

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

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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 practiced 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 1940¹ and King et al in 1951.²

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.³ 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.^{4,8} Dexmedetomidine a newer promising drug which has sedative, analgesic and haemodynamic stabilizing properties due to its highly selective α_2 agonist activity. With this background a study was planned to observe the attenuation of pressor response during laryngoscopy and intubation with dexmedetomidine and fentanyl.

Materials and Methods

After approval from Institutional Ethics Committee (IEC) and taking informed written consent, this prospective, randomized, double blind study was carried out on 128 patients of 18-65yrs age, ASA Grade I-II, both sexes, scheduled for elective surgery under general anaesthesia.

Sample Size: Sample size was calculated on the basis of previous study by Gandhi S et al.⁹ A minimum sample size of 64 patients in each group, is to study the minimum difference of 20 beats per minute in heart rate with power of 80% and confidence interval of 95%.

Exclusion Criteria: The patients with baseline heart rate lesser than 60 per minute & blood pressure <100/50 mm of Hg, Reactive airway disease, History of heart disease, PR interval >0.24 seconds, Mallampatti grade >2, requiring two or more attempts for intubation were excluded.

Randomization and Group Allocation: 130 patients were assessed for eligibility and 2 patients not meeting the inclusion criteria were excluded. Randomization was done, using sealed opaque envelope technique depending on drug received. Group D [n=64] and Group F [n=64] received Dexmedetomidine (0.6mcg/kg) and Fentanyl (2mcg/kg) respectively, and diluted with NS to make 10ml, given I.V. over 10 min. in infusion.

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 (0.01mg/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 byinj. 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
T ₁ : Baseline (Before Premedication)	94.36±15.312	94.42±15.928	0.982
T ₂ : Before Intubation (10 Min after premed)	83.19±18.110	97.75±15.961	0.000
T ₃ : 1 Min after Intubation	92.56±15.227	114.98±14.048	0.000
T ₄ : 2 Min after Intubation	92.33±14.095	108.98±13.173	0.000
T ₅ : 3 Min after Intubation	90.56±13.701	104.45±13.115	0.000
T ₆ : 5 Min after Intubation	88.50±14.379	101.14±11.992	0.000
T ₇ : 7 Min after Intubation	85.94±11.749	98.38±12.188	0.000
T ₈ : 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
T ₁ : Baseline (Before Premedication)	129.73±9.532	130.19±11.576	0.809
T ₂ : Before Intubation (10 Min after premed)	123.00±8.894	126.30±12.716	0.092
T ₃ : 1 Min after Intubation	131.41±10.921	147.06±16.405	0.000
T ₄ : 2 Min after Intubation	131.17±10.047	135.31±12.528	0.041
T ₅ : 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

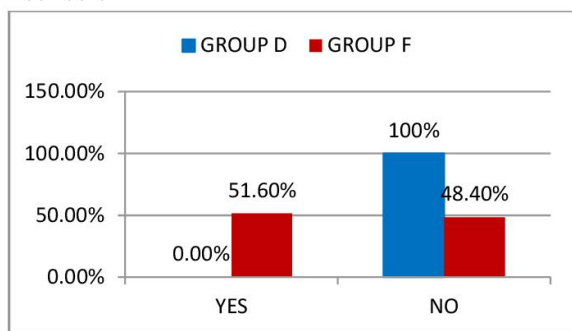


Fig. 1: Distribution of patients according to HR raised > 20% from baseline between the groups

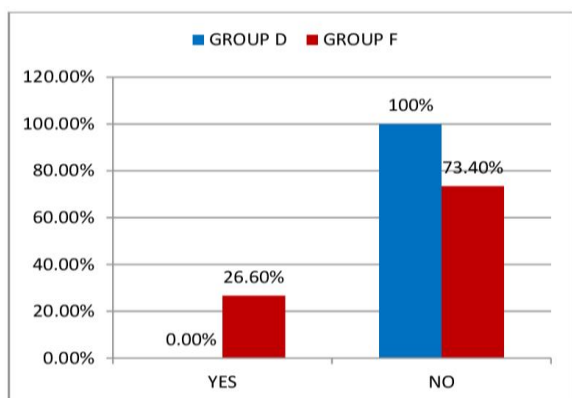


Fig. 2: Distribution of patients according to SBP raised > 20% from baseline between the groups

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.¹⁰⁻¹² 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.¹³

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.¹⁴⁻¹⁷ Several studies^{10,13,18,19} 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.⁴ 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 1min 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,¹³ Scheinin B et al,¹⁸ Sulaiman S et al.¹⁹ But in patients who received fentanyl had statistically significant increase in heart rate at 10 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 al¹³ (used Dexmedetomidine, 1 μ g/kg) and Turgut N et al²² (used Fentanyl, 1 μ g/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 ± 10.921 mm of Hg] from baseline (T1) to 1min after intubation (T3), the mean percentages of rise in 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 percentages of rise in 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

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 studies^{20,21} 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

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