



Original Research Article

An evaluation of efficacy of addition of dexmedetomidine /clonidine to fentanyl in attenuation of pressor response of laryngoscopy and intubation: A prospective double blind randomized controlled trial

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ABSTRACT

Background: Laryngoscopy and intubation have been associated with increased sympathetic responses such as hypertension, tachycardia, arrhythmias, and myocardial infarction. This response is usually transient and variable but might be life threatening in cardiovascular and cerebrovascular compromised patients. So controlling this response is utmost goal of anaesthesia. We evaluated the effectiveness of dexmedetomidine/clonidine to attenuate pressor response.

Aims: Evaluation of efficacy of addition of Dexmedetomidine/ clonidine to fentanyl in attenuation of pressor response of laryngoscopy and intubation.

Materials and Methods: 96 patients were enrolled and randomly divided in three groups having 32 patients each. Group NS received 10 ml normal saline, Group CL received 2mcg/kg Inj. Clonidine and Group DE received 1mcg/kg Inj. Dexmedetomidine infusion over 10 min before laryngoscopy. Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were studied immediately after premedication, 10 min after study drug infusion and then at 1, 2, 3, 4, 5 and 10 min intervals.

Results: There was significant fall in mean HR and mean MAP after 10 min of study drug infusion. Clonidine and dexmedetomidine groups had significantly less rise in heart rate and mean arterial pressure after intubation and then at 1, 2, 3, 4, 5 and 10 min time intervals compared to placebo group. No significant side effects were observed.

Conclusion: Use of dexmedetomidine 10 min before laryngoscopy was associated with significantly less rise in pressor response compared to placebo group. Dexmedetomidine better attenuates the pressor response compared to clonidine but the difference was statistically insignificant.

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1. Introduction

First description of intubation was given by Rowbatham and Magill in 1921. Reid and Brace in 1940¹ and King et al. in 1951² demonstrated the circulatory responses to laryngeal and tracheal stimulation following laryngoscopy and intubation.

Various haemodynamic changes like hypertension, tachycardia, arrhythmias, myocardial ischemia or infarction have been associated with laryngoscopy and intubation. These changes are usually transient and variable and

well tolerated in healthy individuals but can be fatal in patients having hypertension, coronary artery diseases and cerebrovascular diseases. These high risk patients may develop left ventricular failure, myocardial ischemia, cerebral haemorrhage and convulsions may be precipitated in pre-eclamptic patients.

So attenuating this response is utmost goal of safe general anaesthesia. Various methods and drugs have been practiced to blunt these pressor responses like deepening of anaesthesia, use of topical anaesthesia and laryngeal mask airway (LMA), use of opioids, calcium channel blockers, beta blockers, alpha-2 agonist before

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intubation.^{3–10} Presently alpha-2 agonist like clonidine and dexmedetomidine had shown their efficacy to attenuate this response effectively by decreasing the sympathoadrenal stimulation.

With this background we planned the present study to evaluate the efficacy of addition of dexmedetomidine/clonidine to fentanyl in attenuation of pressor response caused by laryngoscopy and intubation during various surgeries under general anaesthesia (GA).

2. Materials and Methods

After taking approval from local institutional ethical committee, this prospective randomized double-blind controlled trial was carried out in Department of Anaesthesiology at RNT Medical College and associated group of hospitals, Udaipur (Raj.). Informed written consent was taken from all patients. Patients having age between 15 to 65 years of both sexes, ASA grade I and II, scheduled for elective surgeries under GA were included in the study. Patients having baseline heart rate < 60/min and blood pressure < 100/50 mm of Hg, reactive airway disease and history of cardiac and hypertensive disease were excluded from the study as well as patients requiring two or more attempts for laryngoscopy and intubation were also excluded from the study.

Sample size- Sample size was calculated on the basis of previous study by Mondal S et al.¹¹ A minimum sample size of 96 was calculated with confidence interval of 95% and probability of having any error in selecting the sample was 10%.

All the patients were randomly divided into three groups having 32 patients in each group. Randomization was done with computer chit method.

Group NS received Inj Normal Saline (NS) 10 ml (control group)

Group DE received Inj dexmedetomidine (1 mcg/kg) + Inj. NS to make total volume up to 10 ml

Group CL received Inj clonidine (2mcg/kg) + Inj. NS to make total volume 10ml.

To ensure double blindness, study drugs were prepared by an independent anaesthesiologist as per group allocation who was not further involved in the study. Study drug administration and data recording was done by another anaesthesiologist who was not aware of group allocation.

Study drug preparation and administration- Inj. dexmedetomidine (100mcg/ml) 1ml was diluted with NS to make total volume 10 ml (10mcg/ml) in 10 ml syringe and then 1mcg/kg was infused over 10 min in group DE. Similarly Inj. clonidine (150mcg/ml) 1 ml was diluted in 9 ml saline to make total volume 10 ml (15mcg/kg) in 10 ml syringe. Then 2mcg/kg was infused over 10 min in group CL, while control group received 10 ml NS over 10 min.

All the patients were thoroughly evaluated in pre-operative check up.

After arrival in the operating room, patients were cannulated with 20 gauge I.V. cannula and Inj. Ringer lactate (RL) infusion was started. Standard monitoring with multi-channel monitor having 5 lead electrocardiogram (ECG), pulse oximetry (SpO₂), non-invasive blood pressure (NIBP) were applied to patients and baseline heart rate (HR), mean arterial pressure (MAP), oxygen saturation were recorded.

All the patients were preloaded with Inj. RL 10ml/kg and preoxygenated with 100% oxygen for 5 min. All the patients were premedicated with Inj. Glycopyrrolate (0.04 mg/kg), Inj. Ondansetron 4 mg and Inj Fentanyl (2mcg/kg) intravenously. Then study drugs were given to patients as per group allocation.

All the patients were induced with Inj. Thiopentone (5 mg/kg) I.V. and after giving Inj. Succinylcholine (2mg/kg) I.V, laryngoscopy was done and patients were intubated with appropriate sized endotracheal tube. Patients who had coughed or bucked during procedure were excluded from study.

HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), MAP were recorded after premedication, 10 minutes after study drug infusion (T₀) and then at 1min (T₁), 2min (T₂), 3min (T₃), 4min (T₄), 5min (T₅) and 10min (T₁₀) intervals after endotracheal intubation. Now the study was considered completed and further patients were maintained with O₂ (50%) + N₂O (50%) + Isoflurane (1%-2%) and non-depolarizing muscle relaxant Inj. Vecuronium bromide (0.08mg/kg) bolus and then 0.1 mg/kg I.V. intermittently.

After completion of surgery, residual neuromuscular blockade was reversed with Inj. Neostigmine (0.05mg/kg) and Inj. Glycopyrrolate (0.01mg/kg) I.V. After extubation all patients were assessed for sedation using Ramsay sedation score¹² (1- Anxious or restless or both, 2- Cooperative, orientated and tranquil, 3- Responding to commands, 4- Brisk response to stimulus, 5- Sluggish response to stimulus, 6- No response to stimulus).

After assuring full recovery, patients were shifted to post anaesthesia care unit (PACU) and monitored for vitals at every 30 minutes up to two hours.

Any adverse events like hypotension, bradycardia, arrhythmias and bronchospasm occurred intraoperatively or postoperatively were recorded.

HR less than 60 was considered as bradycardia and treated with Inj. Atropine 0.2 mg I.V. in incremental doses till desired effect achieved, while SBP less than 90 mmHg was considered as hypotension and treated with intravenous fluid administration or Inj. Mephentermine 6 mg I.V. in incremental doses.

2.1. Statistical analysis

Results obtained in the study were presented using Microsoft Excel and SPSS software for Windows 8. Continuous variables were presented as Mean ± SD

and compared using student's test and ANOVA, whereas categorical data were presented as number (Proportion) and compared using Chi square test. P value <0.05 was regarded as statistically significant, P value <0.001 was taken as highly significant and P value >0.05 was regarded as non-significant.

3. Results

All the patients were comparable demographically among three groups regarding mean age, sex and mean body weight. (Table 1)

In our study baseline HR among three groups were statistically comparable ($p>0.586$). After 10 min of study drug infusion HR reduced up to 5.56%, 13.73%, and 10.16% respectively in group NS, DE and CL which was statistically significant. After 1min of intubation the HR raised up to 16.32%, 9.87% and 7.49% respectively in group NS, DE and CL which was found statistically significant. After that it remained statistically significantly low in group DE and group CL at 2min, 3min, 5min, 7min and 10min intervals compared to control group. Changes in HR at various time intervals remained significant in group NS/DE, group NS/CL but remained insignificant when compared in group DE/CL. (Figure 1)

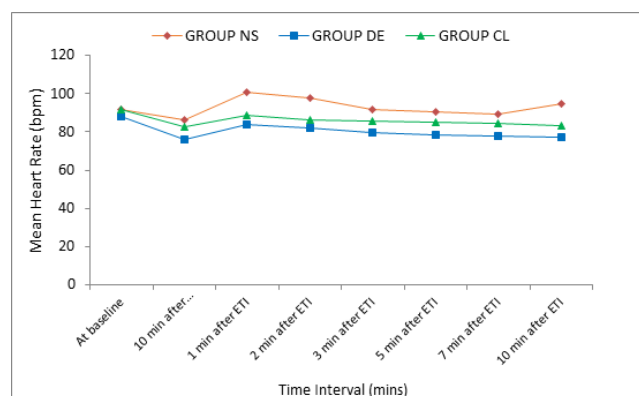


Fig. 1: Distribution of patients according to HR among the groups (NS, DE, CL)

In our study baseline mean MAP among three groups were statistically comparable s12.64% respectively in group NS, DE, CL, which was found statistically significant. After 1min of intubation the MAP raised up to 14.36%, 7.65% and 10.16% respectively in group NS, DE and CL which remained statistically significant among all three groups at 2min, 3min, 5min, 7min and 10min intervals. Changes in MAP at various time intervals remained significant in group NS/DE, group NS/CL but remained insignificant when comparison was done between group DE and CL. (Figure 2)

In our study no one patient developed hypotension and bradycardia in group NS while 3 patients (9.3%)

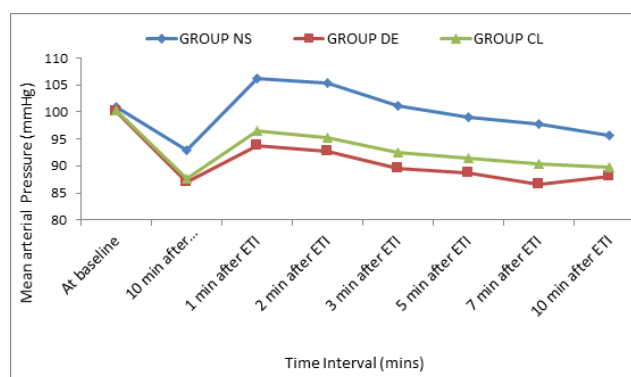


Fig. 2: Changes in mean MAP among three groups at various interval

developed hypotension and bradycardia in group DE while 3 patients (9.3%) developed hypotension and 2 patients (6.2%) developed bradycardia in group CL which was effectively managed with drugs as mentioned in material methods or by decreasing the infusion rate of study drug.

4. Discussion

The pressor response to laryngoscopy and endotracheal intubation may be potentially life threatening, if remained unrecognised or left untreated. These changes are the maximum at 1 min after intubation and last for 5-10 min and well tolerated by patients in the absence of cardiovascular co morbidity and deranged intracranial pressure homeostasis.¹³ Attenuation of this post intubation pressor response is an utmost goal for modern anaesthesia.

Alpha-2 agonists like clonidine and dexmedetomidine have proved their efficacy to attenuate this response by central sympatholytic action. They also offer a unique pharmacological profile with sedation, analgesia, cardiovascular stability and with advantage to avoid respiratory depression.^{14–17}

In our study clonidine and dexmedetomidine had significant fall in HR after 10 min of study drug infusion compared to control group. After 1, 2, 3, 5 and 7min of intubation the rise in HR was statistically insignificant in clonidine and dexmedetomidine group compared to control group. This can be explained due to sympatholytic action of clonidine and dexmedetomidine. Although clonidine and dexmedetomidine didn't show significant difference regarding rise in HR after intubation at different time intervals.

Mondal S et al¹¹ conducted a study to evaluate the effect of dexmedetomidine, clonidine on pressor response after intubation. They found that dexmedetomidine and clonidine group had significantly less rise in HR after intubation at 1 and 3 min ($p < 0.001$) compared to normal saline group. While the fall in heart rate was more in dexmedetomidine group compared to clonidine group but

Table 1: Distribution of patients according to demography

Variables	Group NS (n=32)	Group DE (n=32)	Group CL (n=32)	P value
Age (years)	41.31±15.33	38.19±12.74	40.19±12.79	0.65
Weight (kg)	57.31±9.06	53.03±8.84	55.90±9.83	0.186
Duration of surgery	73.38 ± 7.330	74.50±7.103	75.25±8.629	0.621

difference was statistically insignificant ($p>0.05$). These results coincided with our study.

Similar to our study, Bajwa SJS et al.¹⁸ found that laryngoscopy and intubation was associated with a significant rise of mean HR in fentanyl Group as compared with dexmedetomidine group ($p<0.001$). Mean HR after 1, 3 and 5 min of intubation again returned to lower values, but on comparison of rate of decrease and stabilization of haemodynamic parameters, it was highly significant in group dexmedetomidine ($p<0.001$).

Similarly Gandhi S et al.¹⁹ also found that dexmedetomidine was associated with less increase in HR compared to fentanyl group which was statistically highly significant.

In our study MAP showed significant fall in clonidine and dexmedetomidine group compared to control group after 10 min of study drug infusion. After 1, 2, 3, 5, 10 min of intubation clonidine and dexmedetomidine group had less increase in MAP compared to control group which was statistically significant. But the fall was greater in dexmedetomidine group compared to clonidine group though it was statistically insignificant.

Gandhi S et al.¹⁹ compared dexmedetomidine with fentanyl in attenuation of pressor response during laryngoscopy and intubation. They found that the mean MAP was significantly increased in both the groups after laryngoscopy and intubation ($p<0.05$). The peak increase in mean arterial blood pressure was seen just after intubation and cuff inflation (after 1&2 minute). The increase in MAP was less in group dexmedetomidine as compared to group fentanyl and this difference was statistical highly significant ($p<0.001$).

SJS Bajwa et al.¹⁸ also found that laryngoscopy and intubation was associated with a significant rise of mean MAP in fentanyl group as compared with dexmedetomidine group ($p<0.001$). Mean MAP after 1, 3 and 5 min of intubation again returned to lower values but on comparison of rate of decrease and stabilization of haemodynamic parameters, it was highly significant in dexmedetomidine group ($p<0.0001$). These results also coincided with present study.

Our results also coincided with N. Turgut et al.²⁰ They found that the laryngoscopy and intubation was associated with a significant rise of MAP in fentanyl group as compared with dexmedetomidine group ($p<0.01$). MAP values before and after extubation in Group fentanyl was significantly higher than in group dexmedetomidine.

Shridhar Kalakeri et al.²¹ also found that use of dexmedetomidine was associated with less rise of mean MAP after intubation and it was highly significant.

In our study, immediately after reversal, 28 patients (87.5%) had RSS 2 while 4 patients (12.5%) had RSS 3 in group DE. While in group CL, all 32 patients (100%) have RSS 2 and in group NS 20 patients (62.5%) had RSS 1 while 12 patients (37.5%) had RSS 2. These data suggested that dexmedetomidine and clonidine is associated with more sedation after recovery but it was clinically insignificant ($p>0.05$).

In the present study, after study drug infusion 3 patients (9.37%) in both group (DE and CL) developed hypotension which was successfully managed by fluid administration and slowing the infusion rate while bradycardia observed in 3 patients (9.375%) in group DE and 2 patients (6.25%) in group CL. These all patients were well managed by slowing the infusion rate. No one patient developed hypotension and bradycardia in group NS.

Similar to our study Bajwa et al.¹⁸ and Sridhar et al.²¹ found that patient's developed bradycardia were well managed with either drug or fluid administration.

5. Conclusion

In present study we conclude that use of dexmedetomidine (1mcg/kg)/clonidine (2mcg/kg) 10 minutes before laryngoscopy, significantly attenuate the pressor response associated with laryngoscopy and intubation. Dexmedetomidine better attenuates the pressor response compared to clonidine however the difference was statistically insignificant.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

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