Attenuation of pressor response to laryngoscopy and intubation: Dexmedetomidine Vs. fentanyl premedication

Lalit Kumar Raiger¹, Gokulakrishnan L², Madhan Chandramohan³, Apoorva Aseti⁴, Ravindra Kumar Gehlot⁵*

¹Senior Professor, ²Ex Resident, ³Senior Resident, ⁴Junior Resident, ⁵Assistant Professor, Dept. of Anaesthesiology, RNT Medical College, Udaipur, Rajasthan, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India

*Corresponding Author: Ravindra Kumar Gehlot
Email: dr.rgehlot.2010@gmail.com

Received: 7th August 2018
Accepted: 31st August 2018

Abstract

Introduction: The pressor response during laryngoscopy and intubation is part of a huge spectrum of stress response, results from the increase in sympathetic and sympatho-adrenal activity. The present study was planned to observe the attenuation of pressor response during laryngoscopy and intubation with dexmedetomidine and fentanyl; also to compare the effectiveness between these two drugs.

Materials and Methods: In this study we include 128 patients, of ASA grade I- II, aged 18-65yrs, of either gender, scheduled for elective surgery under general anaesthesia. Groups: Group D – Dexmedetomidine (0.6µg/kg) and Group F – Fentanyl (2µg/kg), these drugs diluted with NS to make 10 ml, given I.V. slow over 10 min. Vital parameters (HR, SBP, DBP and MBP) were recorded as baseline, then at 10 minutes after pre-medication and then at 1,2,3,5,7 and 10 minutes after endotracheal intubation.

Results: There was significant increase in heart rate, systolic blood pressure and diastolic blood pressure during laryngoscopy and intubation in group F as compared to group D (p<0.001). Dexmedetomidine produces more significant attenuation of systolic blood pressure during laryngoscopy and intubation as compared to Fentanyl.

Conclusion: Dexmedetomidine (0.6mcg/kg) is superior to fentanyl (2mcg/kg) in the attenuation of the pressor response and that the ideal time for its administration should be about 10 minutes before a laryngoscopy and intubation.

Keywords: Dexmedetomidine, Fentanyl, Intubation, Laryngoscopy, Pressor response.

Introduction

Intubation has been inpracticed since long following it described by Rowbatham and Magill in 1921. The haemodynamic responses following laryngoscopy and intubation stimulation were documented by Reid and Brace in 1940 and King et al in 1951.

The intubation’s pressor response is part of a huge spectrum of stress response, results from the increase in sympathetic and sympatho-adrenal activity, which as evidence by increased plasma catecholamines concentration in patients undergoing surgery under GA. These changes are the maximum at 1 minute after intubation and last for 5-10 minutes. The major causes of these haemodynamic response are considered as stretching of pharyngeal and laryngeal tissues during laryngoscopy. To blunt these pressor responses - deep anaesthesia, topical anaesthesia, opioids, calcium channel blockers, beta blockers, laryngeal mask airway (LMA) have been tried with varying success.

Dexmedetomidine a newer promising drug which has sedative, analgesic and haemodynamic stabilizing properties due to its highly selective α2 agonist activity. With this background a study was planned to observe the attenuation of pressor response during laryngoscopy and intubation with dexmedetomidine and fentanyl.
All patients were preloaded with crystalloid fluid (8-10 ml/kg). Monitoring includes pulse oximetry (SpO₂), ECG and non-invasive blood pressure (NIBP). Inj. glycopyrrolate (0.01 mg/kg) and inj. ondansetron (0.10 mg/kg) were given intravenously as premedicant. Patients received their study drugs before induction. Induction done with inj. thiopentone (4-7 mg/kg) and laryngoscopy & intubation was facilitated by inj. Succinyl choline (2mg/kg i.v.). Anaesthesia was maintained with sevoflurane 50% N₂O in O₂ and non-depolarizing muscle relaxant – atracurium and residual muscle paralysis reversed with inj. neostigmine (0.05 mg/kg) and inj. glycopyrrolate (0.01 mg/kg). Patients were observed for, any complications like bradycardia, tachycardia, hypotension, hypertension, arrhythmias and bronchospasm during peri-operative period and treated accordingly. For study the intubation had to be accomplished within 15 seconds by an expert anesthesiologist. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean blood pressure (MBP) were recorded before pre-medication (T₁), 10 minutes after pre-medication (T₂) and then at 1 minute (T₃), 2 minutes (T₄), 3 minutes (T₅), 5 minutes (T₆), 7 minutes (T₇) and 10 minutes (T₈) after endotracheal intubation; which were sufficient to assess the pressor response. After confirmation & fixation of tube in position the surgery was allowed to commence as this period assume to prevent the influence of surgical stimulus on haemodynamic parameters.

**Blinding:** Two anaesthesiologists were involved in the study; as one prepared the drugs and administered it to the patients and was not involved in the study further. While another who was not aware about the type of drug received by the patient performed intubation and recorded all the data.

**Statistical Analysis**

**Table 1: Changes in heart rate at various time intervals**

| Time interval          | Group D (n=64) | Group F (n=64) | P-value |
|------------------------|----------------|----------------|---------|
| T₁: Baseline (Before Premedication) | 94.36±15.312   | 94.42±15.928   | 0.982   |
| T₂: Before Intubation (10 Min after premed) | 83.19±18.110   | 97.75±15.961   | 0.000   |
| T₃: 1 Min after Intubation | 92.56±15.227   | 114.98±14.048  | 0.000   |
| T₄: 2 Min after Intubation | 92.33±14.095   | 108.98±13.173  | 0.000   |
| T₅: 3 Min after Intubation | 90.56±13.701   | 104.45±13.115  | 0.000   |
| T₆: 5 Min after Intubation | 88.50±14.379   | 101.14±11.992  | 0.000   |
| T₇: 7 Min after Intubation | 85.94±11.749   | 98.38±12.188   | 0.000   |
| T₈: 10 Min after Intubation | 84.55±10.279   | 99.95±12.474   | 0.000   |

**Table 2: Changes in Systolic Blood Pressure at various time intervals**

| Time interval          | Group D (n=64) | Group F (n=64) | P-value |
|------------------------|----------------|----------------|---------|
| T₁: Baseline (Before Premedication) | 129.73±9.532   | 130.19±11.576  | 0.809   |
| T₂: Before Intubation (10 Min after premed) | 123.00±8.894   | 126.30±12.716  | 0.092   |
| T₃: 1 Min after Intubation | 131.41±10.921  | 147.06±16.405  | 0.000   |
| T₄: 2 Min after Intubation | 131.17±10.047  | 135.31±12.528  | 0.041   |
| T₅: 3 Min after Intubation | 127.19±10.855  | 130.25±12.100  | 0.134   |

Results were presented using MS Excel and SPSS software 16 for Windows. Statistical analysis was carried out using analysis of chi-square test and Student’s t test [paired and unpaired]. P <0.05 was regarded as statistically significant.

**Results**

The gender and age of the all patients in both groups are comparable to each other (p> 0.05). The weight of the patients among two groups was statistically significant (p=0.009) with 48.4% were in the age group of 40-50yrs and 51-60yrs in group D and F respectively. Rise in HR [> 20% from baseline] at 1 min post-intubation was seen in 51.6% patients in group F as compared to no patient in group D (p<0.001) [Fig. 1]. There was >20% rise in SBP from baseline at 1 min post-intubation in group F [26.6%] as compared to group D [statistically highly significant ; p<0.001] [Fig. 2]

Table 1 shows increases in heart rate occurred in group F compared to group D at 10 min after premedication (before intubation) and up to 10 min after intubation[statistically highly significant ; p<0.001].

Table 2 shows increase in systolic blood pressure occurred in group F compared to group D at 1 min and 10 min after intubation [statistically highly significant; p<0.001] and also statistically significant difference between the groups at 2 min after intubation [p<0.05].

Table 3 and 4 shows statistically highly significant increase in diastolic blood pressure and MBP occurred in group F compared to group D at 1 min after intubation [p<0.001]. Significant increase in diastolic blood pressure and MBP from baseline in group F at 2, 3 and 10 min time interval after intubation as compared to group D [p<0.05].
Discussion

Nor-epinephrine, epinephrine and dopamine levels rise during laryngoscopy and intubation, but the rise in nor-epinephrine levels is consistently associated with increase in blood pressure and heart rate. Transient hypertension and tachycardia are probably of no consequence in healthy individuals, but either or both may be hazardous to those with hypertension, myocardial insufficiency and cerebrovascular disease.

Dexmedetomidine (α-2 agonist) having 8-times more affinity for α-2 adrenoceptors as compared with clonidine; it attenuates pressor response; had unique pharmacological profile with sedation, sympatholysis, cardiovascular stability, analgesia, opioid and anaesthetic sparing effect, with great advantage to avoid respiratory depression. Several studies have used 0.5-1 mcg/kg of dexmedetomidine to attenuate stress response to intubation. In our study 0.6 mcg/kg of dexmedetomidine was used.

Patient Demographics: The groups were comparable in patient characteristics (age, sex and type of surgery) except for the weight [p<0.05]. The distribution of patients in the groups were dependent on duration of laryngoscopy [p<0.05]; with group D having maximum percentage distribution at 14 seconds (26.6%) and group F having maximum percentage distribution at 14 and 15 seconds (32.8%). The mean duration of laryngoscopy was 13.23±1.294 seconds in group D and 13.88±1.062 seconds in group F. The present study the duration of laryngoscopy is limited till the insertion of endotracheal tube. Laryngoscopy increases the MAP during the first 30-45 seconds and there after the tracheal intubation contributes to this response. Limiting the duration of laryngoscopy to 15 seconds reduces the intensity of pressor response to an extent and in present study the haemodynamics began to drop after the initial rise within the study period of 10 minutes after intubation. This ensures that we study the effectiveness of the intervention drug, in attenuating the response to laryngoscopy and intubation rather than laryngoscopy alone.

Heart Rate [HR]: In fentanyl group mean heart rate increased to 22% from baseline (T1) to 1 min after intubation (T3). While in dexmedetomidine group mean heart rate decreased to 2% from baseline (T1) to 1 min after intubation (T3). The percentage of HR increase (> 20% from baseline) at T3 interval [1 minute after intubation] in group D was 0.0% but in group F it was 51.6% [p<0.001].10 minutes after laryngoscopy there was highly significant decrease in heart rate from baseline in dexmedetomidine group. [p<0.001]. These observations were comparable to those by Bajwa SJS et al., Scheinin B et al., Sulaiman S et al. But in patients who received fentanyl had statistically significant increase in heart rate at10 minutes after laryngoscopy, which probably due to lack anti-anxiety medication.

In both groups, heart rate was increased immediately after laryngoscopy and intubation. However this increase was more in Group F as compare to Group D,[p<0.001]. These observations were comparable to Bajwa SJS et al. (used Dexmedetomidine, 1 µg/kg) and Turgut N et al. (used Fentanyl, 1 µg/kg).

Systolic Blood Pressure [SBP]: In group D of present study had statistically not significant increase in SBP [129.73±9.532 to 131.41±10.921mm of Hg] from baseline (T1) to 1 min after intubation (T3), the mean percentage rises of SBP was approximately 1% at T3. While in group F there was increase in SBP [130.19±11.576 to 147.06±16.405 mm of Hg] from baseline (T1) to 1 min after intubation (T3), the mean percent rises of SBP was 13% at T3.

The percentage of SBP raised > 20% from baseline at T3 interval [1 minute after intubation] in group D was 0.0% but in group F it was 26.6%, likewise the intergroup mean SBP at T3 shows statistically highly significant rise in group F compared to group D [p<0.001]. In group F there was significant decrease in SBP from baseline i.e., 10 minutes after fentanyl infusion [p<0.05] and similarly in group D there was statistically highly significant decrease in SBP from baseline [p<0.001]. So, it is evident that the systolic blood pressure was significantly increased in both the groups after laryngoscopy and intubation [p<0.05]. The peak increase in systolic blood pressure was seen just before the insertion of endotracheal tube.
after intubation (after 1&2 minute), which was less in group D as compared to group F at 1 minute after intubation.[Statistically highly significant, p<0.001] The systolic blood pressure came back to near normal within 10 minutes post intubation. These results were comparable to Gandhi S et al,9 Menda F et al,10 Yildiz M et al11 and Jain V et al.23

Diastolic Blood Pressure and Mean Blood Pressure: Between the groups there were statistically highly significant rise in DBP and MBP noted only in group F than group D at T3 [P<0.001] whereas the rise in DBP and MBP were statistically significant in group F than group D at T4 [P<0.05] which was in concordance to the observations of Gandhi S et al,9 Jain V et al23 and Chung KS et al.24 The peak increase in DBP was seen just after intubation and cuff inflation (after 1 & 2 minute).

After premedication with study drug, DBP and MBP started decreasing from its baseline value; and these observations were comparable to Gandhi S et al,9 Jain V et al,23 Chung SK et al.24

Similar to Reddy et al25 and Jain et al23 we did not observed any significant differences in HR, SBP, DBP and MBP values between the baseline and post-intubation values in the dexmedetomidine group.

Side Effects: We did not find any excessive reduction in HR or SBP values in the dexmedetomidine group. Although bradycardia and hypotension have been reported in studies20,21 pertaining to the effect of dexmedetomidine on peri-operative haemodynamics. We administered dexmedetomidine 0.6 µg/kg slowly over 10 min in present study, hence no bradycardia or hypotension was found; also in fentanyl group there was no incidence of bradycardia and hypotension.

Conclusion
We conclude that dexmedetomidine (0.6µg/kg) is superior to fentanyl (2µg/kg) in the attenuation of the pressor response and with our study results the ideal time for its administration should be about 10 minutes before a laryngoscopy and intubation. Fentanyl attenuates the pressor response, but its effect was far lower than that of dexmedetomidine at 1 minute after intubation.

Acknowledgement: Nil

Conflict of Interest: Nil

References
1. Reid LC, DE. Irritation of the respiratory tract and its reflex effect upon heart. Surg Gynecol Obst. 1940;70:157–162.
2. King BD, Harris LC Jr, Greifenstein FE, Elder JD Jr, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. Anesthesiology. 1951;12: 556-566.
3. Lindgren L, Yli-Hankala A, Randell T, Kirveli M, Scheinin M, Neuvonen PJ. Haemodynamic and catecholamine responses to induction of anaesthesia and tracheal intubation: Comparison between propofol and thiopentone. Br J Anaesth. 1993;70:306–310.
4. Stoelting RK. Circulatory changes during direct laryngoscopy and tracheal intubation - influence of duration of laryngoscopy with or without prior lidocaine. Anesthesiology. 1977;47(4):381-384.
5. Kautoo UM, Heinonen J. Attenuation of circulatory response to laryngoscopy and tracheal intubation: A comparison of two methods of topical anaesthesia. Acta Anaesthesiol Scand 1982;26:599-602.
6. Vucevic M, Purdy GM, Ellis FR. Esmolol hydrochloride for management of the cardiovascular stress responses to laryngoscopy and tracheal intubation. Br J Anaesth. 1992;68:529-530.
7. Wig J, Sharma M, Baichoo N, Agarwal A. Nicardipine and verapamil attenuate the pressor response to laryngoscopy and intubation. Can J Anaesth. 1994;41:1185-1188.
8. Braude N, Clements EAF, Hodges UM, Andrews BP. The pressor response and laryngeal mask insertion - a comparison with tracheal intubation. Anaesthesia, 1989;44: 551-554.
9. Gandhi S, Goyal V, Radhakrishnan K, Balakrishman M. Comparison of dexmedetomidine with fentanyl in attenuation of pressor response during laryngoscopy and intubation. JOSR Journal of Pharmacy. 2014;4(2):28-38.
10. Menda F, Köner O, Sayin M, Türe H, Imer P, Aykaç B. Dexmedetomidine as an adjunct to anesthetic induction to attenuate haemodynamic response to endotracheal intubation in patients undergoing fast-track CABG. Ann Card Anaesth. 2010;13:16-21.
11. Yildiz M, Tavlan A, Tuncer S, Reislí R, Yosunkaya A, Otelcioglu S. Effect of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation: Perioperative haemodynamics and anaesthetic requirements. Drugs R D. 2006;7:43-52.
12. Charuluxananan S, Kyokong O, Somboonviboon W, Balmongkon B, Chaisomboonpan S, Nicardipine versus lidocaine for attenuating the cardiovascular response to endotracheal intubation. J Anesth. 2000;14:77-81.
13. Bajwa SJS, Kaur J, Singh A, Parmer SS, Singh G, Kulshrestha A, et al. Attenuation of pressor response and dose sparing of opioids and anaesthetics with pre-operative dexmedetomidine. Indian J Anaesth. 2012;56:123-128.
14. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg. 2000;90:699-705.
15. Ebert T, Maze M. Dexmedetomidine: Another arrow for the clinician’s quiver. Anesthesiology. 2004;101:568-570.
16. Gerlach AT, Dasta JF. Dexmedetomidine: An updated review. Ann Pharmacother. 2007;41:245-52.
17. Grewal A. Dexmedetomidine: New avenues. J Anaesthesiol Clin Pharmacol. 2011;27:297-302.
18. Scheinin B, Lindgren L, Randell T, Scheinin H, Scheinin M. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and peroperative fentanyl. Br J Anaesth. 1992;68:126–131.
19. Sulaiman S, Karthekeyan RB, Vakamudi M, Sundar AS, Ravullapalli H, Gandham R. The effects of dexmedetomidine on attenuation of stress response to endotracheal intubation in patients undergoing elective off-pump coronary artery bypass grafting. Ann Card Anaesth. 2012;15:39-43.
20. Ben-Abraham R, Ogorek D, Weinbroum AA. Dexmedetomidine: A promising agent for anesthesia and perioperative care. *Isr Med Assoc J*. 2000;2:793-96.

21. Lawrence CJ, De Lange S. Effects of a single pre-operative dexmedetomidine dose on isoflurane requirements and peri-operative haemodynamic stability. *Anaesthesia*. 1997;52:736-744.

22. Turgut N, Turkmen A, Gokkaya S. Dexmedetomidine based versus fentanyl based total intravenous anesthesia for lumbar laminectomy. *Minerva Anesthesiol*. 2008;74:469-474.

23. Jain V, Chandak A, Gosh A, Kolhar M. Comparison of dexmedetomidine and fentanyl for attenuation of the haemodynamic response to laryngoscopy and tracheal intubation. *Ain-Shams Journal of Anesthesiology*. 2015;08:236-243.

24. Chung KS, Sinatra RS, Halevy JD, Paige D, Silverman DG. A comparison of fentanyl, esmolol, and their combination for blunting the haemodynamic responses during rapid-sequence induction. *Can J Anaesth*. 1992;39(8):774-779.

25. Reddy SV, Balaji D, Ahmed SN. Dexmedetomidine versus esmolol to attenuate the haemodynamic response to laryngoscopy and tracheal intubation: A randomized double blind clinical study. *Int J Appl Basic Med Res*. 2014;4(2):95-100.

**How to cite this article:** Raiger L K, Gokulakrishnan L, Chandramohan M, Aseri A, Gehlot R. K. Attenuation of pressor response to laryngoscopy and intubation: Dexmedetomidine Vs. fentanyl premedication. *Indian J Clin Anaesth*. 2018;5(4):486-490.