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# Research Article
# Observational Study on the Effect of Propofol and Remifentanil Using Modified Topical Anaesthesia Method

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## Abstract

**Background and Objectives:** Topical anaesthesia (TA) is defined as blocking the nerve conduction which is reversibly surrounding the site of application. In this study, we observed the beneficial effect between propofol and remifentanil using modified topical anaesthesia. **Materials and Methods:** A total of 936 patients were categorized into three groups in the ratio of 1:1:1 (312:312:312) and classified based on ASA grading. The three groups were administered with propofol (Group-I), remifentanil (Group-II) and propofol-remifentanil cocktail (Group-III) and proceeded for a modified Awake Fiberoptic Intubation (AFOI) and evaluated for airway assessment and clinical outcome. **Results:** No statistically significant difference was observed based on the coughing and limb motion scores. The mean time for tracheal intubation was 589.3±5.7 sec for Group-I compared to 581.2±4.5 sec for Group-II and 603.7±3.9 sec for Group-III. Fourteen patients (4.49%) of Group-I were observed with severe airway obstruction scores compared to 8 patients (2.56%) of Group-II and 11 patients (3.53%) of Group-III. Group-II patients also scored favourable postoperative episodes without any issues and complicacy. Overall Group-II patients (remifentanil) attained satisfactory and successful airway management compared to Group-I and Group-III patients. **Conclusion:** The study concludes that the infusion of remifentanil with modified topical anaesthesia resulted in more successful and satisfactory airway management and intubating conditions compared to propofol.

Key words: Awake fibreoptic, awake intubation, remifentanil, propofol, tracheal intubation, airway management, topical anaesthesia

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

## INTRODUCTION

The major role of topical anaesthesia is to block nerve conduction which is reversibly surrounding the site of application. A topical anaesthetics drug usually targets the free peripheral nerves of the mucosa and inner layer of the skin causing a short term loss of sensation near the site of application[1]. It is becoming common in numerous surgical operations due to the belief that local anaesthesia requires painful injection[2]. Topical anaesthesia is also preferred by patients who have fears for needle injection and dermal complicacy[3]. However, during local anaesthesia, the risk of serious morbidity and complicacy associated with airway management remains a key issue[4]. Thus, there is an ultimate requirement for the use of Awake Fibreoptic Intubation (AFOI) among those cases that deals with difficult airway management[5]. Awake intubation can be carried out effectively during a difficult airway because a briefed airway evaluation is taking a longer duration and is not possible in case of an emergency. However, it is important to consider AFOI if the equipment and expertise are readily available[6]. The AFOI is the standard of care for difficult airway management and the success rate of AFOI usually depend on the experience of the intubating expertise and behaviour of the patient[7]. The most successful and accepted procedure for performing AFOI is using the flexible fiberoptic scope by nasal intubation or oral approach[8]. The main requirements for this technique depend on the proper preparation of the patient and good maintenance of patient safety. Several drugs have been utilized to provide sedation for this procedure which includes propofol, remifentanil, ketamine and dexmedetomidine etc.[9,10]. The AFOI is also preferred by patients who have anxiety for airway difficulty[11]. It is also reported that 7-8% of patients undergoing surgical procedures faced difficult airways which had to be managed by conventional airway management ultimately[12]. In addition, patients who have severe conditions or high-risk factors require securing the airway before the induction anaesthesia to prevent any potential complications. Hence, AFOI is generally preferred based on the nature and type of the injury[11]. On the other hand, good topical anaesthesia is associated with a successful awake fibreoptic intubation management on a patient. Therefore, there is a direct correlation between TA and AFOI in which both are important procedures for harbouring an effective airway management[13]. However, there are certain disadvantages of TA procedures and therefore a modified method or procedure is required, which involves the application of an epidural catheter on the suction channel through the fiberoptic bronchoscope. This modification will make it easier for spraying the lidocaine/prilocaine through the vocal cord comfortably. Previous studies have reported the efficacy of propofol and remifentanil separately as an intravenous analgesic in preparation of the patient for unpleasant and painful procedures[14,15]. However, the anaesthetic effect of remifentanil and propofol was never compared using modified topical anaesthesia. The study aims to compare the effectiveness of propofol and remifentanil separately and as a mixture of both by using a modified topical anaesthesia method.

## MATERIALS AND METHODS

**Study area:** The study was carried out at the Department of Anesthesiology, The General Hospital of Central Theater Command of People's Liberation Army, Wuhan, Hubei 430000, China from September, 2018 to October, 2021. All the investigations and operating protocols were carried out between September, 2018 to October, 2021.

**Ethical approval:** Ethical approval was obtained from the Medical Ethical Research Board vide Approval No. AKT/28472-65C provided all the procedures and experiments were carried out following the Declaration of Helsinki and its later amendments. Both verbal and written consent was obtained from all participants.

**Patients:** A total of 936 patients including male and female were selected for this investigation who were admitted to the hospital from September, 2018 to October, 2021. The patients were selected based on the grading of ASA (American Society of Anesthesiologists) and only patients who were classified as ASA grade I and ASA grade II were chosen. The age of patients ranges from 26-58. All the patients were screened for sugar test (diabetes), heart disease (cardiovascular complications), blood pressure (hypertension), kidney function test (renal disorder) etc and found to be free from these complications.

**Intubation of the patients:** All intubation procedures were carried out in the standard operating room and scheduled from 9:00 am to 1:00 pm in a quiet environment to evade circadian rhythm influence. The 936 patients were divided into three groups in the ratio of 1:1:1 (312:312:312) viz. Group-I (propofol), Group-II (remifentanil) and Group-III (Both propofol and remifentanil). For Group A, 1.2 mg propofol, 1 mcg of remifentanil for Group B and Group C, 0.5 mg/0.6 mcg propofol-remifentanil was prepared according to their BMI for intravenous administration. Apart from the regular screening, the mean arterial pressure (MAP), heart rate and

hemodynamics were measured again in the standard operating room at the time of intubation, during the initiation of the operation and at the time of extubation. All the data were recorded which includes MAP, $SPO_2$, hemodynamics, heart rate, electrocardiogram and respiratory rate. Preoperative assessment was carried out for extensive airway examination and laryngoscopy procedure was evaluated based on modified SARI score (Simplified Airway Risk Index). The score point ranges from 0-12 wherein a higher point number denotes a difficult airway. The modified SARI score implemented in the patients of this investigation consists of (i) Mouth opening [<4 cm], (ii) Thyromental distance [<6.5 cm], (iii) Prognathism ability, (iv) Mallampati score, (v) Neck movement [<90°] (vi) Body weight [>90 kg], (vii) Prognathism and (viii) Previous intubation history.

**Induction of anaesthesia:** Group-I patients were given 1.2 mg of propofol mixed with 22 mL of 1% saline using a 25 mL syringe. Group-II patients were given 1 mcg of remifentanil mixed with an initial bolus injection of 1 mcg. Whereas, Group-III patients were given 0.5 mg/0.6 mcg propofol-remifentanil with or without initial bolus injection. Group-I patients were maintained with a 0.6 μg $kg^{-1}$ loading dose of propofol infused 0.1 μg $kg^{-1}$ for 8 min. Group-II patients were maintained with 0.5-1 mcg of remifentanil with not more than 8-10 min and slow bolus injections which is given after 2-5 min. Group-III patients were maintained with 3 mg/0.4 mcg propofol-remifentanil with or without bolus injection for another 8-10 min. All patients of the three groups were continuously observed for any requirement of inadequate anaesthesia and checked for low blood pressure. For modified topical anaesthesia, lidocaine/prilocaine was sprayed to the patients of all three groups via their mouth before swallowing which is further maintained with 1% lidocaine/prilocaine mixture in the throat by a catheter. Furthermore, topical anaesthesia was administered using a flexible fiberoptic bronchoscope and lidocaine/prilocaine was sprayed beneath the vocal cords via the larynx.

**Clinical outcome and assessment:** The clinical outcome was measured based on the Intubation Score (1: No cough, 2: Slight cough, 3: Mild cough and 4: Severe cough), Limb motion (1: No movement, 2: Slight movement, 3: Mild movement and 4: Severe movement). Furthermore, the tolerance was measured based on fiberoptic intubation comfort score (1: No facial reaction, 2: Slight facial reaction, 3: Mild facial reaction, 4: Severe facial reaction and 5: Very severe facial reaction). Another three-point scale measurement was applied to assess the Tracheal Intubation Score (1: Interactive, 2: Nervousness with mild resistance and 3: Extreme resistance which requires immediate GA). The airway obstruction score was also measured and scored as 1: Normal airway, 2: With obstruction that can be relaxed and 3: With obstruction that needs jaw retraction.

**Statistical analysis:** Statistical analysis was carried out using GraphPad 6.01 (Prism, LA, California, USA). Sedation parameters are expressed as Mean±SE based on the comparison between the three groups using $\chi^2$ test. Whereas, age, weight, height and BMI are expressed as Mean±SD. Patient reaction, intubation scores and adverse events were expressed as frequency and percentages. A p-value of <0.05 was taken as statistical significant.

## RESULTS

There was no statistically significant variation in the baseline characteristics of the total 936 enrolled patients based on age, sex, height, weight and BMI. There were no variations at all in the ASA status and modified SARI score which determines the overall risk for tracheal intubation (Table 1). Table 2 presents the assessment analysis score of the participants based on successful fiberoptic intubation. There was no significant variation statistically based on the coughing and limb motion scores among the three groups (Table 2). All the 936 enrolled patients accomplished the fiberoptic intubation. However, 15 patients (4.81%) of Group-I were obliged to rescue infusion for bringing back to their conscious state. Whereas, 6 patients (1.92%) and 11 patients (3.53%) were obliged to rescue infusion for Group-II and Group-III, respectively (Table 2). Group-I patients attained a mean time of 589.3±5.7 sec for tracheal intubation compared to 581.2±4.5 sec for Group-II and 603.7±3.9 sec for Group-III (Table 2). Hence, it was revealed that Group-II patients had the lowest tracheal intubation time compared to the other two groups. However, the State entropy and RSS at intubation were observed to be almost similar. Table 3 represents the assessment analysis of adverse events of the three groups of patients. Fourteen patients (4.49%) of Group-I were observed with a severe airway obstruction score of 3 on a 3-point scale compared to 8 patients (2.56%) of Group-II and 11 patients (3.53%) of Group-III (Table 3). Whereas, 10 patients (3.21%) of Group-I occurred transient hypoxia compared to 6 (1.92%) of Group-II and 9 patients (2.88%) of Group-III (Table 3) with SpO2 level between 85-89%. The respiratory rate of Group-I was observed to be the lowest with a mean rate of 10±2.4 bpm compared to 14±1.8 bpm of Group-II and 12±2.1 bpm of Group-III. However, no severe complications

Table 1: Baseline data of the enrolled patients

| Characteristics | Group-I Propofol | Group-II Remifentanil | Group-III Both Prop-Remi |
|---|---|---|---|
| N | 312 | 312 | 312 |
| Age (years) | 48.3±3.2 | 49.5±5.8 | 51.8±2.6 |
| Female | 162 (51.92%) | 164 (52. 56%) | 159 (50.96) |
| Weight (kg) | 59.51±3.1 | 61.45±2.1 | 60.32±6.12 |
| Height (cm) | 164.4±3.8 | 166.9±2.7 | 165.2±4.1 |
| BMI (kg $m^{-2}$) | 22.9±0.8 | 23.1±1.4 | 23.2±0.6 |
| ASA status | 1.6±0.1 | 1.6±0.2 | 1.6±0.1 |
| Modified SARI | 4.2±0.2 | 4.2±0.1 | 4.2±0.3 |
| **Smoking status** | | | |
| Smoker | 131 (41.99%) | 122 (39.10%) | 126 (40.38%) |
| Non-smoker | 181 (58.01%) | 190 (60.90%) | 186 (59.62%) |
| **Drinking status** | | | |
| Drinker | 109 (34.94%) | 98 (31.41%) | 103 (33.01%) |
| Non-drinker | 203 (65.06%) | 214 (68.59%) | 209 (66.99%) |

Table 2: Assessment of intubation score based on the modified awake fiberoptic intubation protocol

| Intubation scores | Group-I (n (%)) Propofol | Group-II (n (%)) Remifentanil | Group-III (n (%)) Both |
|---|---|---|---|
| N | 312 | 312 | 312 |
| **Coughing scores** | | | |
| 1 | 163 (52.24%) | 168 (56.38%) | 164 (52.56%) |
| 2 | 104 (33.33%) | 97 (32.55%) | 108 (34.62%) |
| 3 | 34 (10.90%) | 28 (9.40%) | 32 (10.26%) |
| 4 | 11 (3.53%) | 5 (1.68%) | 8 (2.56%) |
| **Limb motion scores** | | | |
| 1 | 151 (48.40%) | 169 (54.17%) | 157 (50.32%) |
| 2 | 101 (32.37%) | 96 (30.77%) | 108 (34.62%) |
| 3 | 46 (14.74%) | 42 (13.46%) | 36 (11.54%) |
| 4 | 14 (4.49%) | 5 (1.60%) | 11 (3.53%) |
| Intubation time (sec) | 54.8±2.3 | 48.7±1.2 | 52.6±3.1 |
| Drug requirements (μg $kg^{-1}$) | 0.82 | 1 | 0.95 |
| RSS at intubation | 2.4 ±0.3 | 2.5±0.1 | 2.6±0.4 |
| State entropy at intubation | 88.6±2.8 | 87.5±1.5 | 88.4±2.2 |
| Rescue requirement for consciousness | 15 (4.81%) | 6 (1.92%) | 11 (3.53%) |
| Time to tracheal intubation (sec) | 589.3±5.7 | 581.2±4.5 | 603.7±3.9 |

Table 3: Assessment of adverse events based on the modified awake fiberoptic intubation protocol

| Adverse event | Group-I (n (%)) Propofol | Group-II (n (%)) Remifentanil | Group-III (n (%)) Both |
|---|---|---|---|
| N | 312 | 312 | 312 |
| **Airway obstruction score** | | | |
| 1 | 216 (69.23%) | 241 (77.24%) | 232 (74.36%) |
| 2 | 84 (26.92%) | 65 (20.83%) | 72 (23.08%) |
| 3 | 14 (4.49%) | 8 (2.56% ) | 11 (3.53%) |
| Hypoxia (n (%)) | 10 (3.21%) | 6 (1.92%) | 9 (2.88%) |
| Respiratory rate (bpm) | 10±2.4 | 14±1.8 | 12±2.1 |

were reported from the patients of all the three groups with a SpO2 level of 85-92%. Table 4 represents the characteristics of the postoperative adverse events. Topical anaesthesia recall rates were 250 (80.13%), 267 (85.58%) and 259 (83.01%) for Group I, II and III respectively. Hence, it is revealed that Group-II had a higher recall rate compared to the other two groups (Table 4). Additionally, Group-II also had a higher endoscopy recall with 202 (64.74%) patients compared to 189 (60.58%) of Group-I and 195 (62.50%) of Group-III (Table 4). Based on the sore throat score and hoarseness rate, Group-II patients were observed with more favourable and satisfactory postoperative scores (Table 4). The patients of Group-II scored overall favourable postoperative episodes without any issues and complicacy.

Table 4: Characteristics of postoperative assessment

| Follow-up parameters | Group-I (n (%)) Propofol | Group-II (n (%)) Remifentanil | Group-III (n (%)) Both |
|---|---|---|---|
| Sore throat (n (%)) | 82 (26.28%) | 66 (21.15%) | 72 (23.08%) |
| Hoarseness (n (%)) | 29 (9.29%) | 18 (5.77%) | 21 (6.73%) |
| Satisfaction score (1-4) | 2 | 2 | 2 |
| Recall of topical anesthesia (n (%)) | 250 (80.13%) | 267 (85.58%) | 259 (83.01%) |
| Recall of endoscopy (n (%)) | 189 (60.58%) | 202 (64.74%) | 195 (62.50%) |
| Recall of intubation (n (%)) | 86 (27.56%) | 97 (31.09%) | 90 (28.85%) |

## DISCUSSION

The present investigation involved the observational study on the effect of propofol and remifentanil using a modified topical anaesthesia method. The results demonstrate that the use of remifentanil resulted in a significant reduction of recovery time with effective anaesthetic induction compared to propofol and propofol-remifentanil mixture. The process of modified topical anaesthesia in this study includes diffusing the drugs into the airways viz., propofol and remifentanil with the help of a FOB suction tube using a fine catheter[16]. The advantage of topical anaesthesia is that it acts on the periphery of the nerves thereby reducing the impact of the pain on the patient[17]. Topical anaesthesia usually alters the pain limit by controlling its sensation by blocking the transmission signals from the sensory nerve fibers[2]. Topical anaesthesia is used increasingly and gained popularity as reported by the American Society of Cataract and Refractive Surgery in their annual survey of the practice styles and preferences[18]. Moreover, the modified protocol in this study helps prevent the injections such as Trans-Cricothyroid Membrane Injection and open airway injections which is favourable for patients with ENT issues and complications[19]. In this observational study, Group-II patients administered with remifentanil had a superior intubation score using the modified protocol compared to those patients administered with propofol (Group-I) and propofol-remifentanil mixture (Group-II). This unveiled the beneficial effect and favourable scores of remifentanil based on coughing scores, limb motion Scores, intubation time and state entropy. Remifentanil is a powerful analgesic and a potent μ-opioid receptor agonist which possessed poor hypnotic properties with a lesser effect on cognitive function[20]. On the other hand, propofol is thought to possess a stronger hypnotic property which may cause a rapid loss of consciousness by impacting the GABA receptors[21]. In this study, lidocaine/prilocaine was sprayed through the translaryngeal intubation with the help of an epidural catheter. Lidocaine/prilocaine was also applied on-site by injecting via the cricothyroid membrane through the proximal site. However, it is necessary to remain alert of the expertise to observe the conscious state and sedation of the patients since the modified AFOI requires the patient to be calm and co-operative[5]. A similar procedure of modified topical anaesthesia on the application of epidural catheter for effective airway management was reported by Madan *et al.*[22]. The effectiveness of remifentanil over other anaesthetic agents such as propofol, ketamine, midazolam, etc., has been reported by Feldman *et al.*[23]. Remifentanil is reported with improved patient comfort in the ICU and various investigators also reported on the potential role of remifentanil over critically ill and serious neurotrauma patients[20]. This may be due to the unique pharmacological characteristics of remifentanil that showed advantageous among neurotrauma cases, renal dysfunction, chronic obstructive pulmonary disease etc.[24]. However, in the case of propofol, it is different with limiting analgesic characteristics. In the present study, no significant difference was observed between the three groups based on heart rate and blood pressure. In Group-I, 15 patients were observed with SpO2 level >90% compared to 5 patients of Group-II and 9 patients of Group-III. However, no severe complications were reported from all the patients. Thus, it showed the efficacy of remifentanil over propofol by using modified AFOI. Finally, the post-operative assessment also scored an overall favourable score for the patients administered with remifentanil (Group-II) without any issues and complicacy compared to the other two groups.

## CONCLUSION

This investigational study revealed that the infusion of remifentanil with modified topical anaesthesia resulted in successful and satisfactory airway management and intubating conditions. Remifentanil appears to be a safe method of providing sedation for awake fibreoptic intubation in the difficult airway. However, further evaluation of this modified technique is warranted.

## SIGNIFICANCE STATEMENT

The study discovered that remifentanil provides successful and satisfactory airway management and intubating conditions in difficult airway management. Thus remifentanil is beneficial for patients which have difficult airway management issues and complicacy.

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