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# COMPARISON OF HEMODYNAMIC RESPONSE OF DEXMEDETOMIDINE VS FENTANYL-MIDAZOLAM COMBINATION IN CASE OF AWAKE FIBEROPTIC INTUBATION IN PATIENTS WITH ANTICIPATED DIFFICULT AIRWAY: A RANDOMIZED DOUBLE BLIND INTERVENTIONAL STUDY

Anaesthesiology

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## ABSTRACT

**Background:** Awake fiberoptic intubation (AFOI) is a technique of choice in known or anticipated difficult airway. AFOI can cause sympathetic stimulation that can be deleterious. Hence, current guidelines on AFOI recommend offering sedation to all patients. Various drugs have been used previously such as benzodiazepines, opioids, and propofol. These drugs cause sedation, amnesia, and attenuate the hemodynamic response but cause respiratory depression and hypoxemia. Hence, a sedative agent which allays anxiety and discomfort of the patient and decreases the sympathetic response without causing respiratory depression is ideal for such situations. The aim of the present study was to compare the hemodynamic response of dexmedetomidine vs fentanyl-midazolam combination in awake fiberoptic intubation.

**Methods:** Hospital based, prospective, Randomized, double blind interventional study. 60 eligible cases were randomly allocated into 2 study groups (Group A and Group B). Group A patients received Inj. dexmedetomidine (1 µg/kg) i.v. in 10 ml NS over 10 minutes, while Group B patients received Inj. fentanyl (2 µg/kg) i.v. plus inj. midazolam (0.02 mg/kg) i.v. in 10 ml NS over 10 minutes. For statistical analysis unpaired-t-test and chi-square test were used.

**Results:** In dexmedetomidine group the mean heart rate was significantly lower as compared to fentanyl-midazolam group at 4 min after fiberoptic scope insertion and at immediate post intubation ($P < 0.001$). The statistically significant difference in mean of mean arterial pressure was seen at 4 min and 6 min after fiberoptic scope insertion ($P < 0.05$), and highly significant difference at immediate post intubation ($P < 0.001$), while difference in mean rate pressure product was significant at 2 min and 6 min ($P < 0.05$), and highly significant at 4 min and immediate postintubation ($P < 0.001$) having better control with dexmedetomidine group. Cough score and post intubation tolerance score were favourable with dexmedetomidine group ($P < 0.001$). There was no significant difference in proportion of side effects in both study groups.

**Conclusion:** Dexmedetomidine provides better hemodynamic stability and better intubating conditions as compared to fentanyl-midazolam combination.

## KEYWORDS

Dexmedetomidine, Fentanyl, Midazolam, fiberoptic bronchoscope, difficult airway

## INTRODUCTION:

Airway management is a major skill of an anaesthesiologist. Any kind of difficulties during the tracheal intubation significantly contribute to the morbidity and mortality associated with anaesthesia. Fiberoptic intubation is an integral part in patients whose airway access is expected to be difficult. It can be performed either as an initial management in a known difficult airway case, or as a backup technique when there is an unsuccessful direct laryngoscopy.[1]

The need for fiberoptic intubation is anticipated on the basis of a history of difficult intubation or various anatomical and anthropometric features that may predict difficult laryngoscopy. These features includes limited mouth opening, decreased atlanto-occipital extension, decreased thyromental distance, inability to prognath, obesity, limited oropharyngeal space, trauma to face, neck, and upper airway, decreased submandibular compliance, known or suspected cervical spine instability, congenital deformities of the head and neck, anatomical malformations of the mandible or larynx, and tumors of head and neck.[2,3,4]

The difficult airway algorithm devised by the American Society of Anaesthesiologists emphasizes that patients with "difficult airway" should be intubated awake.5 Awake fiberoptic intubation is aided if the patient achieves a state of 'conscious sedation', i.e. the patient receives anxiolysis so optimizing compliance but not so sedated that co-operation is lost. Conscious sedation is a state which provides patient comfort and co-operation, blunting of airway reflex, hemodynamic stability, amnesia and the maintenance of a patent airway with spontaneous ventilation. With sedation and topical anaesthesia, most patient becomes calm and comfortable yet responsive for the awake fiberoptic intubation.[5,6,7]

Various pharmacological agents have been reported to achieve conscious sedation for intubation including midazolam, propofol, fentanyl, remifentanil and ketamine.8-13 However, all of the above-mentioned drugs are respiratory depressants. Though the combination of these drugs may provide better intubation conditions, the incidence of hypoxemia is high. Dexmedetomidine is a novel sedative agent which can be used for awake fiberoptic intubation. It is a highly selective α2-adrenoceptor agonist that acts as an analgesic, sedative, and a moderate anti sialagogue without causing respiratory depression.12,13 Thus, dexmedetomidine has many properties that makes it a suitable drug for management of patients with difficult airway, and it may be feasible when used as a sole agent or as an adjunct.12 In view of the above said statements, we carried out a randomized study to investigate the better drug among the two groups for conducting awake fiberoptic intubation for which we chose to divide the patients into two groups, one receiving dexmedetomidine, and the other receiving fentanyl-midazolam combination. We aimed to derive a comprehensive and integrated picture of the relative safety and effectiveness of one drug over the other.

## METHOD:

After approval from the institutional ethics committee and review board, Patients having anticipated difficult airway, age between 18 to 55 years, either sex, weighing between 45-75 kg, with an American Society of Anaesthesiologists (ASA) grade I or II, Mallampati grade > 2 , willing to give written and informed consent and scheduled to undergo elective surgery under general anaesthesia were included in study. Exclusion criteria included uncooperative patients, pregnant patients, H/o reactive airway diseases, history of allergy or hypersensitivity to any of the study drugs, Heart rate < 60 bpm & Systolic blood pressure < 100 mmHg.

Day before surgery a thorough pre-anaesthetic evaluation of the patient was done including history, complete systemic examination and all routine blood investigation, coagulation profile, electrocardiogram and x-ray chest. All patients were kept nil per oral for a minimum period of 6 hours before the surgical procedure.

60 eligible patients were randomly allocated into 2 study groups (Group A and Group B) using the sealed envelope method, each group consisting of 30 patients.

After confirmation of identity, patients were taken in operation theatre. PAC, fasting status, and informed written consent were checked. A peripheral I.V. line was secured with 18 G/20 G cannula. Inj. Ringer Lactate 10 ml/kg I.V. bolus was administered. Inj. Ranitidine 50 mg I.V., inj. Metoclopramide 10 mg I.V. and Inj. Glycopyrrolate (0.005 mg/kg I.V.) were given as a premedication.

Nebulization was done with 2% lidocaine 4 ml (80 mg) for airway topicalization. Puff of 10 % lidocaine were sprayed over the posterior pharyngeal wall. Xylometazoline nasal drops and lidocaine jelly were applied to both the nostrils.

Baseline parameters such as Heart Rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean Arterial Pressure (MAP), Rate pressure product and SPO2 were recorded.

**After that study drug was given.**
Group A patients received inj. Dexmedetomidine (1 µg/kg) I.V. in 10 ml normal saline over 10 minutes.

Group B patients received inj. Fentanyl (2 µg/kg) I.V. plus Midazolam (0.02 mg/kg) I.V. in 10 ml normal saline over 10 minutes.

Bronchoscope was loaded with an appropriate sized cuffed endotracheal tube after proper lubrication.

Sedation was assessed by Ramsay sedation score (RSS). When RSS was achieved ≥ 2 the fiberoptic bronchoscopy was performed via the nasal approach. Insufflation with 100 % oxygen (at the rate of 4 litre/minute) done via the suction port throughout the procedure.

Heart rate, Systolic blood pressure, Diastolic blood pressure, Mean Arterial Pressure, Rate pressure product and SpO2 were recorded at every 2 minutes interval during process of fiberoptic intubation (from the insertion of fiberoptic bronchoscope till the placement of endotracheal tube in trachea), then at immediate post intubation.

General anaesthesia was induced with Inj. Propofol 2mg/kg I.V. slowly over 1 minute, followed by inj. Atracurium 0.5 mg/kg I.V. and surgery was allowed to be proceed.

Parameters (Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, Rate Pressure Product and SpO2) were recorded at 5 minutes and 10 minutes post intubation.

Anaesthesia was maintained with 40 % O2 + 60 % N2O, Inj. Atracurium 0.1 mg/kg I.V., and Sevoflurane 1-2 MAC.

At the end of surgery neuromuscular blockade reversal was done with Inj. Neostigmine (0.05 mg/kg) and Inj. Glycopyrrolate (0.01 mg/kg). Patient were extubated when they fulfilled the extubation criteria.

Incidences of adverse effects like hypotension, bradycardia, respiratory depression, and laryngospasm were also noted.

Statistical analysis: Statistical analysis was performed with SPSS, version 25 for windows statistical software package (SPSS INC., CHICAGO, IL, USA). The continuous data were presented as mean and standard deviation and compared between groups using student's t-test. The categorical data were presented as numbers and percentage and compared between groups using chi square test. The probability was considered to be statistically significant if < 0.05 and highly significant if < 0.001.

## RESULTS:

**Table 1: Demographic profile, ASA physical status and mallampati grade**

| | | Group A | Group B | P Value |
|---|---|---|---|---|
| Age (years) | | 37.43 ± 13.22 | 34.93 ± 12.12 | 0.448 |
| Sex [N0. (%)] | M | 18 (60 %) | 19 (63.33 %) | 1.000 |
| | F | 12 (40 %) | 11 (36.66 %) | |
| Weight (kg) | | 59.17 ± 7.87 | 57.80 ± 8.91 | 0.531 |
| ASA physical status [N0. (%)] | I | 11 (36.66 %) | 12 (40.00 %) | 1.000 |
| | II | 19 (63.33 %) | 18 (60.00%) | |
| Mallampati Grade [N0. (%)] | 3 | 13 (43.33) | 11 (36.66) | 0.792 |
| | 4 | 17 (56.66) | 19 (63.33) | |

Table 1 shows that both the groups were comparable with respect to age (years), sex, weight (kgs), ASA status, and mallampati grade, so as to ensure that there was no confounding bias.

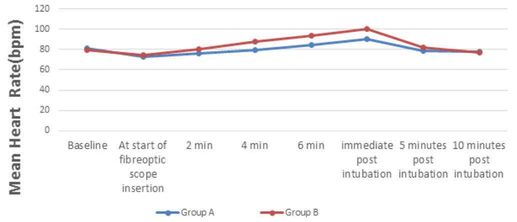


**Figure 1: Mean heart rate:**

**Trend of mean heart rate**
Figure 1 shows the mean heart rate of patients at different intervals in both study groups. There was statistically significant difference between the mean HR in two groups at 4 min after fiberoptic scope insertion (P < 0.05) and highly significant difference at immediate post intubation (p 0.001) with better control of HR in dexmedetomidine group.

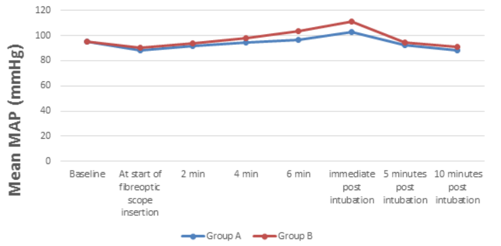


**Figure 2: Mean of mean arterial pressure**

**Trend of mean of MAP**
Figure 2 shows the mean of MAP of patients at different intervals in both study groups. There was statistically significant difference between the mean of MAP in two groups at 4 min, and 6 min after fiberoptic scope insertion (P < 0.05) and highly significant difference at immediate post intubation (P 0.001) with better control of MAP in dexmedetomidine group.

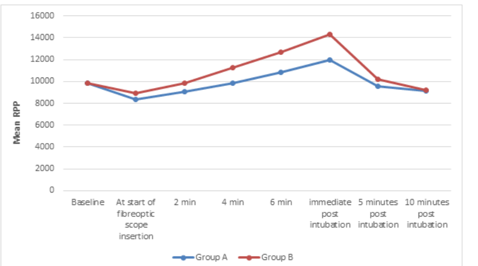


**Figure 3: Mean Rate Pressure Product**

**Trend of mean Rate Pressure Product**
Rate Pressure Product is also called double product (RPP = Heart rate x Systolic blood pressure). Figure 3 shows the mean RPP of patients at different intervals in both the study groups. There was statistically significant difference between the mean RPP in two groups at 2min, and 6 min after fiberoptic scope insertion (P < 0.05) and highly significant difference at 4 min after fiberoptic scope insertion and immediate post intubation (P 0.001) with better control of RPP in dexmedetomidine group. Statistically significant difference was also seen between the mean RPP in two groups at 5 min post intubation (P < 0.05).

**Table 2: Cough score, and Post intubation tolerance score**

| | | Group A | | Group B | | P value |
|---|---|---|---|---|---|---|
| | | No. | % | No. | V | |
| Cough Score | <2 | 23 | 76.67 | 5 | 16.67 | < 0.001 |
| | >3 | 7 | 23.33 | 25 | 83.33 | |
| Post intubation tolerance score | 1 | 24 | 80.00 | 8 | 26.66 | < 0.001 |
| | >2 | 6 | 20.00 | 22 | 73.33 | |

Table 2 shows the cough score and post intubation tolerance score in both the study groups. The difference between two groups was statistically significant (P < 0.001) with a favourable results with group A.

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**Table 3: Complications / Side effects**

| Complications / Side effects | Group A | | Group B | |
|---|---|---|---|---|
| | No. | % | No. | % |
| Bradycardia | 2 | 6.66 | 1 | 3.33 |
| Hypotension | 2 | 6.66 | 3 | 10.00 |
| Respiratory depressions | 0 | 0 | 0 | 0 |
| Other (laryngospasm) | 0 | 0 | 1 | 3.33 |
| Total | 30 | 100.00 | 30 | 100.00 |
| P value = 0.487 | | | | |

The proportion of side effects were comparable between the two groups ($P > 0.05$).

## DISCUSSION

Demographic characteristics (age, weight, sex distribution), ASA physical status, and Mallampati grade distribution, were comparable in both groups ($P > 0.05$).

The mean baseline hemodynamic parameters (HR, MAP, and Rate Pressure Product) were also comparable in both the groups ($P > 0.05$). Thus, the randomization was done adequately and the desired study and control populations were achieved.

### Mean Heart Rate

During fiberoptic scopy the mean heart rate increased in both the groups. When different time points during the fiberoptic scopy were compared between both groups, it was found that the mean heart rates in group A were lower than in group B with highly significant difference at 4 min after fiberoptic scope insertion, and at immediate post intubation ($79.57 \pm 10.09$ bpm vs $87.92 \pm 4.06$ bpm, and $90.67 \pm 10.44$ bpm vs $100.63 \pm 7.60$ bpm respectively; $P < 0.001$).

Similar observations were noted by Murugesan et al14, who conducted study on 40 patients undergoing thyroid surgery and concluded that following fiberoptic intubation the dexmedetomidine group has significantly lower heart rate as compared to fentanyl-midazolam group ($P < 0.001$). The difference in heart rate between the two groups remained significant till 8 min post intubation with better control of heart rate in dexmedetomidine group. Similar study conducted by Hassani et al15 on 52 patients and it was found that dexmedetomidine group compared to fentanyl-midazolam group had lower heart rate following fiberoptic intubation, and the difference was statistically significant ($P < 0.05$).

### Mean of mean arterial pressure :

During fiberoptic scopy the mean of MAP increased in both the groups. When the mean of MAP at different time points during the fiberoptic scopy were compared between both groups, it was lower in group A than in group B with significant differences at 4 min and 6 min after fiberoptic scope insertion ($94.28 \pm 7.10$ mmHg vs $98.25 \pm 6.55$ mmHg, and $96.28 \pm 5.06$ mmHg vs $103.50 \pm 5.23$ mmHg respectively; $P < 0.05$), and highly significant difference at immediate post intubation ($102.93 \pm 6.22$ mmHg vs $111.44 \pm 6.27$ mmHg; $P < 0.001$).

Our results were comparable with the study done by Murugesan et al14, who observed that following fiberoptic intubation there was less increase in MAP in dexmedetomidine group as compared to fentanyl-midazolam group, and the difference was statistically significant ($105.50 \pm 12.50$ mmhg vs $116.55 \pm 14.45$ mmhg; $P < 0.05$). The difference in mean arterial pressure between the two groups remained significant till 6 min post intubation with better control in dexmedetomidine group.

Mean Rate pressure product : During fiberoptic scopy the mean RPP increased in both the groups. When the mean RPP at different time points during the fiberoptic scopy were compared between both groups, it was lower in group A than in group B at all the time points and the difference was statistically significant at 2 min and 6 min ($9059.57 \pm 1254.16$ bpm.mmHg vs $9877.40 \pm 1353.89$ bpm.mmHg and $10806.83 \pm 1229.70$ bpm.mmHg vs $12677.17 \pm 637.42$ bpm.mmHg respectively ; $P < 0.05$), and highly significant at 4 min and immediate postintubation ($9832.39 \pm 1357.69$ bpm.mmHg vs $11243.04 \pm 862.58$ bpm.mmHg, and $12002.33 \pm 1430.24$ bpm.mmHg vs $14339.33 \pm 1347.10$ bpm.mmHg ( at 4 min and immediate post intubation respectively; $P < 0.001$). It was significantly lower in Group A as compared to Group B at 5 min post intubation ($9550.30 \pm 1128.08$ bpm.mmHg vs $10182.73 \pm 1227.14$ bpm.mmHg ; $P < 0.05$).

### Cough score and post intubation tolerance score:

Favourable cough score of $\leq 2$ was found in 23 (76.67 %) patients in group A as compared to 5 (16.67 %) patients in group B, and the difference between two groups was statistically highly significant ($P < 0.001$).

Postintubation tolerance Score of 1 was considered favourable and found in 24 (80.00 %) patients in group A and 8 (26.66 %) patients in group B, and the difference between two groups was statistically significant ($P < 0.001$).

Our observations were similar to study done by Yousuf et al16, who observed that favourable cough score ($\leq 2$) and favourable intubation score (1) was seen in higher number of patients in dexmedetomidine group as compared to fentanyl-midazolam group (27 vs 4, and 22 vs 5 respectively), and the difference between both groups was statistically significant ($P < 0.001$).

### Complications / side effects :

Bradycardia was observed in 2 (6.66 %) patients in group A as compared to 1 (3.33 %) patient in group B.

Hypotension was observed in 2 (6.66 %) patients in group A as compared to 3 (10.00 %) patients in group B.

Respiratory depression was not observed in any patient among both the groups.

No patient among dexmedetomidine group while 1 (3.33 %) patient among the fentanyl-midazolam group developed laryngospasm after giving the study drug.

The proportions of side effects/complication were comparable between two groups ($P > 0.05$).

Our results were similar to the study done by Mariyappa et al17, who performed a randomized prospective study on 60 patients undergoing AFOI and compared the effectiveness of dexmedetomidine and Propofol-fentanyl. It was concluded that there was no significant difference in proportion of side effects like hypotension, bradycardia, laryngospasm and respiratory depression between both the groups ($P > 0.05$).

## CONCLUSION

From the present study we conclude that both dexmedetomidine and fentanyl- midazolam combination show attenuation of hemodynamic response to awake fiberoptic intubation, thus both are effective for awake fiberoptic intubation, but dexmedetomidine provides better hemodynamic stability (HR, SBP, DBP, MAP, RPP) as compared to fentanyl-midazolam combination with preservation of patent airway and spontaneous ventilation.

The favourable intubating conditions as depicted by cough score and post intubation tolerance score are better with dexmedetomidine as compared to fentanyl-midazolam combination.

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