Hemodynamic Responses and Safety of Sedation Following Premedication with Dexmedetomidine and Fentanyl during Fiberoptic-assisted Intubation in Patients with Predicted Difficult Airway

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Abstract

Background: Awake fiberoptic intubation (AFOI) is the gold standard for the management of predicted difficult airway, and inappropriate sedation is a major cause leading to its failure. Aims: The primary objective was to compare the heart rate (HR) changes that accompany AFOI following sedation with dexmedetomidine and fentanyl. Secondary objectives included comparison of changes in blood pressure, patient comfort, ease of intubation, and degree of sedation. Settings and Designs: This prospective double-blinded randomized study was conducted in a tertiary care institution. Subjects and Methods: Forty patients with anticipated difficult airway requiring AFOI were included in the study. Group A received dexmedetomidine 1 µg/kg whereas Group B received fentanyl 2 µg/kg. After topical anesthesia of the airway, AFOI was performed. Statistical Analysis Used: Fisher’s exact test, independent two-sample t-test, and Mann–Whitney U-test were used as applicable. Results: The hemodynamic parameters were comparable in both the groups except at 1 min postintubation when fentanyl group had significantly higher HR. There were lower alertness and muscle tone scores in dexmedetomidine group. Total comfort score was significantly higher in fentanyl group. Though more patients in dexmedetomidine group showed no reaction to intubation and more patients in fentanyl had slight grimacing, the difference was insignificant. The ease of intubation was similar in both the groups. Conclusion: Though dexmedetomidine 1 µg/kg and fentanyl 2 µg/kg premedication results in comparable hemodynamics and ease of intubation, in view of enhanced patient comfort, dexmedetomidine premedication is advantageous in patients with anticipated difficult airway undergoing AFOI.

Keywords: Conscious sedation, dexmedetomidine, fentanyl, fiberoptic, hemodynamics, intubation, premedication

INTRODUCTION

Awake fiberoptic intubation (AFOI) is the gold standard for the management of the predicted difficult airway. The Fourth National Audit Project of the Royal College of Anaesthetists had highlighted the underuse of AFOI in the management of difficult airways and pointed out that inappropriate sedation was a major cause leading to its failure.[1] When AFOI is attempted without sedation, it is usually associated with patient discomfort and severe hemodynamic responses. Benzodiazepines, propofol, opioids, alpha-2-adrenoceptor agonists and ketamine are the main drugs that have been described to facilitate AFOI.[2] Though sedation may enhance the acceptability of awake intubation, it requires careful administration and monitoring as it can lead to airway obstruction and therefore hypoxia.[3] Certain unique characteristics of dexmedetomidine make it an attractive choice for AFOI[4] as it is not associated with respiratory depression when used alone, in spite of deep levels of sedation it can produce. Furthermore, it facilitates a decrease in salivary secretions which is a desirable effect during AFOI. We hypothesized that conscious sedation using dexmedetomidine might attenuate hemodynamic responses to AFOI better than fentanyl.

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Aim of the study
The primary objective of our study was to compare the heart rate (HR) changes that occur immediately following fiberoptic-assisted endotracheal intubation following sedation with dexmedetomidine and fentanyl. Secondary objectives included comparison of changes in the blood pressure following AFOI, patient comfort, ease of intubation process, degree of patient’s alertness/sedation, and incidence of hypoxia between the two groups.

Subjects and Methods
This was a prospective, double-blinded randomized study conducted after obtaining Institutional Ethical Committee Clearance and patients’ consent. Based on the results observed in an earlier publication comparing postintubation HRs in dexmedetomidine and fentanyl groups (75 ± 6.48 vs. 113 ± 16.482), with 95% confidence and 80% power, minimum sample size was calculated to be less than five cases in each group using IBM SPSS V.20 software (Bengaluru, India). However, in the present study, we included 20 cases in each group which gave a 99% confidence and 90% power.

Head and neck surgery patients of the American Society of Anesthesiologists (ASA) physical status 1–3, coming for elective surgery requiring fiberoptic intubation, based on the airway status of the patient, were recruited for the study. Patients of ASA 4 or higher, those with coagulopathies or mass on anterior part of the neck, and those on beta-blockers or angiotensin-converting enzyme inhibitors were excluded. All patients were kept fasting for 6 h for solid foods and 4 h for fluids.

Forty patients were randomly allotted to one of the two groups [Figure 1]. In the operation theater, an intravenous access was secured under local anesthesia, glycopyrrolate 0.2 mg and ondansetron 4 mg were administered, and the patients were hydrated with 500 mL of Ringer’s lactate intravenously. The study drug, either dexmedetomidine 1 µg/kg or fentanyl 2 µg/kg, as per randomization, was diluted to 50 ml with normal saline and was kept in an unlabeled 50cc syringe. Group A patients received dexmedetomidine as a bolus infusion of 1 µg/kg body weight over 10 min using a syringe pump, whereas Group B patients received fentanyl 2 µg/kg body weight over the same time. The allocation of patients randomly to either of the groups based on computer-generated random sequences and the administration of test drug specific to a group was performed by different persons.

Both groups received topical anesthesia of the airway with 10% lignocaine spray and 2% jelly which was followed by a transtracheal injection of 4 mL of 4% lignocaine. AFOI was then performed by an anesthesiologist who was trained in performing AFOI using a flexible bronchoscope (Karl Storz 11301BN1 Germany CE0123, 5 mm). Desaturation to levels <95% during the procedure was treated with supplemental oxygen through the side port of the flexible bronchoscope. After confirming correct endotracheal tube placement with capnography and reservoir bag movements, the patients were induced with propofol 2 mg/kg along with midazolam 2 mg. Muscle relaxation was provided with vecuronium 0.1 mg/kg, and patients were mechanically ventilated with oxygen-nitrous oxide mixture (1:2) with isoflurane 1% keeping end-tidal carbon dioxide levels between 30 and 35 mmHg. Group A patients were administered intravenous fentanyl 2 µg/kg 5 min after AFOI, following documentation of the hemodynamic parameters of the study. An increase in systolic blood pressure >30% above basal values was managed with propofol 30 mg bolus. Bradycardia was defined as HR <50/min, and intravenous atropine 0.6 mg was used to correct it, if occurred.

Baseline hemodynamic parameters were documented before and after study drug administration, immediately after intubation, then at 1 and 5 min later. The ease of intubation process and patient alertness/sedation scale [Table 1] as well as patient comfort scale [Table 2] were assessed and documented. Desaturation to levels <95% and subsequent need of oxygen supplementation were also noted.

Table 1: Assessment and scoring for ease of intubation and degree of alertness

| Score | Description |
|-------|-------------|
| 1     | Easy        |
| 2     | Moderate    |
| 3     | Hard        |
| 1     | No reaction |
| 2     | Slight grimacing |
| 3     | Severe grimacing |
| 4     | Verbal objection |
| 5     | Defensive movement of the head |

FOI = Fiberoptic intubation
Numerical variables such as age, weight, HR, mean arterial pressure (MAP), and comfort scores were expressed as mean and standard deviations. The categorical variables such as sex, ASA status, patient reaction, and ease of intubation were expressed as frequency and percentages. To obtain the association between different characteristics with groups, Fisher’s exact test was used. To obtain the statistical significance of numerical variables between groups, independent two-sample \( t \)-test was applied for parametric data (age, MAP) and Mann–Whitney \( U \)-test was applied for nonparametric data (comfort score, HR, etc.). Statistical analysis was done using IBM SPSS V.20 software (Bengaluru, India).

**RESULTS**

Both the groups were comparable demographically and in distribution of ASA status. The hemodynamic parameters were comparable in both the groups except at 1 min postintubation when the fentanyl group showed a significantly higher HR [Table 3]. Analysis of comfort variables individually revealed significantly lower alertness and muscle tone scores in the dexmedetomidine group, whereas the other variable remained comparable [Figure 2]. However, the total comfort scores were significantly higher in fentanyl group [Table 4]. Though more patients in dexmedetomidine group showed no reaction to intubation and more patients in fentanyl had slight grimacing, the difference was insignificant. The ease of intubation was similar in both the groups [Table 5]. Equal number of patients in each group (16, i.e., 80%) desaturated to <95% and required supplemental oxygen.

**DISCUSSION**

First described in the late 1960s, the role of FOI is now recognized in the guidelines for management of both anticipated and unanticipated difficult airways.[7,8] During FOI, patient comfort should be ensured with adequate anxiolysis while maintaining a patent airway and adequate ventilation.[9] However, commonly, there is a reluctance to use sedative premedicants in these patients for fear of development of airway obstruction and/or apnea. Inadequate sedation could manifest as exaggerated hemodynamic response to FOI.

The present study has shown that the hemodynamics following sedative premedication with both fentanyl 2 µg/kg and dexmedetomidine 1 µg/kg were comparable contrary to our hypothesis that dexmedetomidine premedication might attenuate the stress response better. However, it results in enhanced patient comfort.

Though many sedatives have been tried during FOI, no single agent was found to be ideal. The most commonly used anxiolytic agent, midazolam when used alone may not provide optimal sedation or patient comfort.[10] However, when combined with opioids such as fentanyl or morphine, it resulted

| Parameter       | Assessment                                   | Score |
|-----------------|----------------------------------------------|-------|
| Alertness       | Deeply asleep                                | 1     |
|                 | Lightly asleep                               | 2     |
|                 | Drowsy                                       | 3     |
|                 | Fully awake and alert                        | 4     |
|                 | Hyper-alert                                  | 5     |
| Calmness        | Calm                                         | 1     |
|                 | Slightly anxious                             | 2     |
|                 | Anxious                                      | 3     |
|                 | Very anxious                                 | 4     |
|                 | Panicky                                      | 5     |
| Respiratory     | No coughing and no spontaneous respiration   | 1     |
| response        | Spontaneous respiration                      | 2     |
|                 | Occasional cough                            | 3     |
|                 | Coughing regularly                           | 4     |
|                 | Frequent coughing                            | 5     |
| Crying          | Quiet breathing, no crying                   | 1     |
|                 | Sobbing or gasping                           | 2     |
|                 | Moaning                                      | 3     |
|                 | Crying                                       | 4     |
|                 | Screaming                                    | 5     |
| Physical        | No movement                                  | 1     |
| movement        | Occasional slight movements                 | 2     |
|                 | Frequent slight movement                     | 3     |
|                 | Vigorous movements limited to the extremities| 4     |
|                 | Vigorous movements including torso and head  | 5     |
| Muscle tone     | Muscles totally relaxed, no muscle tone      | 1     |
|                 | Reduced muscle tone                         | 2     |
|                 | Normal muscle tone                           | 3     |
|                 | Increased muscle tone and flexing of fingers, toes| 4     |
|                 | Extreme muscle rigidity and flexing of fingers, toes| 5     |
| Facial tension  | Facial muscle totally relaxed                | 1     |
|                 | Facial muscle tone normal, no tension evident| 2     |
|                 | Tension evident in some facial muscles       | 3     |
|                 | Tension evident throughout facial muscles    | 4     |
|                 | Facial muscles contorted and grimacing       | 5     |
in apnea in half of the subjects, with nearly all experiencing hypoxemia with saturation <90%.

As a strong opioid analgesic with proven analgesic effect, fentanyl has been widely used to reduce the hemodynamic stress response to endotracheal intubation. However, the dose required to blunt this response as a sole agent could be dangerous in patients with anticipated difficult intubation. Combinations of fentanyl and tramadol in tailored doses with respect to age have been successfully used to aid awake endotracheal intubation, guided by fiberoptic bronchoscopy.\(^\text{[11]}\)

We have limited dose of fentanyl to 2 µg/kg as there is no consensus regarding the dose of fentanyl which can be safely used for sedation during AFOI in patients with difficult airway. Doses as high as 3 µg/kg with midazolam 0.05 mg/kg have been safely used during awake blind nasotracheal intubation in patients with temporomandibular joint ankylosis.\(^\text{[12]}\) However, there are reports of significant number of patients desaturating to <95%, following fentanyl 2 µg/kg premedication during AFOI as well. More intense airway manipulation with higher degrees of stimulation during blind nasal intubation might have attenuated the respiratory depressant effect of a higher dose of fentanyl in the study by Dhasmana \(^\text{et al.}\).* Hence, it seems advisable to limit the dose of intravenous fentanyl to a maximum of 2 µg/kg, and at the same time, precautionary measures such as supplementing oxygen through side port of the fiberoptic bronchoscope may be adopted early during the procedure.

Dexmedetomidine and remifentanil are now considered as the two agents which provide optimal sedation without compromising the safety of the patient during FOI.\(^\text{[2,13]}\) Dexmedetomidine, a short-acting alpha-2 agonist, was found to be more effective than fentanyl in producing better intubation conditions, sedation, hemodynamic stability, and less desaturation.\(^\text{[4]}\) When premedicated along with sedative infusion of propofol, it results in complete amnesia of the procedure with hemodynamic stability with a patent airway.\(^\text{[14]}\) Though both 1 and 1.5 µg/kg doses resulted in similar hemodynamic changes during FOI, dexmedetomidine 1.5 µg/kg was proved to be more effective for sedation in young healthy patients as they were significantly calmer, more cooperative, and satisfied during the procedure.\(^\text{[15]}\)

Mondal \(^\text{et al.}\).*\(^\text{[4]}\) had observed that dexmedetomidine was more effective than fentanyl in producing better intubation conditions, sedation along with hemodynamic stability, and less desaturation during AFOI. The study population in their study comprised of patients with normal airway for elective laparoscopic surgeries, whereas we tested the safety of these drugs in patients with difficult airway.

Sedation without airway obstruction and respiratory depression is the unique feature of dexmedetomidine. Though in the study by Mondal \(^\text{et al.}\).*\(^\text{[4]}\) fewer patients desaturated to <95%
following dexmedetomidine premedication, in our study the incidence was much higher and equal in both groups. This could be because of the difference in patient characteristics. Most of the patients in our study were older and had head and neck malignancies which might have resulted in poor nutritional status. The possibility of hypoproteinemia and enhanced drug sensitivity might have resulted in respiratory depression in our patients. However, we were able to correct the desaturation with supplemental oxygen in all the patients. We did not have any consequences requiring any other rescue technique or crisis management.

Though we have not documented the time taken for intubation, it is highly probable that the procedure duration could have been longer in our study, as patients in the study by Mondal et al. had essentially normal airway whereas most of our patients had structurally abnormal airway due to malignancy and/or radiation. Despite all these explanations, it seems reasonable to supplement oxygen through the side port of flexible bronchoscopes, meant for passage of instruments, from the beginning of AFOI to prevent the development of desaturation in patients with anticipated difficult airway who receive sedative premedication.

Hypotension and bradycardia, the two common side effects of dexmedetomidine, were not observed in our study probably because the patients were well hydrated with intravenous fluids before administration of dexmedetomidine and all of them had received glycopyrrolate as well.

One of the limitations of our study was that we compared two drugs which had different sites of action. We investigated hemodynamic stability with a drug which has bradycardia and hypotension as side effects which may be profound in beta-blocked and young adults who run already on lower HRs. Though dexmedetomidine is known not to produce respiratory depression, we observed desaturation in most of the patients in both the groups. The reasons for desaturation other than sedation such as breath holding, coughing, or further narrowing of a compromised airway due to presence of bronchoscope were not analyzed separately in our study. The success of AFOI depends on operator skill as well as adequacy of topical anesthesia. In our study, each patient had independent risk of difficult airway which would have affected the efficacy of topicalization and ease of intubation. Another drawback was that the administration of fentanyl, which might increase the muscle tone, could have partly influenced the comfort scores in the fentanyl group since grading of muscle tone was part of comfort score determination.

The strengths of our study are that it was performed in forty patients with structurally abnormal airway due to head and neck cancers with almost impossible conventional direct laryngoscopy and intubation. There were only two operators who conducted AFOI; the familiarity and experience were almost equal for both. Hence, there were little confounding factors of variability in the skills of the operators.

**Conclusion**

Though dexmedetomidine 1 µg/kg and fentanyl 2 µg/kg premedication result in comparable hemodynamics and ease of intubation, in view of enhanced patient comfort, dexmedetomidine premedication is advantageous in patients with anticipated difficult airway undergoing awake fiberoptic bronchoscope-assisted intubation.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Cook TM, Woodall N, Freer C. The NAP4 Report: Major Complications of Airway Management in the United Kingdom, London: The Royal College of Anaesthetists; 2011. Available from: http://www.rcuk.ac.uk/system/files/CSQ-NAP4. [Last accessed on 2016 Nov 08].
2. Johnston KD, Rai MR. Conscious sedation for awake fibreoptic intubation: A review of the literature. Can J Anaesth 2013;60:584-99.
3. Leslie D, Stacey M. Awake intubation. Contin Educ Anaesth Crit Care Pain 2015;15:64-7.
4. Mondal S, Ghosh S, Bhattacharya S, Choudhury B, Mallick S, Prasad A. Comparison between dexmedetomidine and fentanyl on intubation conditions during awake fiberoptic bronchoscopy: A randomized double-blind prospective study. J Anaesthesiol Clin Pharmacol 2015;31:212-6.
5. Chemik DA, Gillings D, Laine H, Hendler J, Silver JM, Davidson AB, et al. Validity and reliability of the Observer’s Assessment of Alertness/Sedation Scale: Study with intravenous midazolam. J Clin Psychopharmacol 1990;10:244-51.
6. Ambuel B, Hamlett KW, Marx CM, Blumer JL. Assessing distress in pediatric intensive care environments: The COMFORT scale. J Pediatr Psychol 1992;17:95-109.
7. Drogel P. Management of the anticipated difficult airway – A systematic approach: Continuing Professional Development. Can J Anaesth 2009;56:683-701.
8. Apfelbaum JL, Hagberg CA, Caplan RA, Blitt CD, Connis RT, Nickinovich DG, et al. Practice guidelines for management of the difficult airway: An updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Anesthesiology 2013;118:251-70.
9. Collins SR, Blank RS. Fiberoptic intubation: An overview and update. Respir Care 2014;59:865-78.
10. Bergese SD, Patrick Bender S, McSweeney TD, Fernandez S, Dzwonczyk R, Sage K. A comparative study of dexmedetomidine with midazolam and midazolam alone for sedation during elective awake fiberoptic intubation. J Clin Anesth 2010;22:35-40.
11. Wang SY, Mei Y, Sheng H, Li Y, Han R, Quan CX, et al. Tramadol combined with fentanyl in awake endotracheal intubation. J Thorac Dis 2013;5:270-7.
12. Dhasmana S, Singh V, Pal US. Awake blind nasotracheal intubation in temporomandibular joint ankylosis patients under conscious sedation using fentanyl and midazolam. J Maxillofac Oral Surg 2010;9:377-81.
13. Eftekharian HR, Zarei K, Arabion HR, Heydari ST. Remifentanil, ketamine, and propofol in awake nasotracheal fiberoptic intubation in temporomandibular joint ankylosis surgery. J Craniofac Surg 2015;26:206-9.
14. Gupta K, Jain M, Gupta PK, Rastogi B, Saxena SK, Manngo A. Dexmedetomidine premedication for fiberoptic intubation in patients of temporomandibular joint ankylosis: A randomized clinical trial. Saudi J Anaesth 2012;6:219-23.
15. Dhasmana SC. Nasotracheal fiberoptic intubation: Patient comfort, intubating conditions and hemodynamic stability during conscious sedation with different doses of dexmedetomidine. J Maxillofac Oral Surg 2014;13:53-8.