ABSTRACT

Objectives: Awake fiberoptic intubation (AFOI) is a step-forward technique for successful intubation of patients with difficult airways. The popularity of its usage is increasing day by day in handling difficult airways. Our study aims to compare the efficacy and efficiency of Buprenorphine and Fentanyl as sedative agents for AFOI. The primary and secondary outcome measure was to assess hemodynamic response and on intubating condition of the patient after AFOI.

Methods: This randomized, prospective study was conducted in tertiary center hospital. Total of 100 patient were enrolled for study and divided into two groups, Group A patients received intravenous Buprenorphine injection (2.5 μg/kg over 10 min) and Group B Fentanyl injection (2 μg/kg over 10 min) was injected prior to AFOI. The degree of sedation was assessed using the Observer's assessment of alertness/sedation score (OAA/S), and the score of coughing during awake bronchoscopy was used to assess intubation status. Tolerability of intubation was assessed using a 5-point intubation score and a 3-point post-intubation assessment score immediately after the placement of the endotracheal tube into the trachea.

Results: Group A had more favorable OAA score than Group B, whereas other intubation conditions cough score, limb movement, 5-point intubation score, 3-point post intubation score was more favourable in Group B than in Group A.

Conclusion: Intravenous Fentanyl is better than Buprenorphine agent in terms of intubation score for AFOI. Both groups are comparable in terms of hemodynamic changes and stability.

Keywords: Awake intubation, Buprenorphine, Difficult airway, Fentanyl

INTRODUCTION

Tracheal intubation technology in anesthesia care has unexpectedly advanced, one of the developments of new modalities in the modern medical care. Laryngoscopy and endotracheal intubation are difficult in many patients in emergency and in elective settings. Induction of general anesthesia in patients carries the additional risk of loss of muscle tone and airway obstruction.

Awake fiberoptic intubation (AFOI), practiced since 1960, is a step-forward technique for successful intubation of patients with difficult airways. The popularity of its usage is increasing day by day in handling difficult airways. AFOI is an important part of anesthesia management for difficult airways. Awake fibre-optic intubation (AFOI) is an important part of anesthesia management for difficult airways with limited mouth opening due to airway obstruction, jaw fractures, and infection [1]. Attention should be paid to the anesthetic and dosage required to achieve sedation and analgesia for nasal intubation when airway management is difficult. During awake fiberoptic intubation under intravenous (IV) sedation, the patient should remain calm and follow verbal instructions.

Endotracheal fiberoptic intubation by bronchoscope, if performed without adequate sedation, can be a very uncomfortable experience, can be very unpleasant for the patient. Various groups of drugs are recently being used for sedation during AFOI such as propofol, benzodiazepines, opioids, alpha 2 agonists, and ketamine.

Pre-requisite for awake fiberoptic intubation are anxiolysis of the patient, Patient comfort, amnesia, hemodynamically stable and weakening of airway reflexes. Adequate sedation with local airway anesthesia can minimize discomfort, anxiety, and sympathetic surge during awake fibreoptic intubation [2]. Preparing the patient in advance for AFOI is important. Preparation includes anesthesia for airway reflexes, adequate sedation, anxiolytic effects and airway maintenance, and adequate ventilation [3]. An ideal sedation regimen is critical for patient comfort, minimization of airway reflexes, patient compliance, hemodynamic stability, amnesia, and maintaining an open airway with spontaneous breathing [4].

AFOI can cause hemodynamic changes such as increased heart rate, blood pressure, and oxygen desaturation and difficulty for anesthesiologists to manage. Therefore, it is important to prepare the patient’s airway to weaken airway reflexes and ensure good sedation and anxiolytic while maintaining adequate ventilation and without loss of airway patency [5].

Even α-adrenergic blockade minimizes increases in heart rate and myocardial contractility (a major determinant of O2 consumption) due to inhibitory effects due to increased adrenergic activity [6].

Buprenorphine had not been evaluated for intubation status during his AFOI at the time this study was planned. Benzodiazepines, propofol, opioids, alpha2-adrenergic receptor agonists, and ketamine are some of the important drugs reported to promote AFOI [7].

METHODS

This was a prospective randomized double-blind study which was conducted in tertiary care super-speciality hospital after ethical committee approval and CTRI permission (CTRI/2022/02/040614). A total of
100 patients with ASA I and II were selected for the study. Patients were divided into two categories using a computer-generated list.

Group A patients were injected with Buprenorphine (2.5 μg/kg).

Group B patients were injected with Fentanyl (2 μg/kg) 10 min before intubation.

All the patients were kept nil per oral and informed consent was taken. Patients were explained about the procedure before being taken in the operating room. Nebulization was done for 20 min before surgery with 4% of lignocaine 4 mL by facemask for topicalization of upper and lower airway.

Standard monitoring was attached to record baseline heart rate, non-invasive blood pressure, oxygen saturation, and electrocardiogram to all patients. Study drugs were prepared by an anaesthesiologist, which was not included in data collection. Another experienced anaesthesiologist performed and observed the procedure was blinded to the group. Xylocaine nasal drops (0.1%) was administered in both the nostrils and a Lignocaine jelly (2%) was used for greasing the fiberoptic scope and the endotracheal tube. Superior laryngeal block was performed bilaterally with 2 mL of lignocaine (2%) that was introduced in both sides and transtracheal block was performed with 2 mL of (2%) lignocaine for recurrent laryngeal nerve block. For topical anesthesia, lignocaine spray (10%) was used to avoid gag reflex and for desensitization of oropharynx and hypopharynx. The total dose of the drug was calculated according to patient’s weight. After that level of sedation was assessed using the observer’s assessment of alertness score/sedation sore (OAA/S) 1= Verbal response to patient’s name, 2=Lethargic response, 3=reacts when the name is spoken loudly and/ or repeatedly, 4= reaction after mild prodding or shaking, 5= reaction after painful stimuli.

AFOI was performed through nasal route, once the position of fiberoptic scope in the trachea was confirmed; then, the tracheal tube was railroaded and positioned approximately 3 cm above the carina and secure the airway. General anesthesia was induced after the confirmation of end tidal carbon dioxide in the capnography and surgery was allowed to proceed. Various hemodynamics parameters were observed and noted at baseline and just after intubation. The primary outcome measure was to assess hemodynamic response of the patient’s after AFOI.

Secondary outcome measure and intubating condition were evaluated by cough score. Cough score, 1=none, 2=one gag or cough only, 3=more than one gag or cough but acceptable conditions, 4=unacceptable conditions: Limb movement, 1=None, 2=Slight, 3=Moderate, 4=Severe during bronchoscopy. Patient tolerance was assessed by a 5-point intubation comfort score, 1= No reaction, 2=Slight grimacing, 3=Heavy grimacing, 4=Verbal objection and 5=Defensive Movement and Three-Point assessment post-intubation score, immediately after endotracheal intubation, 1=Cooperative, 2=Restless/Minimal resistance, 3=Severe resistance/ GA required immediately.

Hypotension (decrease in mean arterial pressure [MAP] >20% from baseline) was treated with intravenous fluids (1x) and injection ephedrine 6 mg iv in titrated doses. Bradycardia (Heart rate <60/min) was treated with atropine. All recordings were tabulated.

Statistical analysis

All the statistical analyses of data were done with statistical programming software IBM SPSS interpretation 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA).

Test used

Independent sample t-test, Paired sample t-test, and Chi-square test were used. Our estimated sample size was based on OAA/S score Stage III among groups and from the previous study. Total of 100 patients were calculated with a mean difference of 1.26 with 3.2 standard deviation. Calculated sample size with 95% confidence interval, 80% power, and alpha level of 0.05 were obtained. Level of significance was set at [\( p \leq 0.05 \)].

RESULTS

The demographic data are in (Table 1) and (Figures 1-3) showing hemodynamic parameters of the patients at different time intervals and comparison of OAA score, cough score, limb movement, 5-point intubation comfort score, and 3-point post-intubation score are in (Table 2).

Age distribution

In Group A (buprenorphine), heart rate increased post-intubation from (85.52±5.61 to 88.00±4.65) (p=0.005), in Fentanyl group heart rate increased from (88.48±9.30 to 90.18±8.78) which was statistically non-significant (p=0.260) (Fig. 1).

Group A Buprenorphine systolic blood pressure increased from baseline to post-intubation (129.70±10.90 to 130.02±11.52 mmHg) with a p=0.879, which was statistically non-significant and in Group Fentanyl systolic blood pressure was decreased from 135.14±13.91 mmHg to 128.46±10.51 mm Hg, which was statistically significant with a p=0.015 (Fig. 2).

Mean arterial blood pressure data at baseline and after intubation for both groups were analyzed. In the Buprenorphine group from (97.72±9.94 to 100.57±8.87) and in the Fentanyl group from (101.20±11.26 to 98.73±8.40). In both group change in MAP, post-intubation were non-significant (Fig. 5).

DISCUSSION

The ASA difficult airway algorithm highlights awake intubation and tracheostomy as primary or alternate options in difficult airway situations. Nowadays, AFOI is the preferred method for securing a difficult airway.

The search for an ideal sedative regimen for awake fibroptic intubation is being constantly pursued by various clinical studies. Our study aims to compare the efficacy and efficiency of Buprenorphine and Fentanyl as sedative agents for AFOI.

Buprenorphine appears to be a partial \( \mu \) receptor agonist. Buprenorphine produces analgesia and central nervous system effects that are qualitatively similar to those of morphine.

Fentanyl is a phenylpiperidine derivative of a synthetic opioid which provides mild sedation, and analgesia along with hemodynamic stability, which is beneficial for AFOI but there is a risk of respiratory depression, nausea, vomiting, and chest wall rigidity.

Hemodynamic parameters

As like to our study, similar data were found in Rajan et al. [7] study, a comparison of hemodynamic parameters was done in both the group dexmedetomidine and fentanyl. In the dexmedetomidine group, baseline heart rate decreased post-intubation from (87.35±2.49 to 83.30±1.95) and the fentanyl group baseline heart rate increased post-intubation from (87.75±1.58 to 90.20±16.47) with a p=0.120. Similar to that in our study in the buprenorphine group, heart rate increased from (85.52±5.61 to 88.00±4.65), a p=0.005 which was significant whereas in the fentanyl group, it was non-significant.

A study done by Dhiman et al. [8] compared fentanyl 2 mcg/kg and magnesium sulfate 45 mg/kg in 20 patients. Observed a 5% rise in MAP from the baseline in the fentanyl group and a 15% rise in the magnesium sulfate group (p=0.320) post-intubation and an increase in heart rate from baseline to post-intubation 35% in group fentanyl and 19% in group magnesium sulphate (p=0.583). The differences were not significant, similar to this in our study, a post-intubation increase in heart rate was seen in both buprenorphine and fentanyl groups but...
was statistically significant in the buprenorphine group with \( p = 0.005 \). Fentanyl remains hemodynamically stable in our study.

A study done by Chaudhary et al. [5] observed changes in heart rate in nalbuphine and fentanyl at different intervals; heart rate increased post-intubation at 2 min, but it was non-significant. Mean blood pressure was comparable in both the groups at all the time points except at 2-min post-intubation, where it was significantly lower in group fentanyl compared to group nalbuphine (\( p = 0.011 \)). They observed a contrast result from our study. In our study heart rate increased in both the fentanyl group as well as in the buprenorphine group, but there was a statistically significant increase in the buprenorphine group with \( p = 0.05 \).

In contrast to our study a study done by Puchner et al. [9] in their study comparison was done in two groups: Group I received remifentanil and Group II received fentanyl-midazolam. The remifentanil group had better suppressed hemodynamic response to nasal intubation with \( p \)-value of \( p < 0.001 \).

Furthermore, a contrast study done by Hassani et al. [10] in their study heart rate decreased in the dexmedetomidine group post-intubation from \( 81.61 \pm 13.14 \) to \( 81.53 \pm 19.50 \) and increased in fentanyl-midazolam post-intubation from \( 87.03 \pm 10.33 \) to \( 95.52 \pm 16.81 \) with \( p = 0.008 \). In our study, fentanyl group remains more hemodynamically stable.

Yousuf et al. [11] in their study found different results from our study. In the dexmedetomidine group, heart rate increased from \( 77.46 \pm 5.75 \) bpm to \( 75.03 \pm 4.83 \) (mean systolic blood pressure increased from \( 118.47 \pm 8.803 \) bpm to \( 127.37 \pm 7.568 \) bpm) in the dexmedetomidine group and it also increases in the midazolam-fentanyl group from \( 117.27 \pm 10.517 \) bpm to \( 133.26 \pm 9.692 \) bpm) was statistically significant \( p = 0.003 \). They found dexmedetomidine is more hemodynamically stable and we found fentanyl more hemodynamically stable.

A study was done by Chu et al. [12] found contrasting result from our study they compared fentanyl with dexmedetomidine and observed a significantly reduced hemodynamic (heart rate and MAP) response post-intubation in the dexmedetomidine group than the fentanyl group.

In contrast to our study a study done by Mondal et al. [3] compared dexmedetomidine and fentanyl. In dexmedetomidine group, decrease in heart rate post-intubation from \( 77.46 \pm 5.75 \) bpm to \( 75.03 \pm 4.83 \) was statistically non-significant and there was significant increase in heart rate in fentanyl group post-intubation from \( 77.76 \pm 10.52 \) beats/min to \( 111.3 \pm 16.49 \) beats/min with \( p < 0.0001 \). The increase of MAP was minimal in group dexmedetomidine from \( 94.43 \pm 6.678 \) to \( 95.03 \pm 4.83 \) (\( p = 0.347 \)). However, in group fentanyl rise of MAP was from \( 94.23 \pm 4.904 \) to \( 114.17 \pm 11.2 \) and was statistically significant \( p < 0.0001 \).

### Table 1: Comparison of primary measurement outcomes

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Buprenorphine (n=50) (%)</th>
<th>Fentanyl (n=50) (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedation score/observer assessment of alertness score n (%)</td>
<td>46 (92)</td>
<td>37 (74)</td>
<td>0.041*</td>
</tr>
<tr>
<td>Lethargic response</td>
<td>3 (6)</td>
<td>12 (24)</td>
<td></td>
</tr>
<tr>
<td>Reacts only after the name is spoken loudly and repeatedly</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Reaction after mild prodding or shaking</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Reaction after painful stimuli</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Coughing n (%)</td>
<td>11 (22)</td>
<td>22 (44)</td>
<td></td>
</tr>
<tr>
<td>More than one gag or cough but acceptable conditions</td>
<td>36 (72)</td>
<td>18 (36)</td>
<td></td>
</tr>
<tr>
<td>Unacceptable conditions</td>
<td>31 (62)</td>
<td>10 (20)</td>
<td></td>
</tr>
<tr>
<td>Limb movement n (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Slightly</td>
<td>30 (60)</td>
<td>34 (68)</td>
<td>0.191</td>
</tr>
<tr>
<td>Moderate</td>
<td>20 (40%)</td>
<td>14 (28%)</td>
<td></td>
</tr>
<tr>
<td>5-point intubation comfort score n (%)</td>
<td>1 (2)</td>
<td>2 (4)</td>
<td>0.000*</td>
</tr>
<tr>
<td>No reaction</td>
<td>2 (4)</td>
<td>46 (92)</td>
<td></td>
</tr>
<tr>
<td>Slight grimacing</td>
<td>24 (48)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Heavy grimacing</td>
<td>25 (50)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>3-point post-intubation score n (%)</td>
<td>37 (74)</td>
<td>46 (92)</td>
<td>0.017</td>
</tr>
<tr>
<td>Cooperative</td>
<td>13 (26)</td>
<td>4 (8)</td>
<td></td>
</tr>
</tbody>
</table>

\* \( p < 0.01 \) is highly significant, Values are expressed as n (%)
However, in our study in buprenorphine group, both heart rate and MAP increased post-intubation. Heart rate increased from (85.52±5.61 to 88.00±4.65), p=0.005 which was significant, whereas in the fentanyl group, heart rate increased from (88.48±9.30 to 90.18±8.78) with p=0.260 which was non-significant. Mean arterial blood pressure increased post-intubation in the buprenorphine group from (97.72±9.94 to 100.57±8.87), p=0.145 statistically non-significant, whereas in the fentanyl group, it decreased from (101.20±11.26 to 98.73±8.40), p=0.224 which was also non-significant.

A study by Patodi et al. [13] compared two groups dexmedetomidine and fentanyl, in the dexmedetomidine group, the mean heart rate decreased post-intubation from (77.23±11.30 bpm to 77.20±11.12 bpm) which was statistically non-significant. MAP also increased with a p=0.717 which was statistically non-significant, but in fentanyl group, change in heart rate and MAP was statistically significant. They found contrast results to our study. In our study, in the buprenorphine group, both heart rate and MAP are increased post-intubation. Heart rate increased from (85.52±5.61 to 88.00±4.65), p=0.005 which was significant, and mean arterial blood pressure increased post-intubation from (97.72±9.94 to 100.57±8.87), p=0.145 which was statistically non-significant, while in fentanyl group, heart rate and MAP did not change significantly.

**Intubating conditions**

Patodi et al. [13] done a study on intubating condition and two groups were compared, in Group dexmedetomidine the number of patients with a favorable cough score (cough score ≤2) were significantly more (24 out of 30) than in fentanyl group (16 out of 30) with p=0.0285. In group dexmedetomidine, the number of patients with a favorable intubation comfort score (intubation comfort score ≤2) was significantly more, 21 out of 30 in dexmedetomidine compared to 13 out of 30 in group fentanyl of p-value (p=0.037).

In our study, cough score was more favorable in the fentanyl group in which more than one gag or cough was present in 10 patients out of 50 in fentanyl group, whereas in the buprenorphine group, 31 patients out of 50 with p=0.000 which was statistically highly significant. Five-point intubation comfort score was also more favorable in the fentanyl group. Only two patients out of 50 had heavy grimacing in the fentanyl group as compared to 25 patients out of 50 in the buprenorphine group with p=0.000 which was statistically significant. A 3-point post-intubation comfort score was more favorable in the fentanyl group. Post-intubation score with minimal resistance was seen in four patients out of 50 in the fentanyl group and 13 patients out of 50 in the buprenorphine group.

In a study done by Chu et al. [12], intubation score (1–5) representing the condition for nasal intubation was significantly better in the dexmedetomidine group (2 (1–3) as compared to fentanyl which was 3 (2–5). In our study, intubation comfort score was more favorable in the fentanyl group. Patients with heavy grimacing were two patients out of 50 in the fentanyl group as compared to 25 patients 50 in the buprenorphine group and was statistically significant with a p=0.000.

In a study done by Mondal et al. [3], cough score of less or equal to 2 was considered a favorable condition, which was achieved in 28 patients out of 30 patients in the dexmedetomidine group but only in three out of 30 patients in the fentanyl group. In our study in the fentanyl group, out of 50 patients, 10 patients had more than one gag or cough whereas, in the buprenorphine group out of 50 patients, 31 patients had more than one gag or cough. This suggests fentanyl group had a better cough score as compared to the buprenorphine group.

Rajan et al. [7] did a study in which the Analysis of comfort variables individually revealed significantly lower alertness and muscle tone scores in the dexmedetomidine group, whereas the other variables (calmness, respiratory response, and physical movement) remained comparable. However, the total comfort scores were significantly higher in the fentanyl group. In our study, alertness score is more in the buprenorphine group whereas coughing score, limb movement, 5-point intubation score, and 3-point intubation score were more

**Fig. 2: Systolic blood pressure data distribution**

**Fig. 3: Mean arterial blood pressure distribution**

**Fig. 4: Study vignette**
favorable in the fentanyl group than the buprenorphine group; therefore, fentanyl is more favorable for intubating condition.

In the study conducted by Chaudhary et al. [5], cough score was more favorable in the fentanyl group than nalbuphine group but statistically insignificant whereas other scores like the post-intubation score, the Ramsay sedation score was comparable in both groups but there was not a significant difference between nalbuphine and fentanyl group. In our study, cough score and post-intubation score was more favorable in the fentanyl group than in the buprenorphine group and it was statistically significant.

In a study done by Youssuf et al. [11], cough score of ≤2 was considered favorable and was found in 27 patients out of 30 in the dexmedetomidine group and four patients out of 30 in the midazolam-fentanyl group, while three patients out of 30 in the dexmedetomidine group and 26 patients out of 30 in the midazolam-fentanyl group had cough scores of ≥3 and was statistically significant with p<0.001; hence, considered dexmedetomidine was more favorable for cough score.

A post-intubation score of 1 was considered favorable and it was found in 22 patients out of 30 in the dexmedetomidine group and in five patients out of 30 in the midazolam-fentanyl group, while post-intubation scores of ≤2 were presented in eight patients out of 30 in dexmedetomidine group and in 25 patients out of 30 in the midazolam-fentanyl group was statistically significant (p=0.001) and more favorable in the dexmedetomidine group.

In our study, cough score of more than one gag or cough was present in 31 patients out of 50 in the buprenorphine group and 10 patients out of 50 in the fentanyl group. A 3-point intubation score was present in 13 patients out of 50 in the buprenorphine group and in four patients out of 50 in the fentanyl group.

In a study done by Dhiman et al. [8] in which the Ramsay sedation score was used, a score of 3 was observed in four patients out of 10 in the fentanyl group and one patient out of 10 in the magnesium sulphate group. Post-intubation scores one patient out of 10 in the fentanyl group and one patient out of 10 in the magnesium sulfate group. The incidence of recall of the fiberoptic intubation procedure was significantly lower in the fentanyl group with p=0.003. A 3-point intubation score was present in 13 patients out of 50 in the buprenorphine group and in four patients out of 50 in the fentanyl group.

Puchner et al. [9] compared a study in which Group I received remifentanil and Group II received fentanyl and midazolam. Remifentanil patients had better tolerated nasal tube passage with a p-value of (p<0.001) and laryngeal tube advancement with a p-value of p<0.001 compared with a fentanyl-midazolam group. Patients had more recall of the fiberoptic procedure six patients out of 37 in the remifentanil group and zero patient out of 37 in the fentanyl-midazolam group with a p-value of p<0.05.

In our study Observer’s assessment of the alertness, score was present in 46 patients out of 50 in the buprenorphine and in 37 patients out of 50 in the fentanyl group. Alertness is more in the buprenorphine group with p=0.041.

CONCLUSION

Our study, we revealed that using injection fentanyl in dosage of 2 mcg/kg and injection buprenorphine in dosage of 2.5 mcg/kg 10 min before intubation. Injection fentanyl found better in terms of less cough, better sedation, better intubating conditions, and tolerance to intubation. Both investigational drugs produced minimal or no respiratory depression. Both groups are comparable in terms of hemodynamic changes. We conclude that fentanyl is better agent in terms of intubation score for AFOI, but buprenorphine is also a superior alternative or alternative to fentanyl for AFOI.

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CONFLICTS OF INTEREST

The authors declare no competing interests.

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