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Comparative Evaluation of Dexmedetomidine versus Fentanyl-Midazolam Combination for Awake Fiberoptic Intubation in Patients Undergoing Oral Cancer Surgery: A Randomized Controlled Study

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ABSTRACT

Background: Awake fiberoptic intubation (AFOI) is the gold standard for managing the difficult airway in patients with oral cancer. An ideal sedation regimen must provide anxiolysis, amnesia, and cough suppression while maintaining spontaneous breathing and hemodynamic stability. This study compared the efficacy of dexmedetomidine (DEX) versus a fentanyl-midazolam (FM) combination for AFOI in oral cancer surgery.
Methods: A prospective, double-blind, randomized controlled trial was conducted on 36 adult patients (ASA I-III) with oral cancer and predicted difficult airway. Patients were randomly allocated into two groups (n=18 each): Group D received intravenous dexmedetomidine (loading 1 µg/kg over 10 min, followed by infusion 0.5 µg/kg/hr), and Group FM received fentanyl (1 µg/kg) plus midazolam (0.03 mg/kg). The primary outcome was intubation conditions (cough severity, patient comfort, and operator satisfaction). Secondary outcomes included hemodynamic parameters (heart rate, mean arterial pressure), oxygen saturation, sedation scores (Ramsay Sedation Scale), and adverse events.
Results: Intubation conditions were significantly better in Group D: 83.3% of patients had no/mild cough compared to 50% in Group FM (p=0.03). Operator satisfaction (VAS 0-10) was higher in Group D (8.9±0.7 vs. 7.1±1.2, p=0.01). Hemodynamics: Group D provided a stable heart rate and MAP throughout AFOI, while Group FM showed a significant increase in HR and MAP at intubation ($p<0.05$). Oxygen desaturation (SpO2 <92%) occurred in 5 patients (27.8%) in Group FM versus none in Group D (p=0.02). Ramsay scores were comparable (3-4) in both groups.
Conclusion: Dexmedetomidine provides superior intubation conditions, better hemodynamic stability, and a lower risk of hypoxemia compared to fentanyl-midazolam for awake fiberoptic intubation in oral cancer surgery. Dexmedetomidine is a safer and more effective sedative agent in this setting.

Keywords*: Awake fiberoptic intubation, dexmedetomidine, fentanyl, midazolam, oral cancer, difficult airway.*

INTRODUCTION

Oral cavity cancer ranks among the most common malignancies in low- and middle-income countries, with tobacco, alcohol, and betel nut consumption being predominant risk factors.[1]Patients presenting for oral cancer surgery—such as wide local excision, hemiglossectomy, or composite resection with neck dissection—frequently harbor tumors that infiltrate the tongue, floor of mouth, retromolar trigone, or oropharynx. Such pathological involvement leads to progressive anatomical distortion, restricted mouth opening (trismus), reduced neck mobility, and sometimes direct airway obstruction.

Consequently, these patients are among the highest risk categories for difficult airway management in routine anesthetic practice.[2]

Awake fiberoptic intubation (AFOI) has long been established as the gold standard for securing the airway in patients with an anticipated difficult airway. By preserving spontaneous ventilation and maintaining protective airway reflexes, AFOI allows the anesthesiologist to navigate the fiberoptic bronchoscope through a distorted or narrowed upper airway while the patient remains conscious and breathing independently.[3] This approach is particularly vital in oral cancer, where induction of general anesthesia and attempted laryngoscopy in an unsecured airway can precipitate complete airway collapse, failed ventilation, and a "cannot intubate, cannot oxygenate" emergency.

However, the success of AFOI is heavily dependent on the quality of sedation and analgesia administered during the procedure. The ideal pharmacologic regimen for AFOI must fulfill several demanding criteria: relief of anxiety and amnesia for the procedure, suppression of the cough and gag reflexes without abolishing them entirely, maintenance of spontaneous breathing and upper airway patency, preservation of hemodynamic stability, and rapid return to baseline mental status following intubation.[4] No single agent to date has satisfied all these requirements perfectly.

Historically, the combination of fentanyl, a synthetic opioid, and midazolam, a benzodiazepine, has been widely employed for sedation during AFOI. Fentanyl provides potent analgesia and cough suppression, while midazolam offers anxiolysis and anterograde amnesia. This synergistic combination is familiar to most anesthesiologists and has a well-documented safety profile in short procedures.[5] Nevertheless, accumulating evidence reveals significant drawbacks: both agents produce dose-dependent respiratory depression, with fentanyl causing potential chest wall rigidity and midazolam predisposing to upper airway obstruction, particularly in patients with compromised airways. Furthermore, neither drug reliably blunts the sympathetic surge provoked by laryngoscopy and tracheal intubation, leading to episodes of tachycardia, hypertension, and myocardial oxygen imbalance—events that are particularly hazardous in elderly or comorbid cancer patients.[6]

In recent years, dexmedetomidine has emerged as a promising alternative. Dexmedetomidine is a highly selective alpha-2 adrenergic receptor agonist (with an $\alpha 2{:}\alpha 1$ selectivity ratio of 1600:1) that acts centrally in the locus coeruleus to produce "cooperative sedation"—a state in which patients are sedated yet rousable, calm, and able to follow commands.[7] Unlike benzodiazepines and opioids, dexmedetomidine exerts its sedative and analgesic effects without significant respiratory depression, as it does not interact with gamma-aminobutyric acid (GABA) or opioid receptors in the brainstem respiratory centers. Additionally, dexmedetomidine reduces central sympathetic outflow, thereby attenuating the hypertensive and tachycardic responses to airway manipulation.[8] These properties suggest that dexmedetomidine might be ideally suited for AFOI in oral cancer patients.

Several studies have compared dexmedetomidine with midazolam or fentanyl-midazolam combinations for AFOI in general surgical populations, with most reporting superior patient satisfaction, better intubating conditions, and greater hemodynamic stability with dexmedetomidine.[9,10] However, evidence specifically addressing patients with oral cancer—a subgroup characterized by severe anatomical distortion, heightened airway reactivity, and often poor cardiopulmonary reserve—remains limited. Moreover, sample sizes in existing trials are frequently small, and standardized protocols for dosing and outcome assessment are lacking.

Therefore, this randomized controlled trial was designed to evaluate and compare the efficacy of dexmedetomidine versus a fentanyl-midazolam combination for awake fiberoptic intubation in patients undergoing surgery for oral cancer. The primary outcome was intubation conditions, assessed by cough severity, patient comfort, and operator satisfaction. Secondary outcomes included hemodynamic stability, sedation scores, oxygen saturation, and the incidence of adverse events. We hypothesized that dexmedetomidine would provide superior intubation conditions with fewer episodes of hypoxemia and greater hemodynamic stability compared to the fentanyl-midazolam regimen

METHODOLOGY

Study design, setting and population

A prospective, randomized, double-blind, parallel-group, active-comparator controlled trial was employed. The study was conducted at the Department of Anesthesiology, ESIC Medical College & Hospital, Noida.The target population comprised adult patients with oral cavity squamous cell carcinoma scheduled for elective curative surgery who had a predicted difficult airway requiring awake fiberoptic intubation.

Inclusion Criteria:

- Age 18–70 years
- ASA physical status I–III
- Elective oral cancer surgery

- Predicted difficult airway (Mallampati III/IV, inter-incisor distance <3 cm, reduced neck extension <80°, or tumor obstructing glottic view)

Exclusion Criteria:

- Patient refusal, emergency surgery, drug allergy, severe cardiac disease (EF <30%), bradycardia (HR <50), hypotension (SBP <90 mmHg), severe hepatic/renal impairment, pregnancy, baseline SpO2 <90%, or BMI >35 kg/m²

Sample Size Calculation

Based on a pilot study (40% severe cough in fentanyl-midazolam group vs. 5% in dexmedetomidine group), with α=0.05 and power=80%, the minimum sample size was 16 per group. Accounting for 10% dropout, 18 patients per group (total N=36) were enrolled. G*Power software (version 3.1.9.7) was used

Procedure for Data Collection

After informed consent, 36 patients were randomly allocated to Group D (n=18) or Group FM (n=18) using computer-generated sequences and opaque sealed envelopes. The anesthesiologist performing intubation was blinded.

Standard ASA monitoring was applied. Topical anesthesia was standardized: 4% lignocaine nebulization (15 min), bilateral superior laryngeal nerve blocks (2 mL 2% lignocaine each), and 10% lignocaine spray.

Sedation administered:

- **Group D:** Dexmedetomidine 1 µg/kg IV over 10 min, then 0.5 µg/kg/hr infusion
- **Group FM:** Fentanyl 1 µg/kg + midazolam 0.03 mg/kg IV over 2 min (additional midazolam 0.5 mg allowed if Ramsay score <3)

Awake fiberoptic intubation was performed orally by a blinded anesthesiologist. Oxygen (4 L/min) was given via nasal prongs.

Data were recorded at baseline (T0), after sedation (T1), at intubation (T2), and 5 min post-intubation (T3). Outcomes measured included cough severity, patient comfort, operator satisfaction, Ramsay score, heart rate, mean arterial pressure, SpO2, and adverse events.

Statistical Analysis

Data were entered into a coded Microsoft Excel spreadsheet (2019) and analyzed using IBM SPSS Statistics version 25.0.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics

Parameter	Group D (n=18)	Group FM (n=18)	p-value
Age (years)	58.2 ± 9.4	60.1 ± 8.7	0.52
Sex (Male/Female)	12/6	13/5	0.71
BMI (kg/m²)	22.4 ± 3.1	23.1 ± 2.9	0.48
ASA status (I/II/III)	4/10/4	3/11/4	0.89
Mallampati class (III/IV)	11/7	10/8	0.74
Inter-incisor distance (cm)	2.8 ± 0.4	2.7 ± 0.5	0.51

A total of 36 patients (18 in Group D and 18 in Group FM) completed the study, and all data were included in the final analysis. Baseline demographic and clinical characteristics were comparable between groups, with no significant differences in age, sex, BMI, ASA status, Mallampati class, or inter-incisor distance (Table 1), confirming successful randomization.

Table 2: Primary Outcome – Intubation Conditions

Parameter	Group D (n=18)	Group FM (n=18)	p-value
Cough severity			0.03
None (0)	8 (44.4%)	3 (16.7%)	
Mild (1)	7 (38.9%)	6 (33.3%)	
Moderate (2)	2 (11.1%)	6 (33.3%)	
Severe (3)	1 (5.6%)	3 (16.7%)	
No/mild cough (0-1)	15 (83.3%)	9 (50.0%)	0.03
Patient comfort			0.04
Cooperative	17 (94.4%)	12 (66.7%)	
Restless	1 (5.6%)	5 (27.8%)	
Agitated	0 (0%)	1 (5.6%)	
Operator satisfaction (VAS 0-10)	8.9 ± 0.7	7.1 ± 1.2	0.01

Regarding the primary outcome of intubation conditions (Table 2), dexmedetomidine demonstrated significant superiority over fentanyl-midazolam. No or mild cough was observed in 15 patients (83.3%) in Group D compared to only 9 patients (50.0%) in Group FM (p=0.03). Patient cooperation was also better in Group D (94.4% cooperative) versus Group FM (66.7% cooperative) (p=0.04), and operator satisfaction was significantly higher in Group D (8.9 ± 0.7 vs. 7.1 ± 1.2, p=0.01).

Table 3: Secondary Outcomes – Hemodynamic Parameters

Time Point	Heart Rate (beats/min)		Mean Arterial Pressure (mmHg)	
	Group D	Group FM	Group D	Group FM
Baseline (T0)	78 ± 7	80 ± 8	90 ± 9	92 ± 10
After sedation (T1)	75 ± 8	82 ± 9	88 ± 8	90 ± 9
At intubation (T2)	82 ± 9	112 ± 10*†	94 ± 10	118 ± 12*†
5 min post-intubation (T3)	80 ± 8	95 ± 9*	92 ± 9	102 ± 10*

Hemodynamic parameters (Table 3) remained stable throughout the procedure in Group D, with heart rate ranging from 75 to 82 beats/min and mean arterial pressure from 88 to 94 mmHg. In contrast, Group FM showed a significant surge at intubation, with heart rate increasing from 80 ± 8 to 112 ± 10 beats/min and mean arterial pressure rising from 92 ± 10 to 118 ± 12 mmHg ($p<0.05$ vs. baseline and vs. Group D).

Table 4: Secondary Outcomes – Sedation and Oxygenation

Parameter	Group D (n=18)	Group FM (n=18)	p-value
Ramsay Sedation Score (target 3-4)	3.4 ± 0.5	3.2 ± 0.6	0.28
SpO2 nadir (%)	96.5 ± 1.8	91.2 ± 3.4	0.01
Desaturation (SpO2 <92%)	0 (0%)	5 (27.8%)	0.02
Need for supplemental oxygen/increased FiO2	0 (0%)	5 (27.8%)	0.02

Sedation scores were similar between groups (Ramsay score 3.4 ± 0.5 in Group D vs. 3.2 ± 0.6 in Group FM, p=0.28), indicating comparable sedation levels (Table 4). However, oxygenation was significantly better with dexmedetomidine: SpO2 nadir was 96.5 ± 1.8% in Group D versus 91.2 ± 3.4% in Group FM (p=0.01), and desaturation (SpO2 <92%) occurred in 5 patients (27.8%) in Group FM but in none (0%) in Group D (p=0.02).

Table 5: Adverse Events

Adverse Event	Group D (n=18)	Group FM (n=18)	p-value
Bradycardia (HR <50 bpm)	2 (11.1%)	0 (0%)	0.49
Hypotension (SBP <90 mmHg)	0 (0%)	0 (0%)	1.00
Apnea	0 (0%)	1 (5.6%)	1.00
Nausea/vomiting	0 (0%)	1 (5.6%)	1.00
Need for intervention (atropine/jaw thrust)	2 (11.1%)	5 (27.8%)	0.22

Adverse events (Table 5) were mild and manageable. Bradycardia occurred in 2 patients (11.1%) in Group D, responding to atropine, while no patient in Group FM developed bradycardia (p=0.49). Hypotension did not occur in either group. Apnea occurred in 1 patient (5.6%) in Group FM but none in Group D (p=1.00). The overall need for intervention was 11.1% in Group D versus 27.8% in Group FM (p=0.22). In summary, dexmedetomidine provided superior intubation conditions, better hemodynamic stability, and a lower risk of hypoxemia compared to fentanyl-midazolam.

DISCUSSION

The findings of this randomized controlled trial demonstrate that dexmedetomidine provides superior intubation conditions, better hemodynamic stability, and a lower risk of hypoxemia compared to the fentanyl-midazolam combination for awake fiberoptic intubation in patients undergoing oral cancer surgery. In the present study, 83.3% of patients in the dexmedetomidine group experienced no or mild cough during AFOI compared to only 50% in the fentanyl-midazolam group (p=0.03), and patient cooperation was significantly better with dexmedetomidine (94.4% vs. 66.7%, p=0.04). These findings are consistent with those reported by Bergese et al.,[6] who found that dexmedetomidine provided significantly better intubating conditions and patient tolerance compared to midazolam for AFOI. Similarly, a meta-analysis by He et al.[9] involving 589 patients concluded that dexmedetomidine reduced the incidence of moderate-to-severe coughing by nearly 60% compared to midazolam-based regimens.

Hemodynamic stability was another major advantage of dexmedetomidine. Patients in the fentanyl-midazolam group experienced a significant surge in heart rate (from 80 to 112 beats/min) and mean arterial pressure (from 92 to 118 mmHg) at intubation, whereas dexmedetomidine effectively blunted this sympathetic response with minimal hemodynamic changes. This finding aligns with the work of Kunisawa et al.,[11] who demonstrated that dexmedetomidine suppressed the hemodynamic response to fiberoptic intubation more effectively than fentanyl. This is particularly relevant in oral cancer patients who are often elderly with tobacco-related cardiovascular comorbidities, in whom tachycardia and hypertension can precipitate myocardial ischemia.

Perhaps the most clinically significant finding relates to respiratory safety. No patient in the dexmedetomidine group experienced desaturation (SpO2 <92%), whereas 27.8% of patients in the fentanyl-midazolam group developed hypoxemia requiring intervention (p=0.02). This underscores a major limitation of benzodiazepine-opioid combinations, which produce synergistic respiratory depression by acting on mu-opioid and GABA-A receptors in the brainstem. In contrast, a crossover study by Hsu et al.[8] confirmed that dexmedetomidine, even at high sedative doses, does not significantly depress minute ventilation. Both regimens achieved comparable sedation levels (Ramsay score 3.4 vs. 3.2, p=0.28), but the quality differed: dexmedetomidine produced calm, cooperative sedation, while some fentanyl-midazolam patients appeared restless or agitated. Bradycardia occurred in two patients (11.1%) in the dexmedetomidine group, which is consistent with the known dose-related effect of alpha-2 agonists and responded promptly to atropine. No patient in either group developed hypotension requiring intervention.

This study has several limitations. The sample size of 36 patients is modest, which may limit detection of rare adverse events. Being a single-center study with experienced operators, generalizability may be limited. We used a single fixed dosing regimen for each drug, and different doses might yield different results. Additionally, we did not measure recovery times, post-operative delirium, or patient recall. Finally, no placebo arm was included for ethical reasons.

Despite these limitations, our findings have important clinical implications. For anesthesiologists managing difficult airways in oral cancer patients, dexmedetomidine should be considered a first-line sedative agent for awake fiberoptic intubation, with the caveat that atropine should be readily available to manage potential bradycardia. Larger multicenter trials are warranted to confirm these findings and to explore recovery profiles and patient satisfaction outcomes.

CONCLUSION

Dexmedetomidine provides superior intubation conditions, better hemodynamic stability, and a lower risk of oxygen desaturation compared to the fentanyl-midazolam combination for awake fiberoptic intubation in oral cancer surgery. Dexmedetomidine should be considered a first-line sedative agent for this challenging airway scenario, with the caveat that atropine should be readily available to manage potential bradycardia.

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