A comparative study of hemodynamic changes in dexmedetomidine versus midazolam and fentanyl combination during awake fibreoptic intubation

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ABSTRACT

Background: The hemodynamic changes during awake fibreoptic intubation (AFOI) are attributed to patient's anxiety, poor topicalization of the airway, excessive sedation, lack of expertise, pain, prolonged time to intubation, stimulation of oropharyngeal structures, and jaw thrust to aid intubation. In this study, we compared hemodynamic changes of dexmedetomidine (DEX) with midazolam (MDZ) and fentanyl during AFOI. **Aims and Objectives:** The objective of the study is to compare the hemodynamic changes in DEX alone versus fentanyl- MDZ combination during AFOI. **Materials and Methods:** Group-I patients (n = 30) received DEX 1 µg/kg bolus infusion over 10 min, followed by infusion of 0.1 µg/kg/h titrated to 0.7 µg/kg/h whereas Group-II patients (n = 30) received iv fentanyl 2 µg/kg bolus followed by MDZ infusion of 0.02–0.1 mg/kg/h until they were adequately sedated, i.e. Ramsay Sedation Score (RSS) of 3. Hemodynamics including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation (SpO$_2$) were recorded when patient is sedated, i.e. at RSS-3, every min of fibrescopy till 5 min and at intubation and every 3rd min post-intubation till 30 min. **Results:** Measurements of the HRs in the two groups showed significant differences between the two groups at RSS-3, during FOS and post-intubation with the DEX group showing lower mean HRs compared with the MDZ and fentanyl group. SBP and DBP showed a fall in both the groups as compared with the baseline at RSS-3, during FOS and post-intubation; however, no significant differences were noted between the two groups. The mean SpO$_2$ values show significant difference between the two groups. (P < 0.05) at RSS-3, FOS, post intubation upto 18 min (P < 0.05). **Conclusion:** The use of DEX at 1 mcg/kg bolus slowly over 10 min, with maintenance rates of 0.1–0.7 µg/kg/h, is safe and beneficial for patients undergoing AFOI. Thus, DEX acts like an ideal drug for AFOI. It provides excellent intubating conditions without significant hemodynamic perturbations and risk of hypoxia.

Key words: Awake fibreoptic intubation; Dexmedetomidine; Fentanyl; Midazolam

INTRODUCTION

Hemodynamic response to laryngoscopy and intubation was first described by Reid and Brace in 1940. Healthy individuals are able to tolerate it well, but these changes may prove to be fatal in high-risk patients.[1,2]

The hemodynamic changes during awake fibreoptic intubation (AFOI) are attributed to patient's anxiety, poor topicalization of the airway, excessive sedation, lack of expertise, pain, prolonged time to intubation, stimulation of oropharyngeal structures, and jaw thrust to aid intubation.[3]

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Thus, drugs used for blunting of this response must have analgesic, sedative, amnesic, and sympatholytic properties. Various drugs have been tried in the recent past, including benzodiazepines such as midazolam (MDZ), opioids such as fentanyl, sufentanil, ramifentanil, sedative hypnotics such as propofol, ketamine, alpha-2 agonists such as clonidine and dexmedetomidine (DEX).[4-7] DEX, revolutionized the concept of sedation in AFOI. Sedation without airway obstruction and respiratory depression is a unique feature of DEX.[8]

During AFOI deep sedation may lead to apnea but very light sedation may have adverse cardiovascular consequences in form of hypertension and tachycardia, especially in high-risk patients. Hence, an ideal sedative is expected to provide comfort and elicit patient's cooperation while maintaining hemodynamic stability and spontaneous ventilation.

Due to risk of respiratory depression and poor analgesia, benzodiazepines alone are not a good choice for AFOI. Fentanyl on the other hand helps to attenuate pressor response to intubation when used in combination with BZP. In this study, we compared hemodynamic changes of DEX with MDZ and fentanyl during AFOI.

Aims and objectives
To compare the hemodynamic changes in DEX alone versus fentanyl-MDZ combination during AFOI.

MATERIALS AND METHODS

After the Institutional Ethical Committee approval, the study was conducted in Government Medical College, Patiala in 60 patients aged between 18 and 60 years, ASA Grade I and II scheduled for elective surgery. A written informed consent was obtained from each patient. The patients were randomly divided into two groups of 30 each.

Exclusion criteria
Patient's refusal, baseline heart rate (HR) <60, baseline blood pressure <100/50, coagulopathy, history of nasal surgery/nasal trauma, nasal polyp, cardiovascular disease, liver cirrhosis, alcohol and drug abusers, mentally ill patients, allergic to the drugs used in the study, patients on drugs such as digitalis, beta-blockers, and calcium channel blockers are known to produce changes in HR and blood pressure.

Pre-anesthetic checkup was done in every patient. All patients were given injection. Glycopyrrolate (0.2 mg) i.m 30 min before the elective surgery. Baseline vital parameters of all the patients such as HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), and oxygen saturation (SpO_2) were documented.

Group-I patients (n=30) were received DEX 1 μg/kg bolus infusion over 10 min, followed by an infusion of 0.1 μg/kg/h titrated to 0.7 μg/kg/h until they are adequately sedated, i.e., Ramsay Sedation Score (RSS) of 3.

Group-II patients (n=30) were received iv fentanyl 2 μg/kg bolus followed by MDZ infusion of 0.02–0.1 mg/kg/h until they are adequately sedated, i.e., RSS of 3.

Patients were placed in the supine position. Each nostril was checked for patency. The nostril with least resistance was chosen for nasal intubation. Nasal mucosa was sprayed with vasoconstrictor xylometazoline (0.1%) and with two puffs of 10% lignocaine. 2% lignocaine viscous gargles were done to achieve adequate topical anesthesia. For further topical anesthesia two puffs of 10% lignocaine were sprayed over tonsillar pillars and back of the throat. Spray as you go technique was used for airway topicalization. When fiberscope reached up to the vocal cords, 2 ml of 2% lignocaine with some air was injected through the epidural catheter inserted over the working channel of the fiberscope. After crossing vocal cords 2 ml of 2% lignocaine with some air was injected in the upper part of the trachea. Supplemental doses of lignocaine up to a maximum of 9 mg/kg were administered to the airway. On reaching the carina endotracheal tube was railroaded over the fibrescope. The endotracheal tube was secured and G.A was administered. Hemodynamics including HR, SBP, diastolic blood pressure, SpO_2 were recorded when patient is sedated, i.e. at RSS-3, every min of fibrescopy till 5 min and at intubation, and every 3rd min post-intubation till 30 min. The surgical procedure was then proceeded as planned.

Statistical analysis
The results obtained in the study were analyzed using IBM SPSS statistics software version 20.0. Statistical analysis was carried out using Student's t-test. Hemodynamic variables were expressed as Mean±SD. P<0.05 was regarded as statistically significant, and P>0.05 was regarded as non-significant.

Observations
Age : The mean age of patients in group 1 and 2 was 43.80±12.3 years and 40.50±12.06 years, respectively. The difference was statistically insignificant (p>0.05). (Figure 1). Both the groups had predominance of females but the sex ratio was comparable in both groups. (p>0.05). (Figure 2).

BASELINE HEART RATE

The mean heart rate (mean±S.D) at baseline was 82.7±8.07 in group 1 and 83.77±7.30 in group 2. There was no statistically significant difference between the two groups at baseline. (p>0.05). (Figure 3)
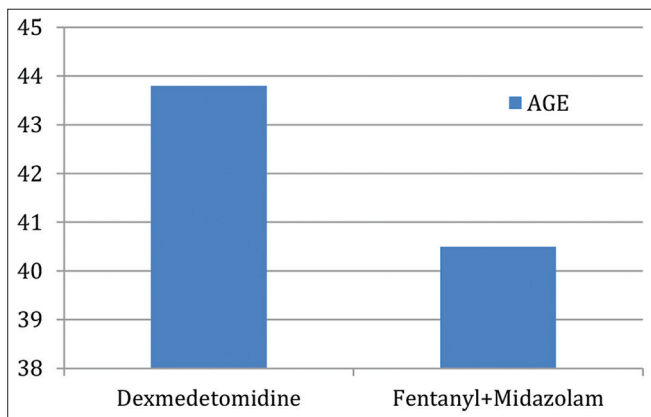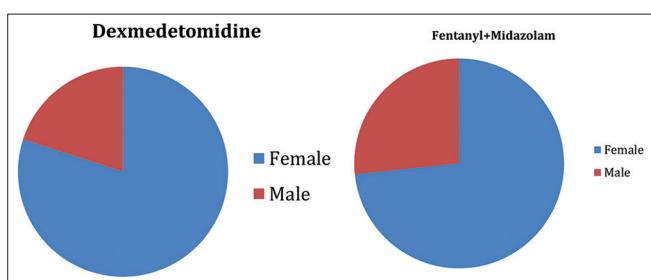
Figure 1: Age distribution in both groups

Figure 2: Gender distribution in both groups

AT RSS 3

The mean heart rate at RSS 3 was 75.50±7.39 in group 1 and 81.97 ± 9.06 in group 2. The difference in heart rate between the two groups was statistically significant (p<0.05). (Figure 3).

Compared with baseline, the mean heart rate decreased by 7.2 beats/min in the dexmedetomidine group and 1.8 beats/min in fentanyl and midazolam group. This decline in heart rate was statistically significant for dexmedetomidine group (p<0.001); whereas it was statistically insignificant for fentanyl and midazolam group (p=0.072). Compared with baseline, the mean heart rate at the time of insertion of fiberoscope (0 min) decreased by 11.83 beats/min in the dexmedetomidine group and 7.63 beats/min in fentanyl and midazolam group. The fall in heart rate for both groups was statistically significant (p<0.001).

On comparison between the 2 groups, significant differences were found in heart rate during FOS (p < 0.05) (Figure 3) Compared with baseline, the mean heart rate at the time of intubation (0 min) decreased by 15.06 beats/min in the dexmedetomidine group and 12.83 beats/min in fentanyl and midazolam group. The fall in heart rate for both groups was statistically significant (p<0.001). On comparison between the 2 groups, significant differences were found in the heart rate after endotracheal intubation upto 15 mins (p<0.05) after which the difference was statistically insignificant (p> 0.05) (Figure 3).
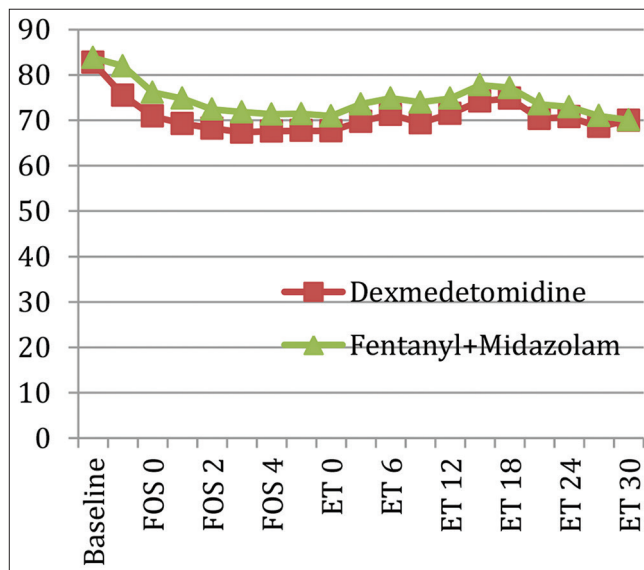
Figure 3: Comparison of heart rate in both groups

BASELINE SYSTOLIC BP

The mean SBP (mean ±S.D) was 127.33 ±2.89 in group 1 and 127.6±4.14 in group 2. There was no significant difference between the two groups. (p>0.05). (Figure 4)

AT RSS 3

The mean SBP (mean±S.D) was 126±3.76 in group 1 and 124.87±3.47 in group 2. Compared with baseline, the mean SBP decreased by 1.26 mm Hg in the dexmedetomidine group and 2.73 mm Hg in fentanyl and midazolam group. There was no significant difference between the two groups. (p>0.05) (Figure 4). Compared with baseline, the mean SBP at the time of insertion of fiberoscope (0 min) decreased by 8.86 mm Hg in the dexmedetomidine group (p=0.014) and 10.2 mm Hg in fentanyl and midazolam group (p<0.001). No significant difference was found in the SBP measurements during FOS between the two groups. (p>0.05) (Figure 4)

Compared with baseline, the mean SBP at the time of intubation (0 min) decreased by 18.73 mm Hg in the dexmedetomidine group and 19.80 mm Hg in fentanyl and midazolam group. On comparison between the 2 groups, no significant difference was found in the SBP measurement after intubation between the two groups. (p>0.05) (Figure 4).

BASELINE DIASTOLIC BP

The mean DBP (mean ±S.D) at baseline was 82.80±3.66 in group 1 and 81.60±3.72 in group 2. There was no significant difference between the two groups. (p>0.05). (Figure 5).
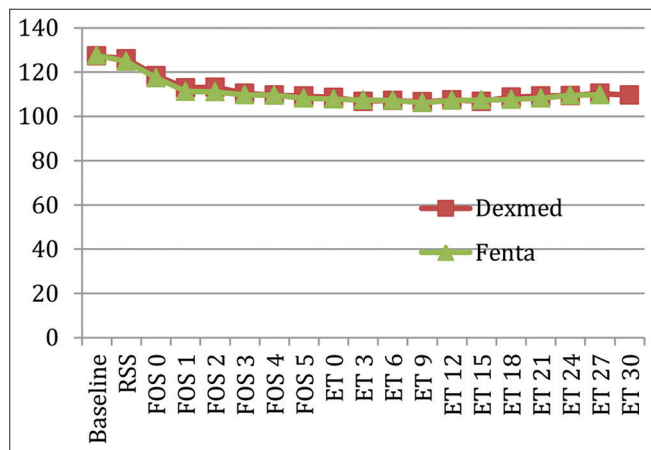
Figure 4: Comparison of systolic blood pressure in both groups

AT RSS 3

The mean DBP (mean ±S.D) at RSS 3 was 76.73±2.85 in group 1 and 76.13±2.72 in group 2. Compared with baseline, the mean DBP decreased by 6.06 mm Hg in the dexmedetomidine group and 5.46 mm Hg in fentanyl and midazolam group. There was no significant difference between the two groups. ($p > 0.05$). (Figure 5).

Compared with baseline, the mean SBP at the time of insertion of fiberoscope (0 min) decreased by 7.20 mm Hg in the dexmedetomidine group and 6.20 mm Hg in fentanyl and midazolam group. No significant difference was found in the DBP measurements before intubation between the two groups. ($p > 0.05$) (Figure 5).

Compared with baseline, the mean DBP at the time of intubation (0 min) decreased by 14.4 mm Hg in the dexmedetomidine group and 13 mm Hg in fentanyl and midazolam group. On comparison between the 2 groups, no significant difference was found in the DBP measurement after intubation between the two groups. ($p > 0.05$) (Figure 5).

BASELINE SpO2

The mean SpO2 (mean ±S.D) was 99.87±0.34 in group 1 and 99.73±0.58 in group 2. There was no significant difference between the two groups. ($p > 0.05$). (Figure 6).

AT RSS 3

The mean SpO2 (mean ±S.D) was 97.67±2.24 in group 1 and 95.47±2.51 in group 2. There was significant difference between the two groups. ($p < 0.05$). (Figure 6) Significant difference was found in the SpO2 measurements before intubation between the two groups. ($p < 0.05$) (Figure 6) Significant differences were found in the SpO2 measurements after endotracheal intubation between the two groups upto 18 mins ($p < 0.05$). No significant difference was found after 15 mins ($P > 0.05$). (Figure 6).
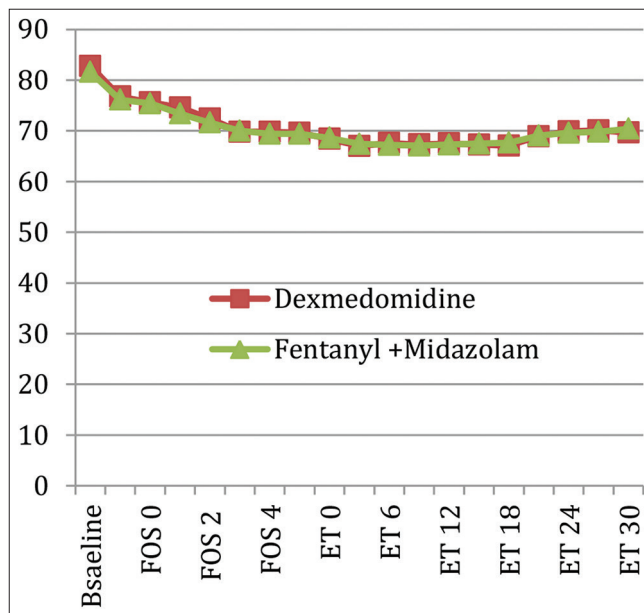

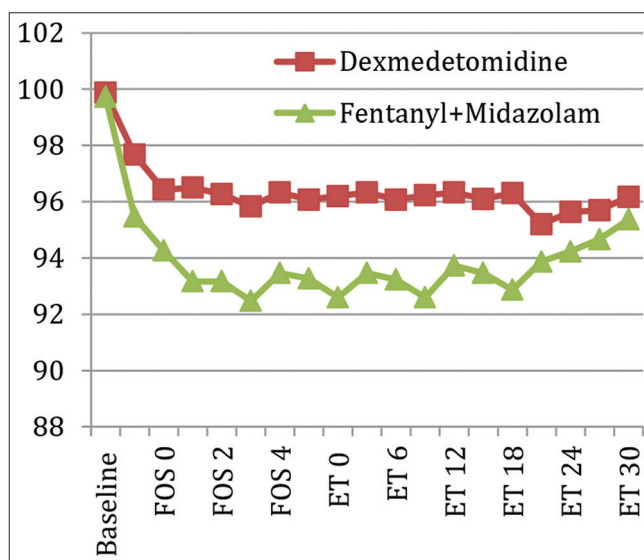**Figure 5:** Comparison of diastolic blood pressure in both groups

Figure 6: Comparison of oxygen saturation in both groups

RESULTS

Both groups were comparable demographically in terms of mean age, weight, and M: F. Both groups underwent uncomplicated AFOI. Measurements of the HRs in the two groups showed significant differences between the two groups at RSS-3, during FOS and post-intubation with the DEX group showing lower mean HRs compared with the MDZ and fentanyl group.

SBP and DBP showed a fall in both the groups as compared with the baseline at RSS-3, during FOS and post intubation; however, no significant differences were noted between

the two groups. Hypotension and bradycardia, the two common side effects of DEX, were not observed in our study probably because the patients were received glycopyrrolate as premedication.

The mean SpO_2 values show significant difference between the two groups. (P<0.05) at RSS-3, FOS, post intubation upto 18 min (P<0.05).

DISCUSSION

Fibreoptic intubation is a wonderful technique for securing airway in both anticipated and unanticipated difficult airways.[9,10]

Tolerability of the procedure by the patients during awake intubation requires good topicalization as well as adequate sedation. Inadequate sedation can be devastating as it could lead to exaggerated hemodynamic response to intubation. On the other hand sedation in excess can lead to airway collapse and therefore hypoxia.[11] Sedation offered by DEX is unique where patients remain sleepy but are arousable. DEX is a highly selective, centrally acting α2 agonist producing hypnosis, amnesia, analgesia, anxiolysis, sympatholysis, and antisialogogue effects all of which are desirable during AFOI. Its sedative properties are mediated by locus ceruleus α2 receptors while spinal alpha-2 receptors mediate analgesic effects.[12,13] Post-synaptic alpha-2 receptors in the central nervous system and presynatic alpha-2 receptors in the peripheral nervous system mediate cardiovascular effects of this drug.

A combination of fentanyl and MDZ for AFOI has good acceptability but risk of fall in SpO_2 is reported in literature.

In our study DEX at 1 mcg/kg bolus infusion over 10 min, with maintenance rates of 0.1–0.7 μg/kg/h, is proved to be safer and beneficial for patients undergoing AFOI. DEX appeared to offer better tolerance, preservation of a patent airway, and spontaneous ventilation, while maintaining hemodynamic stability. The patients in DEX group had a lower mean HR as compared to fentanyl and MDZ group at RSS-3, during fibrescope insertion and post endotracheal tube placement. However, in none of our patients significant bradycardia is noted probably due to glycopyrrolate premedication. Reasons for bradycardia due to DEX as explained in literature are the baroreceptor response of high vascular tone, increased vagal tone that occurs with the bolus, and decreased circulating levels of norepinephrine.[14]

Bloor et al., initially demonstrated the negative chronotropic action of DEX in 1992.[15] Findings of our study are corroborated by Jain et al., Kharwar et al., comparing attenuation of hemodynamic response with DEX versus fentanyl in 60 patients and demonstrated lower HR with DEX.[16,17]

Gandhi et al., compared DEX with fentanyl in attenuation of pressor response during intubation among 100 patients and observed that the HR was significantly lower in DEX group and the difference persisted for 10 min after intubation. These findings are in concordance with our results.[18]

DEX is reported to have dose-dependent biphasic response in blood pressure.[19] Direct stimulation of alpha-2 receptors on blood vessels leads to hypertension with higher doses. On the other hand, hypotension is due to inhibition of the release of norepinephrine from sympathetic nerve terminals by lower doses.[20] However, the typical biphasic response was not noted in our study. Jorden et al., also observed that high bolus doses of DEX do not always result in hypertension,[14] while Venn et al.,[21] reported that high doses of DEX may be used safely without changes in hemodynamics when they are infused slowly over 10 min. However in our study, no significant changes were found in systolic as well as diastolic blood pressure. Combination of MDZ with opioids for sedation during AFOI poses a significant risk of desaturation, cessation of respiration, airway collapse which may even lead to aspiration.[22,23]

Mondal et al., compared intubating conditions and degree of desaturation between DEX and fentanyl in 60 patients and observed higher incidence of desaturation with fentanyl than with DEX.[8]

Similarly Agrawal et al., also compared DEX versus fentanyl and MDZ combination as sedative adjunct to fibreoptic intubation under topical anaesthesia and observed that respiratory rate and SpO_2 were significantly lower in fentanyl plus MDZ group before intubation.[24]

CONCLUSION

The use of DEX at 1 mcg/kg bolus slowly over 10 min, with maintenance rates of 0.1–0.7 μg/kg/h, is safe and beneficial for patients undergoing AFOI. Thus, DEX acts like an ideal drug for AFOI. It provides excellent intubating conditions without significant hemodynamic perturbations and risk of hypoxia.

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