for airway management. We used iv dexmedetomidine 1µg/kg and iv fentanyl 2µg/kg. **Aim:** To compare attenuation of pressor response and compare the effect of maintaining the haemodynamic stability during laryngoscopy and endotracheal intubation.

Methods and Materials: 15 to 65 years of ASA grade I and II posted for surgery. Patients were selected randomly and allocated into Group D: (n-30) received 1µg/kg of dexmedetomidine iv slowly after recording baseline vitals, diluted with normal saline to make 10ml Group F: (n-30) received 2µg/kg fentanyl iv slowly diluted with normal saline to make 10ml.

Results: The demographic data was comparable, we found that iv Dexmedetomidine in the dose of 1 µg/kg and iv Fentanyl 2 µg/kg given ten minutes prior to induction, both attenuated the hemodynamic responses to laryngoscopy and endotracheal intubation. The attenuation of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was better in group D.

Conclusion: Intravenous Dexmedetomidine 1 µg/kg given 10 minutes prior to surgery was superior to intravenous Fentanyl 2µg/kg.

KEYWORDS : Dexmedetomidine, Fentanyl, Laryngoscopy.

INTRODUCTION

In 1940, Reid and Brace first described hemodynamic response to laryngoscopy and intubation. But this evokes a stress response which is exhibited in the form of changes in heart rate, blood pressure and arrhythmias. These undesirable changes are transitory in nature and well tolerated in healthy individuals, it may result in potentially deleterious effects in patients with co-morbid conditions like hypertension, raised intracranial pressure or coronary artery disease.¹

Manipulation of respiratory tract such as in laryngoscopy and tracheal intubation are associated with hemodynamic and cardiovascular responses consisting of increase in circulating catecholamines, with subsequent increase in heart rate, blood pressure and dysrhythmias as well.^{2,3} The cardiovascular response is also directly related to the force and duration of laryngoscopy.⁴

Fentanyl is an opioid analgesic and is popular to be used as premedicant to provide cardiovascular stability during laryngoscopy and intubation. It has a rapid onset and short duration of action and is strong agonist at the µ-opioid receptors.^{6,7}

Dexmedetomidine is an imidazole derivative and selective alpha 2 adrenergic receptor agonist. α2-agonists produce hyperpolarization of noradrenergic neurons and suppression of neuronal firing in the locus ceruleus which leads to decreased systemic noradrenaline release resulting in attenuation of sympathoadrenal responses and hemodynamic stability during laryngoscopy and tracheal intubation. It provides sedation, analgesia, sympatholytic and anxiolytic effects that blunt many of cardiovascular responses.^{8,9}

MATERIAL AND METHODS

The study was conducted in a randomized double blind manner, in the department of Anaesthesiology at Dr. D. Y. Patil Medical College and Hospital. Written informed consent was obtained from all patients. After the approval of the institutional ethics committee, the study was conducted on 60 healthy patients of both sex aged between 15- 65 years, belonging to ASA (American society of Anaesthesiologists) grade I and II, scheduled for elective surgical procedures under general anaesthesia.

Group D: (n-30) received 1µg/kg of dexmedetomidine iv slowly after recording baseline vitals, diluted with normal saline to make 10ml.

Group F: (n-30) received 2µg/kg fentanyl iv slowly, after recording baseline vitals, diluted with normal saline to make 10ml.

Patients were NBM 6 hours before surgery. General and systemic examination of cardiovascular, respiratory and central nervous system were done.

The study drug was given first followed by rest of pre medication inj. Glycopyrrolate, inj. Emeset. Anaesthesia induced with inj propofol 2mg/kg, inj. Suxamethonium 2mg/k. All parameters were recorded at 0, 1, 3 and 5 minutes after intubation.

Heart rate, systolic and diastolic blood pressure, mean arterial blood pressure, respiratory rate, SpO2 and ECG were recorded.

All intubation was accomplished within 15 to 50 seconds by an expert anaesthesiologist who was the same for all cases.

Only one attempt of intubation was accepted by the study. Intubation exceeding 50 seconds was excluded. Maintenance with isoflurane (0.8-1%), O2 (50%), N2O (50%) and non depolarizing muscle relaxant (vecuronium) in the required dose.

At the end of the surgery, patients were reversed with inj. Glycopyrrolate 0.008mg/kg and inj. Neostigmine 0.05mg/kg. In case of bradycardia intraoperatively, inj. Atropine 0.6mg IV stat was given.

STATISTICAL ANALYSIS

The statistical analysis was done using parametric test and final interpretation by using 'Z' test (standard normal variant) with 95% significance. Quantitative data was analyzed by student 't' test

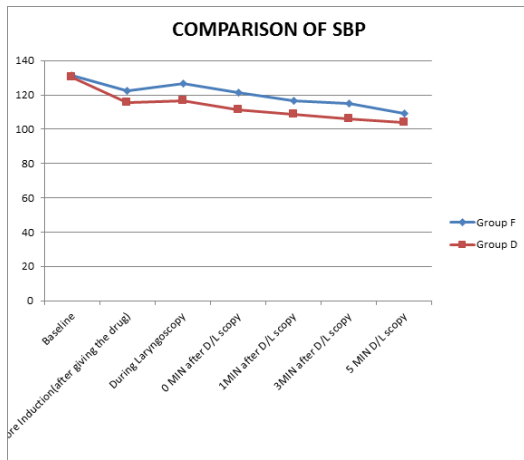
OBSERVATIONS AND RESULTS

The demographic data was comparable in both the groups.

FIGURE 1: Comparison of Heart Rate

HEART RATE	GROUP D MEAN ± SD	GROUP F MEAN ± SD	P VALUE	SIGNIFICANCE
Baseline	90.17±12.02	93.77±9.601	0.2	Not significant
Before Induction(after giving the drug)	81.5±13.66	85.13±14.048	0.3	Not significant
During Laryngoscopy	83.06±9.92	88.13±9.383	0.04680	significant
0 MIN after D/L scopy	80.7±15.44	87.96±7.721	0.02607	Significant
1MIN after D/L scopy	80.3±15.82	84.3±10.87	0.02	Significant
3MIN after D/L scopy	74.37±10.4	80.73±9.979	0.019	significant
5 MIN D/L scopy	72±8.35	77.93±10.71	0.02	significant

FIGURE 2 : Comparison of SBP



The peak is due to increase during intubation . Group D has better hemodynamic response on systolic blood pressure than group F. P value <0.05

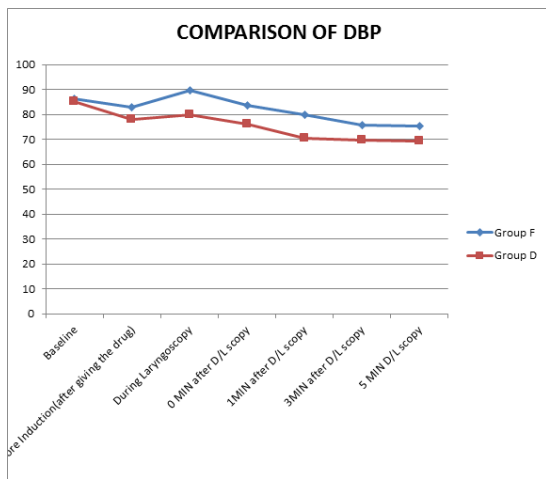


FIGURE 3 : Comparison Of Diastolic Blood Pressure

P value was very significant at 0, 1, 3 and 5 minutes after intubation , Group D has better attenuation of DBP than group F.

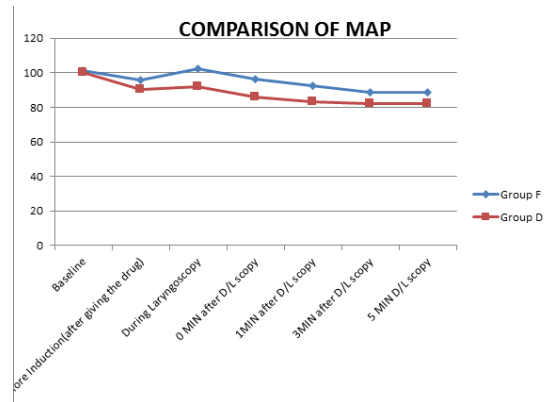


FIGURE 4 : COMPARISON OF MEAN ARTERIAL PRESSURE .

There is significant difference in this hemodynamic parameter before induction and 0,1,3,5 minutes after intubation . This implies that sympathetic responses were lesser in group D as compared to patients of group F .

No significant differences were found in respiratory rates (RR) between group D and F.

No significant changes in the ECG ,SpO2 and duration of surgery in both the groups.

DISCUSSION

Tracheal intubation is a crucial skill it needs direct laryngoscopy to view the vocal cords for insertion of the endotracheal tube .Both laryngoscopy and passage of a tracheal tube are noxious stimuli that can incite adverse events in the respiratory, cardiovascular and other physiologic systems.¹⁰

These responses can be detrimental in those with systemic hypertension , coronary artery disease, cerebrovascular disease or intracranial aneurysms, even the transient changes can result in dangerous effects like left ventricular failure, pulmonary edema, myocardial ischemia,ventricular dysrhythmias and cerebral haemorrhage. ^{2,3} Therefore controlling this perioperative stress response is an important goal of modern anaesthesia.^{11,12,13}

The cardiovascular response is related to the force and duration of laryngoscopy .³ Many studies have reported that 10-18% of the patients develop ischemic ST segment changes during the procedure .¹⁴ Several techniques have been proposed to attenuate the hemodynamic responses such as⁵–

- Deeper plane of anaesthesia with intravenous or inhalation agents.
- Use of opioids prior to induction e.g. Fentanyl , Sufentanyl or Alfentanyl
- Use of intravenous lidocaine
- Lidocaine sprays 10% or 1%/2%/4% lignocaine gargles 3 minutes prior to intubation.
- Use of ACE inhibitors e.g. Captopril, Enalapril 45 minutes prior intubation.
- Various antihypertensives and vasodilators e.g. IV Hydralazine, Calcium Channel blockers like Nifedipine, Beta Blockers like Esmolol.
- Alpha -2 agonists like Dexmedetomidine, Clonidine.
- Use of oral gabapentin

The cardiovascular responses to noxious airway manipulation are initiated by proprioceptors responding to tissue irritation in the supraglottic region and trachea. The glossopharyngeal and vagal afferent nerves transmit these impulses to the brain stem which causes autonomic activation through the sympathetic and parasympathetic nervous systems. In adults, the more common response to airway manipulation is hypertension and tachycardia, mediated by the cardioaccelerator nerves and sympathetic chain ganglia. There is widespread release of norepinephrine from adrenergic nerve terminals and secretion of epinephrine from the adrenal medulla. Some of the hypertensive response also results from activation of the renin-angiotensin system, with the release of renin from the renal juxtaglomerular apparatus, which is innervated by Beta- adrenergic terminals.¹⁵

Stress releases hormones such as cortisol, catecholamines and cytokinin. These hormones increase negative nitrogen balance and catabolism and delay wound repair postoperatively.¹⁶

Bajwa SJS et al in 2012 studied Attenuation of pressor response and dose sparing of opioids and anaesthetics with pre operative dexmedetomidine .They compared dexmedetomidine 1µg/kg with fentanyl 2µg/kg. The pressor response to laryngoscopy, intubation, were attenuated by dexmedetomidine (P<0.001). The mean dose of fentanyl and isoflurane were also decreased significantly (>50%) by the administration of dexmedetomidine.¹⁷ Similar doses were used in our study and we found significant differences in the two groups.

Raval DL et al in 2014 conducted a study with different doses of Dexmedetomidine and found that the dose of 1µg/kg is more effective than 0.5µg/kg in attenuating haemodynamic responses .¹⁸ Hence we had taken a dose of 1µg/kg of dexmedetomidine.

DEMOGRAPHIC PROFILE

There was no statistically significant difference between the two groups.

HEMODYNAMIC PROFILE

HR : The mean heart rate was lesser in group D than group F after giving the drug (P <0.05).Mean heart rate increased after intubation , but the increase in heart rate is significantly lower in group D compared to group F .

Laha et al in 2013 studied the effects of pre induction loading doses of Dexmedetomidine 1 µg/kg on attenuation of sympathoadrenal responses and requirements of anaesthetic agents and concluded that administration of dexmedetomidine not only attenuates the rise in heart rate after intubation at 1, 2, 3 and 5 minutes but also significantly reduces the requirement of anaesthetic drugs.¹⁹ The dose of dexmedetomidine used was similar to our study.

In a study concluded by Patel et al in 2012, it was observed that Dexmedetomidine significantly attenuates stress response at intubation with lower increase in HR (10%) as compared with fentanyl (17%).²⁰ This is in concordance with our study.

Neil L et al in 2017 studied the Effect of Dexmedetomidine versus fentanyl on hemodynamic response to patients undergoing elective laparoscopic surgery: At intubation heart rate decreased by 3.51% in Group D as compared to 11.11% rise in Group F. Post intubate on, heart rate fell by 2% in Group D vs 15% rise in Group F.²¹

In our study, with Dexmedetomidine there was significant increase in HR after laryngoscopy. Till 5 minutes, after intubation the HR showed significant fall at all points, the difference between two groups is significant as P value is less than 0.05 at all time points.

SBP: sympathetic responses were lesser in group D as compared to patients of group F.

Lomate P et al in 2015 evaluated and compared effects of Dexmedetomidine (1 µg/kg) and Fentanyl (2µg/kg) in attenuation of the haemodynamic response to laryngoscopy and intubation. The responses were better in dexmedetomidine (P<0.001) 2 minutes after intubation.²² Similar results seen in our study, we found P value <0.05 (significant) between the two groups after giving the drug till 5 minutes after intubation.

DBP: Patel ND et al conducted a study and concluded that dexmedetomidine provides all anxiolysis, sedation, analgesia, anaesthetic sparing and hemodynamic stability without respiratory depression during general anaesthesia.²³ In their study the DBP results were similar to our study i.e the fall in DBP was more in group D, (P <0.05) than group F at 0,3 and 5 minutes after intubation.

In a study conducted by Gunalan S et al in 2015, they found the diastolic blood pressure had a very significant fall in group D, immediately after intubation (P <0.001) which was similar to our results.²⁴

MAP: The MAP was significantly lower in the group D after giving the drug as compared with group F. Hypotension is caused by activation of receptors in the brain and spinal cord level, inhibiting neuronal firing. Presynaptic activation of α2 adrenergic receptors inhibits release of norepinephrine and postsynaptic activation in the central nervous system inhibits sympathetic activity and, therefore, can decrease blood pressure and HR. There is inhibition of central sympathetic outflow.

Kataria AP et al in 2016 studied Efficacy of these two drugs on pressor response and pneumoperitoneum in laparoscopic cholecystectomy. Control of vitals was better in dexmedetomidine group. Smooth extubation, less sedation and better control of pain in dexmedetomidine group.²⁵

We had similar observations, the MAP was significantly lesser in group D as compared to group F at 0,1, 3 and 5 minutes after intubation.

Limitations -Patients with ASA status I and II were enrolled in the study, so the results cannot be generalized to patients with higher ASA status. The study was conducted in a single centre. A multi centered larger study may be more informative. Measurement of plasma catecholamines level was necessary to demonstrate effectiveness of the study drugs in decreasing sympathetic nervous system activity.

CONCLUSION- Dexmedetomidine attenuates pressor response better than fentanyl

ACKNOWLEDGEMENTS: Thankful to my PG guide and Ex HOD, Dr(Prof) W.S.Thatte.

REFERENCES

- Iannuzzi E, Iannuzzi M, Cirillo V, Viola G, Parisi R, Cerulli A, et al. Periintubation cardiovascular response during low dose remifentanyl or sufentanil administration in association with propofol TCI. A double blind comparison. *Minerva Anesthesiol.* 2004 Mar; 70(3):109-15.
- Fassoulaki A, Melemini A, Paraskeva A, Petropoulos G. Gabapentin attenuates the pressor response to direct laryngoscopy and tracheal intubation. *British Journal of Anaesthesia.* 2006;96:769-73.
- Matot I, Sichel J, Yofe V, Gozal Y. The Effect of clonidine premedication on hemodynamic responses to microlaryngoscopy and rigid bronchoscopy. *Anesth Analg.* 2000;91:828-33.
- King BD, Harris LC, Griefenstein FE, Elder JD, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anaesthesia. *Br J Anaesth.* 1951; 12:556-66.
- Gandhi S, Goyal V, Radhakrishnan K, Balakrishnan M: Comparison of Dexmedetomidine with Fentanyl in Attenuation of pressor Response during Laryngoscopy and Intubation. *IOSR Journal of Pharmacy.* 2014;4(2):28-38.
- Yushiv U, Maiko S, Hideyuki U. Fentanyl attenuates the hemodynamic response to endotracheal intubation more than response to laryngoscopy. *Anaesthetic Analg.* 2002;95:233-237.
- Robert K Stoelting *Pain Pharmacology and physiology Anaesthesia practice*; Robert K Stoltzing and Simon Hillier, 4th edition: 104-108.
- Wijesundara DN, Naik JS, Beattie WS. Alpha-2 adrenergic agonists to prevent perioperative cardiovascular complications: a meta analysis. *Am J Med.* 2003;114:742-52.
- Jalojen J, Hynynen M, Kuitunen A. Dexmedetomidine as an anaesthetic adjunct in Coronary Artery Bypass Grafting. *Anesthesiology.* 1997;86:331-45.
- Henderson J. Airway management in the adult. In: Miller RD, editor. *Miller's Anesthesia*, 7th ed. Churchill livingstone: Philadelphia; 2010.
- Shribman AJ, Smith G, Achola J. Cardiovascular and catecholamine responses to laryngoscopy with or without tracheal intubation. *Br J Anaesth.* 1987;59:295-9.
- Saif GM, Singh V, Kumar A, Wahal R, Bhatia VK. A study of cardiovascular response during laryngoscopy and intubation and their attenuation by ultra short-acting beta blockers esmolol. *Ind J Anaesth.* 2002;46:104-6.
- Joris JL, Chiche JD, Canivet JL, Jacquet NJ, Legros JJ, Lamy ML. Hemodynamic changes induced by laparoscopy and their endocrine correlates: Effects of clonidine. *J Am Coll Cardiol.* 1998;32:1389-96.
- Derbyshire DR, Smith G. Sympatho adrenal responses to anaesthesia and surgery. *Br J Anaesth.* 1984;56:725-39.
- Paul F White, Alejandro R F. *Ambulatory anaesthesia.* Miller's Anaesthesia 6th ed. 2005; Chapter 68:p5759-5863.
- Ashgan R A. Efficacy of pre-operative gabapentin in attenuation of neuroendocrine response to laryngoscopy & endotracheal intubation. *J Med Sci.* 2009;9:24-29.
- Bajwa SJS, Kaur J, Singh A. Attenuation of pressor response and dose sparing of opioids and anaesthetics with pre-operative dexmedetomidine. *Indian Journal of Anaesthesia.* 2012;56(2):123-128.
- Raval DL, Yadav VP. A comparative study of two different doses of dexmedetomidine on haemodynamic responses to induction of anaesthesia and tracheal intubation. *J Clin Exp Res.* 2014;2:163-168.
- Laha A, Ghosh S, Sarkar S. Attenuation of sympathoadrenal responses and anaesthetic requirement by dexmedetomidine. *Anaesth Essays Res.* 2013;7:65-70.
- Patel CR, Engineer SR, Shah BJ, Madhu S. Effect of intravenous infusion of dexmedetomidine on perioperative haemodynamic changes and postoperative recovery: a study with entropy analysis. *Indian J Anaesth.* 2012; 56:542-546.
- Neil L, Patel A. Effect of Dexmedetomidine Versus Fentanyl on Haemodynamic Response to Patients Undergoing Elective Laparoscopic Surgery: A Double Blinded Randomized Controlled Study. *Journal of Clinical and Diagnostic Research.* 2017;11(4):UC01-UC04.
- Lomate P, Thote R, Patil D, Lomate P, Paranjpe J. Attenuation of hemodynamic response during laryngoscopy and intubation: A comparative study between intravenous Dexmedetomidine and Fentanyl. *International J. of Healthcare and Biomedical Research* 2015;4(01):144-156.
- Patel ND, Patel J, Patel D. A study on comparison of intravenous dexmedetomidine with intravenous fentanyl for suppression of hemodynamic responses to laryngoscopy and endotracheal intubation during general anaesthesia. *National Journal of Medical Research.* 2015;Vol5(2):127-131.
- Gunalan S, Venkatraman R, Sivarajan G, Sunder P. Comparative Evaluation of Bolus Administration of Dexmedetomidine and Fentanyl for Stress Attenuation During Laryngoscopy and Endotracheal Intubation. *Journal of Clinical and Diagnostic Research.* 2015 Sep;Vol9(9).
- Kataria AP, Attri JP, Kashyap R, Mahajan L. Efficacy of dexmedetomidine and fentanyl on pressor response and pneumoperitoneum in laparoscopic cholecystectomy. *Anesth Essays Res.* 2016;10:446-50.