

Comparison of Dexmedetomidine Plus Fentanyl Versus Dexmedetomidine Plus Butorphanol for Conscious Sedation in Patients undergoing awake Fiberoptic Nasotracheal Intubation A Prospective Randomized and Controlled Clinical Study.

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Abstract

Background: The aim of this study is to compare conscious sedation in patients receiving dexmedetomidine plus fentanyl versus dexmedetomidine plus butorphanol in awake fiberoptic intubation. Comfort score, patient reaction and hemodynamic parameters will be statistically compared in both the groups.

Methods: After local ethics committee approval, 100 patients were selected according to eligibility criteria and randomly allocated in two groups of 50 each. GROUP DF: patients received bolus of i.v. dexmedetomidine 1µg/kg + i.v. fentanyl 2µg/kg so as to achieve an adequate level of sedation i.e. RSS=3. GROUP DB: patients received bolus of i.v. dexmedetomidine 1µg/kg + i.v. butorphanol 20µg/kg to achieve an adequate level of sedation. Fiberoptic intubation was performed by two anaesthesiologist consultants. Patients were monitored for Comfort score, Ramsay sedation score, 5-Point fiberoptic score. Hemodynamics were compared in both the groups.

Results : It was observed that hemodynamic parameters were comparable in both the groups. However, total comfort score values were better in group-DF as compared to group-DB. Patients in group DF had better tolerance to the procedure and sedation scores were significantly better in group – DF at the time of procedure.

Conclusion: Dexmedetomidine plus fentanyl is better in providing adequate comfort and tolerance to patients undergoing AFOI.

Keywords: AFOI, Dexmedetomidine, Fentanyl, Butorphanol, Total Comfort Score.

Introduction

Awake Fiberoptic Intubation (AFOI) is an effective technique for establishing airway access in patients who have both anticipated and unanticipated difficult airways. It was first described in late 1960s. This procedure facilitates in airway management provided proper patient preparation is done and technique is mastered [1].

It is a valuable technique in securing airway in predicted difficult intubation scenario, compromised airway, airway pathology, when neck extension is to be avoided,

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vertebral artery insufficiency, Arnold Chiari malformation, limited mouth opening as in temporomandibular joint disease, mandibular-maxillary fixation and severe facial burns [2]. Other indications include patients who are at risk of aspiration of gastric contents [3].

AFOI can be performed nasally or orally in awake patients with topical or regional anaesthesia, or in sedated or anesthetized patients [4]. The technique is usually performed with the patient in supine position. Standard airway and emergency equipments should be available all the time. In circumstances in which mask ventilation may be difficult and risk of airway loss is high, an awake technique is preferred. A nasal approach is particularly useful in patients with a large tongue, limited mouth opening, receding lower jaw or tracheal deviation or in cases where an unobstructed surgical field is beneficial (e.g., dental surgery). This approach is also anatomically favorable as

the laryngeal opening is more easily seen with the fiberscope as it courses past the nasopharynx with less obstruction by the tongue. The final decision depends on patient parameters and skill of the anaesthesiologist [5].

The main aim of awake intubation is to have a calm and cooperative patient who can follow verbal commands while maintaining adequate oxygenation and ventilation. Good topical anaesthesia is essential to obtund the sensory afferent stimuli of the oropharyngeal and laryngotracheal region. Establishing topical anaesthesia before intubation prevents coughing, swallowing, laryngospasm and excessive salivation. Both patient comfort and optimal intubating conditions are necessary when we are preparing the patient for fiberoptic intubation [6,7].

Conscious sedation is desirable not only to make the procedure more tolerable for patients but also to ensure optimal intubating conditions, particularly in the presence of abnormal laryngeal anatomy and pathology. The ideal sedative for AFOI would provide anxiolysis and some degree of amnesia with a low incidence of recall of the procedure. It would have analgesic properties, suppress the cough, gag reflex, be safe and easy to titrate with minimal respiratory and cardiovascular side effects. In the last three decades, the use of several classes of drugs have been described benzodiazepines (e.g. diazepam and midazolam), opioids (e.g. morphine, fentanyl and remifentanyl), alpha-2 agonists (e.g. clonidine and dexmedetomidine) and intravenous induction agents (e.g. ketamine and propofol) [8].

The need for conscious sedation during an AFOI is now widely accepted. Kopman et al highlighted its advantages in 1975 in a review of 267 awake intubations. The study concluded that drugs that are most suitable for AFOI have both anxiolytic and analgesic properties. The ideal choice of drug may vary depending upon the patient characteristics and indication for AFOI [9]. The search for the ideal drug for conscious sedation for an AFOI is an ongoing process. The use of local anaesthetic can be partially compensated in terms of eliminating pain and discomfort; still there may be significant psychological obstacles in the tolerance of the procedure which should not be neglected [10]. The last decade has seen the practice of conscious sedation being revolutionized by the introduction of drugs with unique pharmacokinetic and pharmacodynamic properties, such as propofol, remifentanyl and dexmedetomidine.

Rajan S et al in 2018 conducted a study to see the hemodynamic responses and safety of sedation following premedication with dexmedetomidine and fentanyl during fiberoptic assisted intubation in patients with predicted difficult airway. From the study it was concluded that

dexmedetomidine 1 µg/kg and fentanyl 2 µg/kg premedication resulted in comparable hemodynamics. Dexmedetomidine premedication was advantageous in patients with anticipated difficult airway undergoing awake fiberoptic bronchoscope-assisted intubation [11]. Some authors successfully used dexmedetomidine as a single agent for sedation during AFOI and others combined it with agents like fentanyl as a trial to improve its sedation criteria, but the combination of butorphanol with dexmedetomidine was not used before in awake fiberoptic intubation. Butorphanol and fentanyl have been compared in many studies in order to see their effect as a component of balanced general anaesthesia, but none has been done in awake fiberoptic intubation.

To establish a better and safe regimen of sedation while maintaining patency of airway, we compared dexmedetomidine-butorphanol with dexmedetomidine-fentanyl to see which one could improve the sedative criteria of dexmedetomidine in the form of improving tolerance of patients to intubation during AFOI technique without the need to increase the dose of dexmedetomidine which may be associated with airway compromise.

Methods and Materials

The present prospective, comparative and randomized study was conducted in Rajindra Hospital, Patiala, after obtaining the approval from ethical committee Government Medical College, Patiala. Total 100 patients scheduled to undergo elective surgery under general anaesthesia fulfilling the eligibility criteria were selected and randomly divided into two groups of 50 each. Randomization was done by simple envelope method.

Eligibility

- Age: 18 to 60 years
- Gender(s): Both male and female
- ASA Grade I and II
- Patient consent to participate in this study

Exclusion Criteria

- History of severe bradycardia
- Any type of A-V block in ECG
- Thrombocytopenia
- Liver cirrhosis
- Nasal polyp
- History of previous nasal surgery/nasal trauma
- Mentally ill patients
- Pregnant females

- Drug abuse
- Coagulopathy
- Patient's refusal
- Allergic to the drugs involved in the study

A written informed consent was obtained from each patient after explaining the technique prior to inclusion in this study in their own vernacular language. A detailed pre-anaesthetic check-up was done in every patient. All patients received Inj. Glycopyrrolate (0.2mg) i/m 30 minutes before the procedure.

Patients were placed in supine position. Nasal mucosa was sprayed with vasoconstrictor xylometazoline 0.1%. Each nostril was checked for patency. Nasopharyngeal dilator with lignocaine jelly was introduced in either nostril with greater patency. The nostril with least resistance was chosen for nasal intubation. 2% lignocaine viscous gargles were done to achieve adequate topical anaesthesia. For further topical anaesthesia 2 puffs of

10% lignocaine were sprayed over tonsillar pillars and posterior pharyngeal wall. The local anaesthetic dose was not exceeding 4mg/kg [12]. Tanstracheal block was given in cricothyroid membrane after locating it in the midline of the neck with 4% lignocaine.

Insertion of Fiberscope

Lidocaine jelly was applied to fiberscope and nostril. Under the guidance of video, fiberscope was advanced. On reaching the carina, endotracheal tube was railroaded over the fiberscope. Tracheal placement was confirmed by locating murphy's eye while removing the fiberscope. Fiberoptic nasotracheal intubation was done in both groups of patients. Duration of fiberoptic intubation was different in different patients ranging from 1 to 5 minutes. Once tracheal intubation was completed and the tube was secured, general anaesthesia was administered. Clinically patients were monitored and following observations were recorded during the course of intubation:

- Ramsay Sedation Scale at the time of fibroscopy

| Score | Response |
|-------|--|
| 1 | Patient is anxious and agitated or restless, or both. |
| 2 | Patient is cooperative, oriented and tranquil. |
| 3 | Patient responds to commands only. |
| 4 | Patient exhibits brisk response to light glabellar tap or loud auditory stimulus. |
| 5 | Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus. |
| 6 | Patient exhibits no response. |

- Comfort scale values were recorded by the anaesthesiologist during pre-oxygenation, during introduction of fiberscope and at the introduction of ET tube.

Comfort scale, as modified from Ambuel et al [13]

| Parameter | 1 | 2 | 3 | 4 | 5 |
|-----------------------------|---|----------------------------|--|---|---|
| Alertness | Deeply asleep | Lightly asleep | Drowsy | Fully awake and alert | Hyper-alert |
| Calmness | Calm | Slightly anxious | Anxious | Very anxious | Panicky |
| Respiratory Response | No coughing and no spontaneous respiration | Spontaneous respiration | Occasional cough | Coughing regularly | Frequent coughing or choking |
| Crying | Quiet breathing, no crying | Sobbing or gasping | Moaning | Crying | Screaming |
| Physical movement | No movement | occasional slight movement | Slight frequent movement | Vigorous movement restricted to extremities | Vigorous movement including head and chest |
| Muscle movement | Muscles totally relaxed, no muscle movement | Reduced muscle tone | Normal muscle tone | Increased muscle tone and flexing of fingers and toes | Extreme muscle rigidity and flexing of fingers and toes |
| Facial tension | Facial muscle totally relaxed | No facial tension evident | Tension evident throughout facial muscle | Facial muscle contorted | Grimacing |
| Total Score | 35 | | | | |

- Patient's tolerance was assessed by an independent observer on the basis of 5 point FOI score [14]: No reaction (1), Slight grimacing (2), Severe grimacing (3), Verbal objection (4), Defensive movement of head, hands or feet (5).
- Patient baseline vitals (HR, SBP, DBP, MAP, EtCO₂, SpO₂) were recorded during pre-oxygenation, during sedation and fiberoptic insertion, ETT placement every minute up till five minutes.

Results

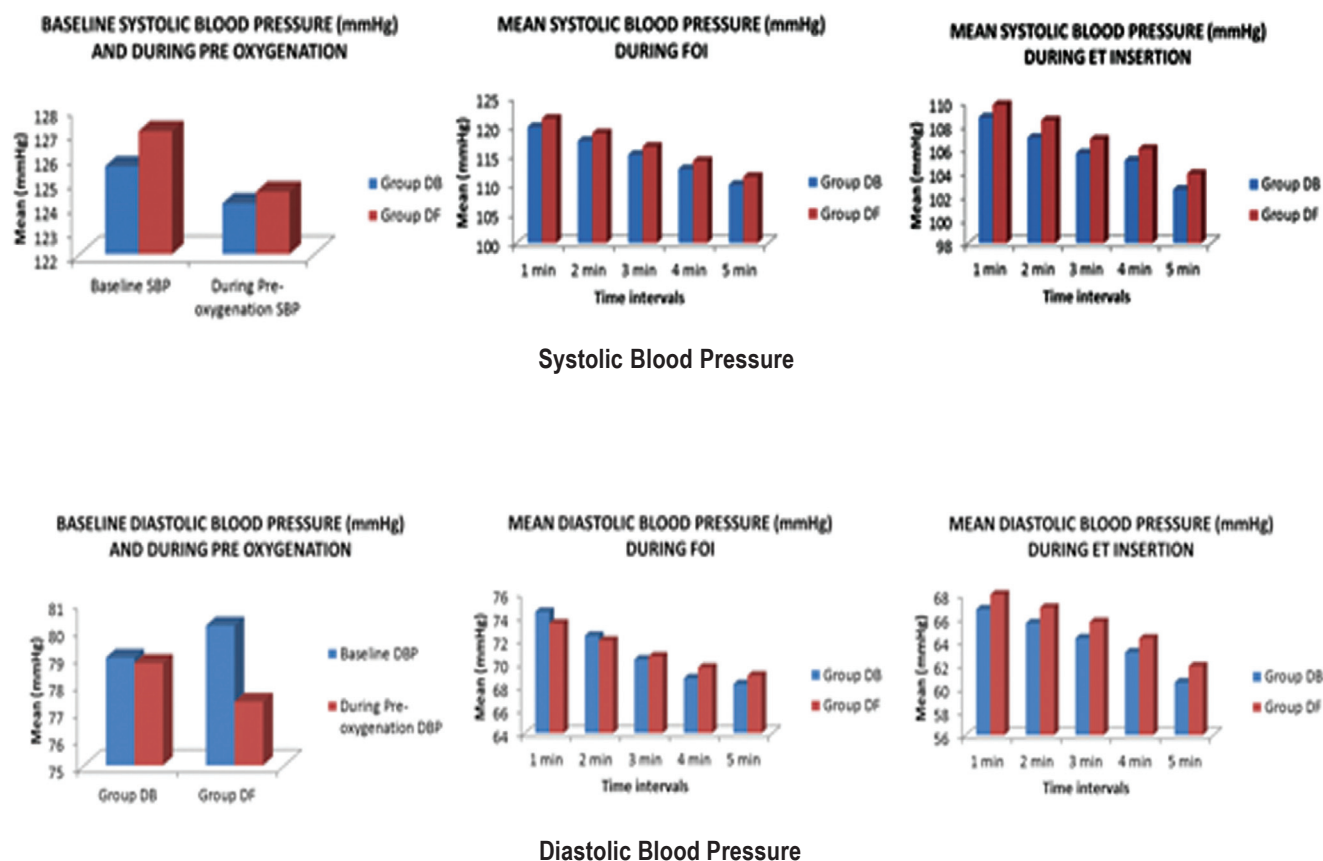
In our study, analysis was conducted using IBM SPSS statistics (version 22.0). Numerical data was expressed as mean and standard deviation and statistical analysis was done using the independent t-test to compare the two groups. For skewed data/scores Mann-Whitney U-test was used.

Gender was compared using Chi square test

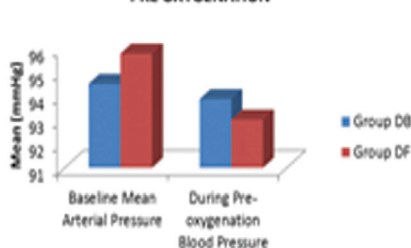
The demographic parameters – age, weight and gender in both the groups were statistically not significant. The hemodynamic parameters – heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, SpO₂, EtCO₂ were statistically not significant in both the groups. The data was comparable. The comfort level of patients during fiberoptic intubation was better in group DF as compared to group DB and the difference was highly significant statistically. Patient tolerance which was estimated using 5 point fiberoptic score was better in group DF than group DB and the difference was highly significant. Sedation score was again better in Group DF at the time of procedure as compared to group DB and the difference was statistically highly significant.

Demographic Parameters

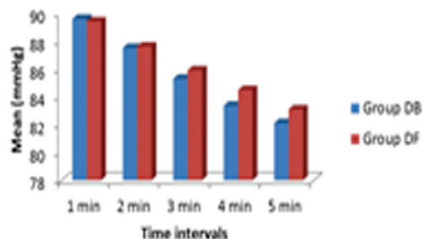
| GROUP | Group DB | Group DF | P value | Significance |
|--------------|---------------|---------------|---------|--------------|
| Age | 39.32 ± 12.31 | 37.90 ± 11.94 | 0.963 | NS |
| Weight | 62.36 ± 8.38 | 60.82 ± 11.21 | 0.438 | NS |
| Gender (F/M) | 32/18 | 40/10 | 0.075 | NS |



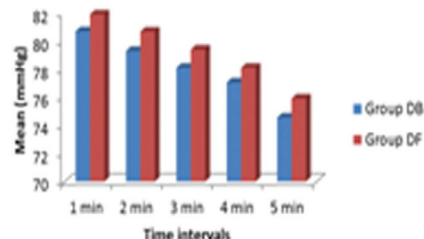
BASELINE MEAN MAP (mmHg) AND DURING PRE OXYGENATION



MEAN MAP (mmHg) DURING FOI

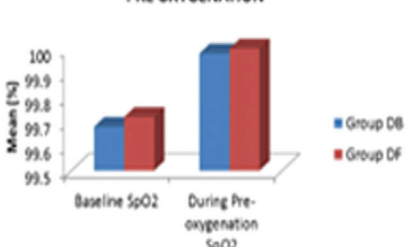


MEAN MAP (mmHg) DURING ET INSERTION

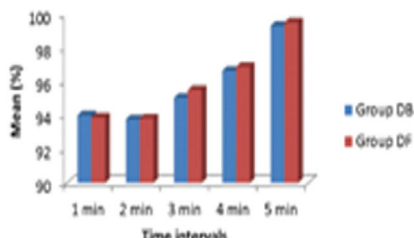


Mean Arterial Pressure

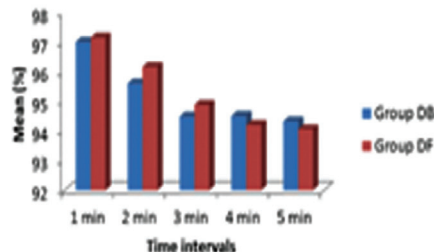
BASELINE MEAN SpO2(%) AND SpO2 DURING PRE OXYGENATION



MEAN SpO2(%) DURING ET INSERTION

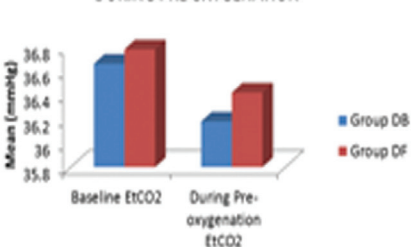


MEAN SpO2 (%) DURING FOI

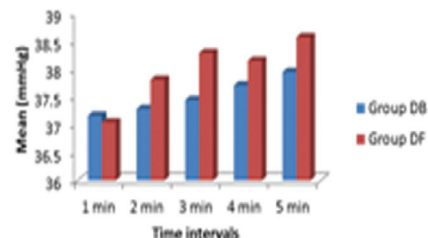


Mean SpO₂

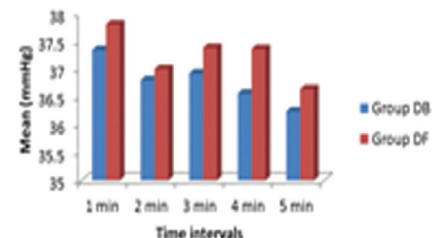
BASELINE MEAN EtCO2 (mmHg) AND EtCO2 DURING PRE OXYGENATION



MEAN EtCO2 (mmHg) DURING FOI



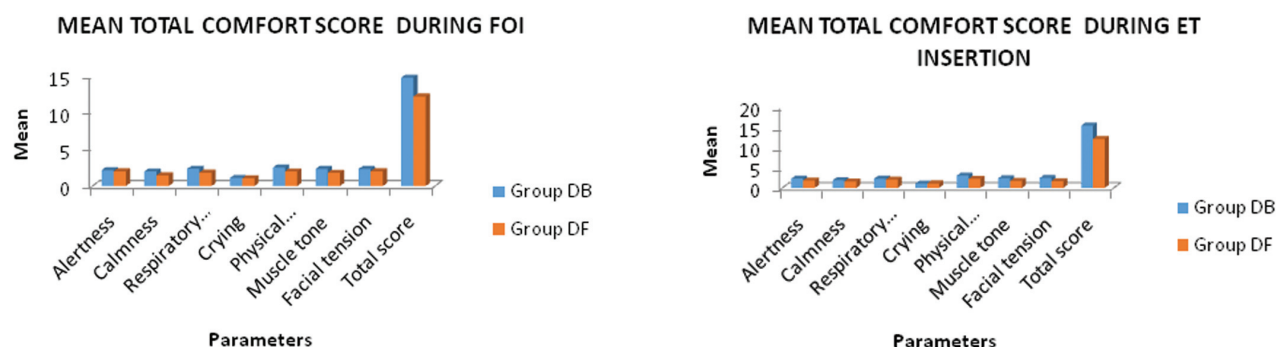
MEAN EtCO2 (mmHg) DURING ET INSERTION



EtCO₂

Total Comfort Score

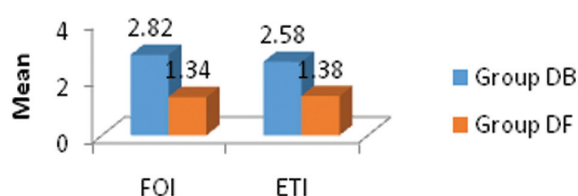
| | | Group | Mean | S.D | P value | Significance |
|---------------------|------------------------|----------|---------|---------|---------|--------------|
| Total comfort score | During pre-oxygenation | Group DB | 17.7200 | 0.90441 | 0.787 | NS |
| | | Group DF | 17.6800 | 0.71257 | | |
| | FOI | Group DB | 14.8200 | 1.66218 | <0.001 | HS |
| | | Group DF | 12.2400 | 1.70904 | | |
| | ETI | Group DB | 15.3600 | 1.97701 | <0.001 | HS |
| | | Group DF | 12.1000 | 2.16889 | | |



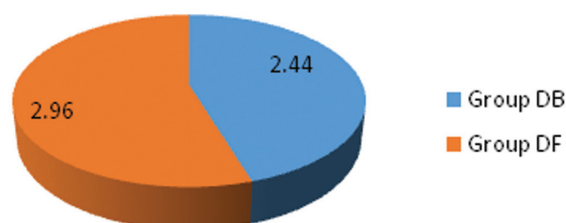
Patient Tolerance

| | | Group | Mean | S.D | P value | Significance |
|-------------------|-----|----------|--------|---------|---------|--------------|
| Patient Tolerance | FOI | Group DB | 2.8200 | 1.02400 | <0.001 | HS |
| | | Group DF | 1.3400 | 0.62629 | | |
| | ETI | Group DB | 2.5800 | 0.88271 | <0.001 | HS |
| | | Group DF | 1.3800 | 0.69664 | | |

PATIENT'S TOLERANCE BASED ON 5 POINT FIBEROPTIC INDEX SCORE



RAMSAY SEDATION SCALE



Ramsay Sedation Scale

| Groups | Mean | S.D | P value | Significance |
|----------|--------|---------|---------|--------------|
| Group DB | 2.4400 | 0.50143 | <0.001 | HS |
| Group DF | 2.9600 | 0.40204 | | |

Discussion

In our study, distribution of patients according to age, weight and gender was similar in both groups and statistically no significant difference was seen between the two groups ($p > 0.05$).

Both groups were given an initial bolus dose of dexmedetomidine $1\mu\text{g}/\text{kg}$ over 10 minutes. It has a diverse action profile which includes sedation, analgesia, anxiolysis, perioperative sympatholysis, cardiovascular stabilizing effects, reduced anesthetic requirements and

preservation of respiratory function [11].

Shoukry RA in 2016 conducted a study on safety and efficacy of dexmedetomidine sedation for elective fiberoptic bronchoscopy and concluded that dexmedetomidine and propofol-fentanyl were effective for patients undergoing flexible fiberoptic bronchoscopy but the sympatholytic and respiratory stability effects of dexmedetomidine made it a safe alternative for sedation during the procedure [15].

The mean heart rate in our study during preoxygenation, during fiberscope insertion and during endotracheal tube

insertion was comparable in both the groups and was statistically non-significant. However a progressive decrease in heart rate was seen in both the groups.

In our study, there was no statistically significant difference in SBP, DBP and MAP in both the groups. Both the groups were hemodynamically stable and cardiostable as well. There was a progressive fall in SBP and DBP owing to the sympatholytic effect of dexmedetomidine which was given in same concentration in both the groups.

Inhibition of sympathetic pathway involved in α_1 receptors done by dexmedetomidine explains its action of decreasing HR and blood pressure. This action was very useful in attenuating the hemodynamic sympathetic response seen in AFOI [16]. Inhibition of sympathetic supply of upper airways by dexmedetomidine resulted in blunting of airway reflexes, with more comfort to patients during intubation. This was helpful in allowing smooth intubation and easy ensuring of endotracheal tube position.

SpO₂ and EtCO₂ were also comparable in both the groups.

Total comfort score was superior in Dexmedetomidine-fentanyl group as compared to Dexmedetomidine-buttorphanol group. Patients were more comfortable owing to the early onset of action of fentanyl as compared to buttorphanol. Patients tolerance as seen in 5-point Fiberoptic scale was significantly better in Dexmedetomidine-Fentanyl group. Patients were intubated using AFOI technique with preparation of airway with local anaesthetic. The mean value of total comfort score during fiberscope insertion in group DB was 14.82 ± 1.66 and in group DF was 12.24 ± 1.70 . The statistical difference for TCS between both the groups during fiberscope insertion was highly significant ($p < 0.001$). The mean value of total comfort score during endotracheal tube insertion in group DB was 15.36 ± 1.97 and in group DF was 12.10 ± 2.16 . The statistical difference for TCS between both the groups during endotracheal tube insertion was highly significant ($p < 0.001$). Thus our study showed that dexmedetomidine-fentanyl group provided better intubating conditions than dexmedetomidine-buttorphanol group.

The mean 5 point fiberoptic intubation index score during fiberscope insertion was 2.82 ± 1.02 and 1.34 ± 0.62 and at endotracheal tube insertion was 2.58 ± 0.88 and 1.38 ± 0.69 in the Group DB and Group DF respectively. Statistically highly significant difference in the patient's tolerance was found during FOI and during endotracheal tube placement between the two groups ($p < 0.001$). Hassan ME et al (2017) conducted a study to evaluate different doses of dexmedetomidine alone versus the combination of dexmedetomidine and fentanyl in sedation during awake fiberoptic intubation in oral cancer surgery patients in a

prospective, randomized, double blind clinical trial. It was concluded from the study that addition of small dose of fentanyl to dexmedetomidine improved patient tolerance to procedure while maintaining airway patency. The results in our study were supported by this study.

The mean Ramsay Sedation Scale in Group DB was 2.44 ± 0.50 and in Group DF was 2.96 ± 0.40 . There was statistically highly significant difference between the two groups ($p < 0.001$). The onset of action of fentanyl is 5 minutes as compared to buttorphanol which is approximately 15 minutes. In our study, we were comparing dexmedetomidine - buttorphanol versus dexmedetomidine-fentanyl. Fentanyl reaches its peak effect within 5 minutes whereas buttorphanol reaches its peak effect later. Due to this difference the sedation score at the time of fiberscopy was better in dexmedetomidine-fentanyl group. The addition of an opioid to dexmedetomidine was useful because of the antitussive effect of opioids and the enhancement of sedation quality. Our study concluded that dexmedetomidine-fentanyl group maintained better sedation score at the time of procedure as compared to dexmedetomidine-buttorphanol group.

Conclusion

The study aimed to evaluate the comparison of intubating conditions using dexmedetomidine plus buttorphanol versus dexmedetomidine plus fentanyl during fiberoptic intubation. Both dexmedetomidine ($1\mu\text{g}/\text{kg}$) – fentanyl ($2\mu\text{g}/\text{kg}$) (group DF) and dexmedetomidine ($1\mu\text{g}/\text{kg}$) – buttorphanol ($20\mu\text{g}/\text{kg}$) (group DB) provided similar hemodynamic changes (HR, SBP, DBP, MAP, SpO₂, EtCO₂) which were statistically non-significant during AFOI but DF group provided better comfort score and tolerance to patients for the procedure as compared to DB group. Sedation scores were better maintained in group DF as compared to group DB at the time of procedure.

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|------------------------------|---|
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| Ethics: | There is no ethical violation as it is based on voluntary anonymous interviews |
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