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**ORIGINAL ARTICLE**

# A prospective randomized controlled trial comparing the effects of dexmedetomidine and fentanyl on attenuation of pressor response during laryngoscopy and intubation

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## ABSTRACT

**Background:** Conduct of general anesthesia requires an ideal premedication and induction agent. Adequate premedication blunts the laryngoscopy and intubation response effectively, which is required in specific groups of people like cardiac patients, hypertensive patients and patients with raised intracranial tension. Our study examines the effectiveness of two drugs, fentanyl and dexmedetomidine in blunting these responses.

**Objectives:** Dexmedetomidine and fentanyl are known for their analgesic and sedative properties. However, there are not sufficient data comparing the two drugs as premedication agents .In the present study we compared the hemodynamic effects of a single pre induction dose of fentanyl and dexmedetomidine on laryngoscopy and intubation.

**Methodology:** Sixty ASA I-II patients were randomized into two groups; Group D (dexmedetomidine group) received 1 µg/kg dexmedetomidine and Group F (fentanyl group) received 2 µg/kg fentanyl intravenously over ten min. The parameters measured included mean arterial pressure, heart rate, systolic and diastolic blood pressure at specified time intervals. The statistical methods used in this study were chi square test and Students unpaired "t" test.

**Results:** Dexmedetomidine was found superior to fentanyl in blunting the cardiovascular response to laryngoscopy and intubation. There was statistically significant difference in heart rate in dexmedetomidine group compared to fentanyl group. The heart rate in group D was 62 ± 47 per min and in group F 76 ± 23 per min, ten minutes post drug administration. Statistically significant differences were also noted in heart rate within one minute after laryngoscopy with Group D (82 ± 13) having a lower value compared to group F (90 ± 50) and also at ten minutes after laryngoscopy and intubation, Group D (63.1 ± 8.70 per min) and Group F (75.07 ± 13.23 per min). Three patients in Group D had bradycardia and had to be supplemented with 0.6 mg atropine. There was no statistically significant differences in mean arterial pressure, systolic and diastolic blood pressures.

**Conclusion:** We conclude that dexmedetomidine (1 µg/kg) is superior to fentanyl (2 µg/kg) as premedication agent in supressing cardiovascular response to laryngoscopy and intubation

**Key words:** Analgesia; Premedication; Ramsay sedation score; Airway management.

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## BACKGROUND

The hemodynamic response for laryngoscopy and intubation was first described by Reid and Brace in 1940 which is widely used as gold standard for airway management.[1] A typical pressor response can include a 40-50% increase in blood pressure, a 20% increase in heart rate, and an elevation of both epinephrine and nor epinephrine levels in blood.[2]

During general anaesthesia, direct laryngoscopy and intubation evokes increase in sympathoadrenal activity by increase in catecholamines levels, exhibited in the form of change in heart rate, blood pressure and arrhythmia. Controlling this intubation response is an important goal for modern anaesthesia.[3]

Dexmedetomidine, a highly selective short acting central alpha 2 agonist has gained popularity as an adjuvant to general and regional anaesthesia. It has analgesic and sympatholytic properties; it decreases the release of catecholamines and also lowers plasma catecholamine level during intubation and surgery without respiratory depression.[3,4]

Fentanyl is a short acting opioid, popularly used as premedicant to provide cardiovascular stability during laryngoscopy and intubation and during intraoperative period, its works as an excellent analgesic.[5]

The present study compares fentanyl and dexmedetomidine as premedication drugs, as there is a need among anaesthesiologists to select the appropriate drug based on their ability to attenuate laryngoscopic reflexes.

To assess the hemodynamic response of dexmedetomidine and fentanyl as premedication agents, to direct laryngoscopy and intubation.

## METHODOLOGY

Sixty ASA 1 and II patients were selected for this prospective randomized double blinded study. Ethics committee approval and written informed consent were obtained from the patients. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a prior approval by the institution's human research committee.

Inclusion criteria included, age between 18 – 60 years, ASA grade I and II patients posted for elective surgery. Exclusion criteria included history of allergy to any study drugs, history of cardiac disease, hypertension, thyroid dysfunction, uncontrolled diabetes mellitus, liver and renal diseases, patients receiving other $\alpha$-agonists or $\beta$-blockers, pregnancy and lactating women, obesity, addiction, psychological disease and predicted difficult intubation.

Patients were divided into two study groups; Group D — dexmedetomidine group and Group F — fentanyl group. Randomisation was done by block randomisation technique. The concealment was achieved with computer generated block selection. A thorough general and systemic examination was undertaken and patients were kept fasting for a period of 8 h before surgery.

All patients received tablet alprazolam 0.25 mg and tablet ranitidine 150 mg on the previous night and 2 h before surgery.

Once the patients were shifted to the operating theatre, baseline vitals were recorded. Patients in Group D received dexmedetomidine 1 $\mu$g/kg (Dexem™ - Themis Medicare Private Limited) and patients in Group F received fentanyl 2 $\mu$g/kg (Fendrop™ – Sun Pharmaceuticals) intravenously. Both the drugs were diluted in ten ml of normal saline and was given over ten minutes. The drugs were prepared by an anesthesiologist who was not involved with the study.

Patients were pre oxygenated with 100% oxygen for 3 min, inj midazolam 0.03 mg/kg was given and induction was done with intravenous Propofol , given in incremental doses till loss of response to verbal commands were attained. Neuromuscular blockade was attained by inj rocuronium bromide 1.2 mg/kg. After 90 sec, laryngoscopy and intubation was done using standard Macintosh laryngoscope. The procedure was done by an experienced anesthesiologist. Only single attempt at laryngoscopy and intubation were considered in the study. Anaesthesia was maintained with isoflurane 0.5% and nitrous oxide 60% and oxygen 40%.

The primary outcomes measured include heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and room air saturation ($SpO_2$), recorded ten minutes post- test drug administration and at 1 minute, 5 and 10 min post intubation. The secondary outcomes measured include Ramsay sedation score post- test drug administration and propofol consumption at the time of induction.[6]

Intraoperative and postoperative assessments were performed by an anesthesiologist blinded to the patient allocation and study groups

Hypotension was defined as SBP $<$ 25% of baseline value or less than 90 mmHg, whichever is lower. Hypertension was defined as SBP $>$ 25% of baseline value or more than 150 mmHg, whichever is higher.

Tachycardia was defined as HR > 25% of baseline value. Bradycardia was defined as HR < 50 beats/min. Hypotension was treated with intravenous fluids and inj ephedrine 5 mg boluses. Bradycardia was treated with 0.6 mg atropine.

The statistical methods used in this study were chi square test and Students unpaired "t" test.

**Table 1: Comparison of mean heart rates between the two groups. Data given as mean (SD)**

| Time | Group D N = 30 | Group F N = 30 | t | p-value |
|---|---|---|---|---|
| Predrug | 74.63 (15.33) | 80.87 (10.734) | 1.824 | *P = 0.073 |
| Post-test drug | 62.47 (12.077) | 76.23 (11.732) | 4.478 | ***P < 0.001 |
| T1 | 82.13 (11.907) | 90.50 (11.434) | 2.776 | **P = 0.007 |
| T5 | 74.17 (11.948) | 78.63 (9.456) | 1.606 | *P = 0.114 |
| T10 | 63.10 (8.707) | 75.07 (13.235) | 4.137 | ***P < 0.001 |

SD Standard deviation, *P – Statistically not significant, **P Statistically significant
***P Statistically highly significant

A statistical package SPSS version 17 was used to do the analysis. A $p < 0.05$ was considered statistically significant.

## RESULTS

Sixty patients, divided into two groups underwent the study. There were no drop outs from the study. Both the groups were comparable with regard to age and gender distribution.

The heart rate response to laryngoscopy and intubation was more with fentanyl group than dexmedetomidine group.

The baseline heart rate was 74 ± 63 vs. 80 ± 87 per min in Group D and Group F respectively. There was statistically significant differences between Group D (62 ± 47) and Group F (76 ± 23) ten minutes post drug administration. Statistically significant differences were also noted within one minute after laryngoscopy with Group D (82 ± 13) having a lower value for heart rate compared to Group F (90 ± 50) and also ten minutes after laryngoscopy and intubation (Group D 63.1 ± 8.707 and Group F 75.07 ± 13.23) (Table 1).

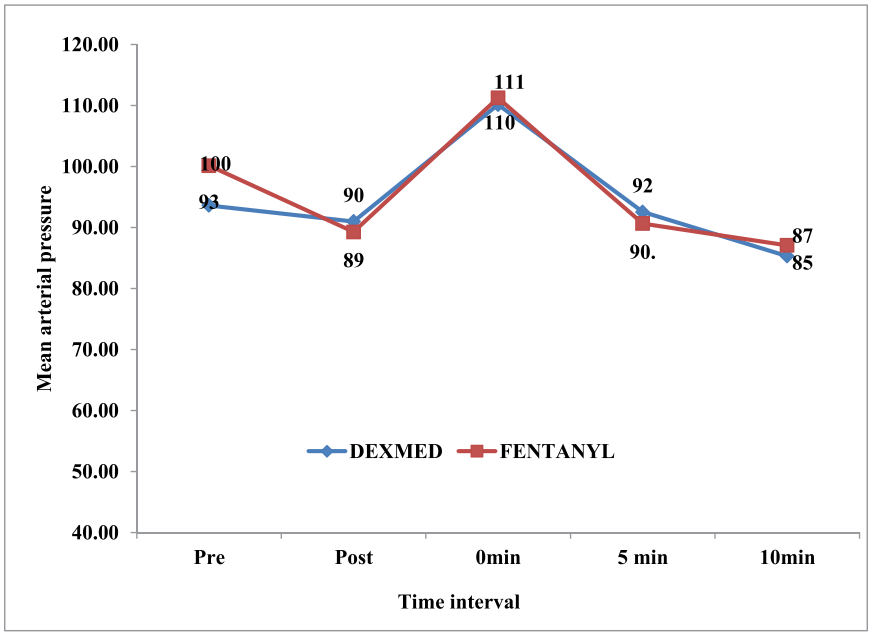
There was no statistically significant difference between mean arterial pressures post-test drug administration in the two groups (Graph 1), systolic blood pressure diastolic blood pressure and saturation ($p > 0.05$). There was no statistically significant difference between the two groups on the amount of propofol consumption (Graph 2).

While a significant difference was observed for Ramsay sedation score between the two drugs post-test drug administration ($p = 0.016$). A higher sedation score (score 4) was observed in Group D (36%) compared to Group F (Table 2).

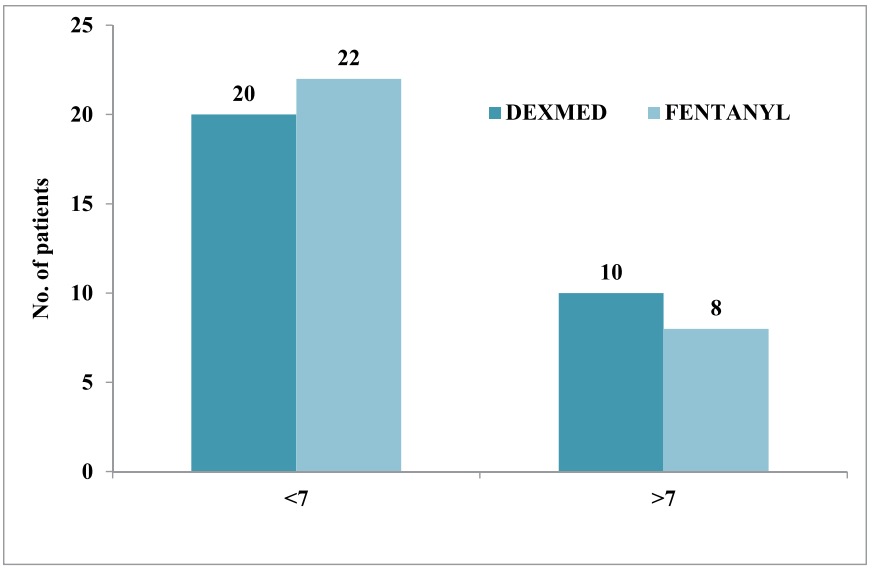
Three patients in Group D had bradycardia which was treated with inj atropine 0.6 mg.

## DISCUSSION

Dexmedetomidine is widely used in anesthesia practice as a sedative drug in view of its minimal effects on respiration compared to opioids. The biphasic response in arterial blood pressure and the risks for bradycardia are well documented.[7] It has limited safety profile in cardiac patients with limited stroke volume, hypovolemic shock and patients on β blockers and digitalis.[8] The safety profile of fentanyl




**Graph 1: Comparison of mean arterial pressure**




**Graph 2: Propofol consumption**

in providing cardiovascular stability has been well documented.[9]

The present study shows that dexmedetomidine, as a premedication agent has significant effects in suppressing the pressor response to laryngoscopy and intubation compared to fentanyl. Both the drugs caused fall in blood pressure post- test drug administration but there was no statistically significant difference between the two groups.

**Table 2: Ramsay sedation score [N(%)]**

| Ramsay sedation score | Group | | Total |
|---|---|---|---|
| | Dexmedetomidine | Fentanyl | |
| 2 | 0 | 6 (20) | 6 (10) |
| 3 | 19 (63.3) | 19 (63.3) | 38 (63.3) |
| 4 | 11 (36.7) | 5 (16.7) | 16 (26.7) |

In a study conducted in 60 patients undergoing laparotomies, the patients were premedicated with fentanyl 2 $\mu$g/kg and dexmedetomidine 1 $\mu$g/kg. The results showed that the hemodynamic stability was more in dexmedetomidine group than fentanyl group. Our study showed that both the drugs caused fall in blood pressure, but there was no statistically significant difference between the two groups. The dexmedetomidine group had a higher Ramsay sedation score than fentanyl group which was similar to our study.[10]

In another study done on ninety patients undergoing general anesthesia, patients were divided into 3 groups receiving dexmedetomidine 1 $\mu$g/kg, fentanyl 2 $\mu$g/kg and esmolol 2 mg/kg. It was found that the reductions in heart rate was profound with dexmedetomidine group compared to the other groups, These findings were similar to our findings.[11] The same observations in heart rate was found in a study conducted by Kamalesh et al. in dexmedetomidine group. But there was a statistically significant fall in blood pressure in dexmedetomidine group compared to fentanyl group which was contradicting our findings.[12]

Gulabani M et al. conducted comparative analysis of the efficacy of lignocaine 1.5 mg/kg and two different doses of dexmedetomidine (0.5 $\mu$g/kg and 1 $\mu$g/kg) in attenuating the hemodynamic pressor response to laryngoscopy and intubation and concluded that dexmedetomidine 1 $\mu$g/kg is effective than 0.5 $\mu$g/kg and lignocaine 1.5 mg/kg without significant side effects.[13]

Our findings were also similar to another study conducted on one hundred patients who received fentanyl 2 $\mu$g/kg and dexmedetomidine 1 $\mu$g/kg. The pressor response to laryngoscopy and intubation was significantly lower in dexmedetomidine group than fentanyl group. The dose of isoflurane was also less in the same group.[14]

Dexmedetomidine has a wide range of applications in current anesthesia practice. The use range from intraoperative procedures to procedures in remote locations like magnetic resonance imaging and endoscopies.[15]

Dexmedetomidine is an excellent 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 decreases the dose of opioids and isoflurane in achieving an adequate analgesia and anaesthesia, respectively.[14]

Use of dexmedetomidine along with other hypotensive drugs should be done with caution and should be

carefully titrated in view of its hemodynamic effects. A dose reduction is recommended in such situations.[16]

## LIMITATIONS

Our study had certain limitations. A larger sample size could improve the authenticity of the results. The hemodynamic effects of both drugs could have been evaluated from the preoperative till the postoperative period. Studying the fixed single dose of drugs limits the evaluation of the dose-response effects.

## CONCLUSION

We conclude that dexmedetomidine (1 $\mu$g/kg) is superior to fentanyl (2 $\mu$g/kg) in supressing cardiovascular response to laryngoscopy and intubation. Both the drugs caused proportional fall in blood pressure post-test drug administration. So dexmedetomidine can be a safe premedication drug compared with fentanyl in patients who are susceptible to adverse cardiovascular consequences of high pressor response.

**Conflict of interest:** Nil

**Authors' contribution:**

NS – Concept, conduct of study, manuscript editing, data acquisition

SBV – Literature search, manuscript editing, data acquisition

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