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Original Research Article

Comparison of the safety and efficacy of propofol and dexmedetomidine as sedatives when used as a modified topical formulation

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Abstract

Purpose: *To evaluate the safety and efficacy of propofol and dexmedetomidine as sedatives in patients with anticipated difficult airways, used as a modified topical preparation.*
Methods: *A total of 432 patients were enrolled in this study. They were classified as ASA I and ASA II. The patients were equally divided into group A (propofol group) and group B (dexmedetomidine group). A modified Awake Fiberoptic Intubation (AFOI) was carried out for these patients, followed by airway assessment and evaluation of clinical outcome based on intubation scores, adverse events, and postoperative data.*
Results: *Patients in both groups had successful intubation at the first attempt. There was no significant difference in baseline characteristics between the two groups. The SARI scores which characterized the overall score for tracheal intubation were 4.6 and 4.2 for groups A and B, respectively. With respect to rescue infusion and consciousness, 11 patients (5.09 %) in group A required rescue, as against 5 patients (2.31 %) in group B. Seven (7) patients (3.24 %) in group A (propofol group) had severe airway obstruction, while only 4 patients (1.85) in group B had the same adverse reaction. Patients in group B had more satisfactory and favourable outcomes than those in group A who were treated with modified AFOI.*
Conclusion: *The use of dexmedetomidine based on modified topical anaesthesia is safe and comfortable in terms of patient convenience and difficult airway management. Thus, dexmedetomidine is a safe, feasible and effective method for managing difficult airway when applied using the modified AFOI.*

Keywords: *Dexmedetomidine, Propofol, Topical anaesthesia, Fiberoptic Intubation*

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INTRODUCTION

Topical anaesthesia refers to superficial loss of sensation due to direct application of local anaesthetic solutions and sprays [1]. It is widely used in numerous surgical procedures, and it has become a routine clinical practice because many people consider local anaesthetic injections painful [2]. Topical anaesthesia is also preferred among patients who have concerns for

needle and tissue oedema [3]. The mechanism of action of a topical anaesthetic agent is that it causes reversible blockage of nerve conduction near the site of application, thereby creating a temporary loss of sensation on that site [4]. On the other hand, fiberoptic intubation (FOI) is often regarded as the standard for difficult airway management because it can be easily applied, irrespective of whether the patient is awake or asleep. Fiberoptic intubation is usually performed when the patient is awake in order to preserve the respiratory drive of the patient and conserve ventilation [5]. On the other hand, awake FOI (AFOI) is achieved using nasal or oral spray to sedate and numb the airways. Awake Fiberoptic Intubation is used more often because the route is shorter, and larger endotracheal tubes (ETTs) can be used, thereby avoiding epistaxis.

Awake Fibreoptic Intubation (AFOI) is mostly recommended for patients with expected difficult airways [6]. In fact, about 6 % of the population of patients have difficult airways which are managed in most cases using a conventional method such as bougie airway management [7]. Moreover, there is need for securing the airways of patients who have serious conditions and high risk of complications before anaesthesia induction or awake intubation, in order to avoid any potential complication such as failed mask ventilation [8]. Therefore, Awake FOI and awake tracheostomy are increasingly preferred, based on the nature and location of the lesion. Thus, there is a direct relationship between topical anesthesia and the AFOI sedation technique which is a crucial procedure for sustaining the airway management of the patient [9]. In addition, good topical anaesthesia often leads to successful AFOI. The technique of thyrocricocentesis is useful, but it has disadvantages among subjects with tumors and neck infection [10]. Therefore, there is need for a modified technique or method that involves the application of an epidural catheter on the suction channel of the fibreoptic bronchoscope. This will help to comfortably spray the lidocaine through the epidural catheter beneath the vocal cord.

For a successful modified AFOI, the most favorable conditions for the patient are that it should result in comfortable and blunted airway reflexes. Till date, various agents are such as propofol, ketamine, sevoflurane and dexmedetomidine are utilized for AFOI sedation [11]. Dexmedetomidine and propofol are widely used, and their adverse effects require evaluation. Dexmedetomidine is an anxiolytic drug which acts as an agonist of α2-adrenergic receptors in the brain. It is used for sedation and pain relief [12]. In contrast, propofol is an anaesthetic agent frequently used for sedation in general anaesthesia during various surgical procedures.

In fact, different protocols have resulted in successful sedation, thereby increasing success rate. The present study was carried out to compare propofol and dexmedetomidine among patients with an anticipated difficult airway, with respect to safety and efficacy of sedation using the modified topical anaesthesia method.

METHODS

Ethical approval

Ethical approval for this study was granted by the Research and Review Board of National Medicine Gezhouba Central Hospital, China. Written informed consent was obtained from all participants. The study was conducted from July 2016 to March 2021. All experiments were carried out in accordance with the Declaration of Helsinki and its later amendments.

Patients

A total of 432 participants who went through a modified AFOI, followed by an airway assessment from July 2016 to March 2021, were enrolled in this study. The patients were considered eligible for enrolment only if they were classified under American Society of Anaesthesiologists' grade 1 and grade II. The study included only patients within the age group of 25 - 55 years who were free from diabetes, hypertension, cardiovascular disease, and renal dysfunction. Patients older than 55 years or younger than 25 years were excluded from the study. Pregnant women and patients who requested/opted for nasal intubation were also excluded.

Intubation procedure

The drug administration process was carried out in the operating room in a calm environment. The patients were equally assigned to two groups: group A (propofol group) and group B [dexmedetomidine (Dex) group]. The study drugs propofol (1 mg) and Dex (200 μg) were prepared for intravenous (*i.v.*) application based on the body weights and BMIs of the patients. The patients were subjected to preoperative assessment, and extensive examination of the airway was carried out. Furthermore, laryngoscopy and intubation procedure were assessed based on a simplified airway risk index (SARI) score which is a multivariate risk score

for predicting difficult tracheal intubation. The SARI score used in the present assessment consisted of information from the patients regarding mouth opening, thyromental distance, Mallampati classification, neck mobility, body mass index (kg/m^2), prognathism potential, weight, thyromental distance, and history of difficult intubations. The airway administration was managed by two experienced anaesthesia staff of the hospital, while the fibreoptic intubation and the drug infusion were performed by two senior residents. All follow-up data on MAP, electrocardiogram, SPO_2 level, and respiratory rate were obtained and recorded.

Drug administration and anaesthesia

Group A patients were administered anaesthesia with 1 mg propofol mixed with 20 mL of saline (0.8 %) using a 25-mL syringe, whereas 2 mL of Dex was mixed with 48 mL saline (0.8 %) and administered to group B patients using a 50 mL syringe. Group A patients were administered propofol at a loading dose of 0.75 µg/k at an infusion rate of 0.15 µg/kg/min for 7 min. This was continued at an infusion rate of 0.1 µg/kg/min. Group B patients were administered Dex at loading dose of 1 µg/kg which was infused at a rate of 0.3 µg/kg/h for 12 min. For topical anaesthesia, the patients were administered lidocaine through the oral route. This was followed by administration of 5 mL of 2 % lidocaine the buccal cavity and throat using a catheter. Thereafter, a very fine plastic catheter was threaded via the controlled suction of the flexible TOOL. At this stage, the modified topical anaesthesia procedure was performed in which a 4-cm flexible fibreoptic bronchoscope was inserted and used to spray the lidocaine through the fine plastic catheter via the larynx which comprised the vocal cords.

Assessment of anaesthesia

The Ramsay Sedation Scale (RSS) was used to assess the level of sedation. The patients were administered 1.5-2 mg of ketamine if the RSS score was < 2. In both groups, drug infusion was stopped if the intubation was successful. Anaesthesia induction was done by administering 1.5 -2.0 mg of ketamine (*i.v.*) maintained with 3 - 4 µg/kg fentanyl (*i.v.*) along with isoflurane (1 – 2 %) and vecuronium (1 mg/kg, *i.v.*) for muscle relaxation. Fibreoptic intubation was applied until the sedation scale was higher than two scores or above, otherwise the endotracheal tube was placed which was verified using capnography.

Assessment of clinical outcomes

The primary outcomes were based on the following:

(a) *Intubation score*: This was based on assessment of coughing which was scored 1 (no cough), 2 (mild cough), 3 (moderate cough) or 4 (severe cough).

(b) *Limb movement*: This was scored 1 (no movement), 2 (mild movement), 3 (moderate movement) or 4 (intensive movement).

(c) *Pain tolerance*: This was assessed based on comfort in fibreoptic intubation which was scored 1 (no facial reaction), 2 (slight facial reaction), 3 (moderate facial reaction), 4 (heavy facial reaction) or 5 (defensive posture using head or limbs).

(d) 3-point assessment after the tracheal intubation: This was scored 1 (cooperative), 2 (minimal resistance) or 3 (severe resistance with the immediate requirement of GA).

(e) Other anaesthetic parameters linked with modified AFOI, which included the level of consciousness.

(f) *Airway obstruction*: This was scored 1 (patient airway), 2 (obstruction which could be relieved by extension of neck) or 3 (obstruction which required retraction of the jaw).

Moreover, hypoxic episode (SpO_2 < 90 %) and requirement of rescue doses of adrenaline for consciousness, were recorded. Post-operative visit was carried out on the next day after the operation in order to assess memory recall, pre-anaesthetic preparations, adverse events and satisfaction scores of the patients.

Statistical analysis

SPSS 170.0 package (SPSS Inc, Chicago, IL, USA) was utilized for statistical analysis. Numerical variables such as age, weight, height, and BMI are expressed as mean ± standard deviation (SD). Pain reaction in patients, intubation scores, and adverse events are expressed as frequency and percentages [n (%)].

The baseline characteristics of groups A and B were compared using Chi square (χ^2) test. A p value < 0.05 was considered statistically significant.

RESULTS

There were no significant differences in data between groups A and B (Table 1). None of the patients had a previous episode of anaesthesia administration. The SARI score was 4.6 ± 0.6 for group A, and 4.2 ± 0.3 for group B. SARI score was used as index of the general score on individual risk for tracheal intubation.

Table 1: Baseline characteristics of the enrolled patients

Characteristics	Group A (Propofol)	Group B (Dexmedetomidine)
Age (years)	52.3 ± 6.1	54.8 ± 7.2
Female	116 (53.70 %)	112 (51.85 %)
Weight (kg)	62.4 ± 5.6	64.3 ± 4.5
Height (cm)	167.3 ± 2.6	169.2 ± 3.2
BMI (kg/m^2)	22.8 ± 1.2	23.4 ± 2.1
ASA status	1.6 ± 0.3	1.6 ± 0.2
Modified SARI	4.6 ± 0.6	4.2 ± 0.3
Smoking status		
Smoker	91 (42.13 %)	87 (40.28 %)
Non-Smoker	125 (57.87 %)	129 (59.72 %)
Drinking status		
Drinker	79 (36.57 %)	74 (34.26 %)
Non-drinker	137 (63.43 %)	142 (65.74 %)

The results of assessment of success of fibreoptic intubation are shown in Table 2. In both groups, all patients had successful fibreoptic intubation. Eleven patients (5.09 %) in group A (propofol group) required rescue infusion for consciousness, relative to five patients (2.31 %) in group B (Dex group). The mean duration of tracheal intubation before attaining sedation was 596.4 ± 3.1 sec in group A patients, whereas it was 664.3±2.6 in group B patients. Thus, the time taken before tracheal intubation was shorter in group A patients than in group B patients. As also shown in Table 2, with respect to cough reflex, patients in group B (Dex) had more successful intubation in the course of inserting the endoscopy, than those in group A (propofol). There were no marked differences between the two groups with respect to RSS score, response entropy, intubation time, and movement scores. Seven patients (3.24 %) in group A (propofol group) and four patients (1.85 %) in group B (Dex group) experienced severe airway obstruction, with airway obstruction score of 3, as shown in Table 3. In group A, eight patients (3.70 %) developed transient hypoxia, while five patients (2.31 %) had transient hypoxia in group B. There was no statistically significant difference in SpO_2 levels (range: 87-91 %) between the two groups.

Table 2: Intubation score based in the modified AFOI protocol

Intubation score	Group A (n= 216), n (%)	Group B (n= 216), n (%)
Cough scores		
1	110 (50.93)	118 (54.63)
2	78 (36.11	80 (37.04)
3	21 (9.72)	16 (7.41)
4	7 (3.24)	2 (0.93)
Movement Scores		
1	101 (46.76)	114 (52.78)
2	72 (33.33)	78 (28.8)
3	34 (15.74)	21 (15.5)
4	9 (4.17)	3 (4.4)
Intubation time, sec	55.3 ± 4.1	49.5 ± 3.3
Drug requirements, µg	0.75 µg/kg	1 µg/kg
RSS at intubation	2.3 ± 0.4	2.6 ± 0.5
State entropy at intubation	87.3 ± 1.4	88.4 ± 2.3
Rescue requirement for consciousness	11 (5.09)	5 (2.31)
Time to tracheal intubation, sec	596.4 ± 3.1	664.3±2.6

However, as shown in Table 3, the mean respiratory rate of group A was 11 ± 1.5 bpm, while that of group B was 13 ± 2.1 bpm. In fact, two patients in group A had their respiratory rate reduced to 9 bpm. However, there were no severe complications during the AFOI procedures in both groups. Moreover, there were no statistical differences in pulse rate and mean arterial pressure (MAP) between group A and group B.

Table 3: Assessment of adverse events based in the modified AFOI protocol

Adverse event	Group A (n= 216)	Group B (n= 216)
Airway obstruction score		
1	155 (71.76)	169 (78.24)
2	54 (25.0)	43 (19.91)
3	7 (3.24)	4 (1.85)
Hypoxia, n (%)	8 (3.70)	5 (2.31)
Respiratory rate, bpm	11 ± 1.5	13 ± 2.1

Results from postoperative monitoring showed only slight variations in adverse events between the two groups. Withdrawal of topical anaesthesia, endoscopy, and intubation occurred in 179 (82.87 %), 127 (58.80 %), and 58 patients (26.85 %), respectively in group A (propofol), relative to 190 (87.96 %), 137 (63.43 %) and 70 (32.41 %) patients respectively in group B. These data are shown in Table 4.

Overall, patients in group B (Dex group) had more satisfactory postoperative scores than those in group A (propofol group).

Table 4: Characteristics of postoperative episodes

Follow-up variable	Group A (n= 216) (Propofol)	Group B (n= 216) (Dexmedetomidine)
Sore throat {n (%)}	54 (25.0)	49 (22.69)
Hoarseness {n (%)}	16 (7.41)	11 (5.09)
Satisfaction score (1-4)	2	2
Recall of topical anesthesia {n (%)}	179 (82.87)	190 (87.96)
Recall of endoscopy {n (%)}	127 (58.80)	137 (63.43)
Recall of intubation {n (%)}	58 (26.85)	70 (32.41)

DISCUSSION

The present study investigated the safety and clinical efficiency of propofol and dexmedetomidine as sedatives using the modified topical anaesthesia and AFOI. The drugs were dispersed into the airways using a fine plastic catheter via FOB suction tube [13]. Indeed, the modified procedure eliminates cricothyroid membrane injections and open airway injections, making it beneficial for patients with neck cancers and ear, nose and throat infections [14].

In the present investigation, patients given dexmedetomidine had more favourable scores than those given propofol, with respect to coughing assessment. The present investigation focused on the comparative efficacy of propofol and dexmedetomidine with regard to modified AFOI. In fact, dexmedetomidine produced desirable intubation scores with respect to coughing. There were no significant differences between the two groups with respect to other factors such as Ramsay Sedation Scale and state entropy at intubation. Cabrini *et al* reported a similar application of modified topical anaesthesia of epidural catheter which proved to be an effective airway topical anaesthesia [15]. However, in this case, an epidural catheter was applied for trans-laryngeal spraying of lidocaine. Moreover, lidocaine was spread by injection through the cricothyroid membrane via coughing. In both situations, the case proximal site was selected for airway management. It is also quite important to achieve conscious sedation because in AFOI, it is necessary for the patient to remain cooperative and relaxed [16]. There are reports on the effectiveness of several anaesthetic agents such as propofol, dexmedetomidine, ketamine, sevoflurane and midazolam. In most of the reports, dexmedetomidine was shown to be more effective than any of the other agents [17,18]. There are also studies that reported intense analgesic characteristics of dexmedetomidine, with favourable airway management and little effect on cognitive process, all of which make it an effective agent for sedation using AFOI [19,20]. In contrast, propofol has certain limitations, especially with respect to its analgesic characteristics [21]. Moreover, Mondal *et al* reported that dexmedetomidine and other topical anaesthetics produce tremendous benefit for AFOI based on the conditions of intubation, ease of intubation, and hemodynamic parameters [22].

In this study, the intubation time for group B patients (49.5 ± 3.3 s) was slightly shorter than that of group A patients (55.3 ± 4.1 s). This was due to the fact that differences in mechanism of action between dexmedetomidine and propofol impacted the sedation. In another study by Xu *et al*, the use of a lower loading dose of dexmedetomidine resulted in insufficient sedation for AFOI in the first attempt [23]. In contrast, in the present study, a higher loading dose of dexmedetomidine (1 µg/kg over 12 min) was administered, and this was followed with a lower infusion dose (0.3 µg/kg/h). There was no statistical significance in hemodynamic stability between the two groups during the intubation period, as evidenced from the MAP and pulse rate.

The SpO_2 values of 10 patients in the propofol group were less than 90 %, whereas only 3 patients in the dexmedetomidine group had SpO_2 level less than 90%. Thus, these findings indicate higher clinical efficacy of dexmedetomidine over propofol, using modified AFOI. However, the level was easily overcome by force inspiration in both groups. There were no significant differences in hoarseness and sore throat between the two groups during intubation and postoperative periods. Moreover, the state entropy scores at intubation between group A (propofol) and group B (dexmedetomidine) showed similar levels of consciousness. However, postoperative infusion of the patients revealed a more favourable score for group B than for group A, with regard to the withdrawal of topical anaesthesia (82.87 vs. 87.96 %), recall of endoscopy (58.80 vs. 63.43 %), and recall of intubation (26.85 vs. 32.41 %).

CONCLUSION

The study has demonstrated that the use of dexmedetomidine produces more satisfactory and favourable sedation in patients who underwent treatment with modified AFOI, than propofol. Moreover, dexmedetomidine results in higher sedation efficacy than propofol. Therefore, dexmedetomidine is a safe, feasible and effective method for managing difficult airways when applied using the modified AFOI.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the author(s) named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors, all authors read and approved the manuscript for publication. Shixiong Wen, Zhengyang Li, Xiuying Xiao, Weiwei Zhan and Yuanyuan Zheng conceived and designed the study. Shixiong Wen, Zhengyang Li, Xiuying Xiao collected and analysed the data. Shixiong Wen, Zhengyang Li and Yuanyuan Zheng wrote the manuscript. Shixiong Wen and Zhengyang Li contributed equally to this work.

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