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Original Article

Effectiveness of Dexmedetomidine versus Propofol Target Controlled Infusion for Sedation during Fiber-optic Nasotracheal Intubation: A Comparative Analysis

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Abstract

Introduction: Fiber-optic intubation has evolved overtime as one of the most valuable modalities for difficult airway management.

Materials and Methods: This study aimed to compare and analyze the efficacy of dexmedetomidine versus target controlled propofol infusion for sedation during nasal fiber-optic intubation. Forty patients with anticipated difficult airways and due to undergo nasotracheal intubation for elective surgery were randomly allocated into the dexmedetomidine group (1.0 μg/kg over 10 min) (n = 20) or the propofol target controlled infusion (TCI) group (n = 20). Intubating conditions and patient tolerance were evaluated as primary outcomes by a graded scoring system.

Results: Intubation was successful in all patients. Satisfactory intubating conditions were found in both groups (19/20 in each group). The median (IOR [range]) comfort score was 2 (1–2 [1–4]) in the dexmedetomidine group and 3 (2–4 [2–5]) in the propofol group (P = 0.027), favoring the former. The dexmedetomidine group experienced fewer airway events and less heart rate response to intubation than the propofol group (P < 0.003 and P = 0.007, respectively).

Conclusion: Both dexmedetomidine and propofol TCI are effective for fiber-optic intubation. Dexmedetomidine allows better tolerance, more stable hemodynamic status and preserves a patent airway.

Key words: Dexmedetomidine, Fiberoptic nasal intubation, Propofol

INTRODUCTION

Fiber-optic nasotracheal intubation is an effective technique for the management of patients with difficult airways. Both optimal intubating conditions and patient comfort are paramount while preparing the patient for fiber-optic intubation. One challenge associated with this procedure is to provide adequate sedation while maintaining a patent airway and ensuring ventilation. An ideal sedation regimen would provide patient comfort, blunting of airway reflexes, patient cooperation, hemodynamic stability, amnesia, and maintenance of patent airway with spontaneous ventilation.

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Many agents have been reported to achieve conscious sedation for intubation including fentanyl, midazolam, ketamine, propofol, remifentanil, and dexmedetomidine.[1-5] The development of target controlled infusion (TCI) technology has increased the potential for propofol and remifentanil sedation in clinical practice. TCIs can provide consistent pharmacodynamic effects with a safe and predictable sedation level to avoid complications related to deep sedation. Dexmedetomidine, an α_2- adrenoceptor agonist, may be a valuable drug for use during fiber-optic intubation as it induces sedation and analgesia without depressing respiratory function.[6,7] Thus, dexmedetomidine has many properties that make it a suitable drug for use in managing patients with difficult airways and it is feasible that when used as a sole agent or an adjuvant, it is efficacious for conscious sedation.[3,8-10]

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Chu *et al.*[11] reported that a loading dose (1 μg/kg) of intravenous dexmedetomidine provided conscious sedation without respiratory depression or upper airway obstruction for fiber-optic nasotracheal intubation. However, there is no study comparing the effectiveness of dexmedetomidine with other sedatives and sedation techniques. The purpose of this study was to compare the effectiveness of a single dose of dexmedetomidine administered over 10 min with propofol TCI for providing conscious sedation during fiber-optic intubation in patients with oral cancer.

MATERIALS AND METHODS

The study was approved by the Institutional Review Board and Ethical Committee. Written informed consent was obtained from each patient. Power calculation identified a minimum requirement for 10 patients to be randomized to each group to demonstrate a 20% difference in intubation scores with a power of 0.9 and a Type-1 error of 0.05. To allow for study error and attrition, we recruited 40 consecutive adult patients of ASA physical status 1–3 and scheduled to undergo elective surgery for the treatment of oral cancer. Fiber-optic nasal intubation using conscious sedation was planned for all patients because of the limited mouth opening arising from the cancer. Patients were randomly allocated into either the dexmedetomidine ($n = 20$) or the propofol ($n = 20$) group. Exclusion criteria included severe bradycardia, any type of atrioventricular block on the ECG, heart failure, emergency surgery, liver cirrhosis, thrombocytopenia, or coagulopathy contraindicating nasal intubation.

Two experienced consultant anesthetists certified in advanced airway life support performed airway management for all study subjects. While one anesthetist performed fiber-optic intubation, the other anesthetist controlled the drug infusion. Anesthetic data and postoperative visits were documented by a study nurse. Intubation conditions were graded by the consultant anesthetist who performed the fiber-optic intubation. The intubating anesthetist, patients, and the study nurse who recorded details of the procedures were all blinded to the study.

No premedication was given to any of the patients. In the operating room, nasal oxygen (2 L/min) was administered. Vital signs such as heart rate (HR), arterial pressure, and arterial oxygen saturation were recorded at baseline and then every 3 min thereafter. Following infusion of study drug, the patient's conscious level was evaluated using state entropy monitoring (Datex-Ohmeda, Helsinki, Finland).

Patients in the dexmedetomidine group received a loading dose of dexmedetomidine (1.0 μg/kg) infused over 10 min. The infusion was prepared by an independent nurse who added 200 μg (2 ml) of dexmedetomidine to 48 ml of 0.9% saline solution in a 50 ml syringe. Each patient in the propofol group received propofol administrated by a TCI pump (Fresenius Kabi) using the Schnider pharmacokinetic model.[12] The initial target effect site concentration (C_e) was set at 3 μg/ml. This was adjusted by 1.0 μg/ml according to patient comfort during the procedure. If a comfort score exceeded 3 or a persistent cough occurred during the procedure, the TCI was titrated upward following which the intubating anesthetist waited for 60 s before proceeding. While waiting for the desired level of sedation to be achieved, topical anesthesia was applied to the airway. Cocaine 6% (60 mg) packs were applied bilaterally to the inferior nasal canals following which the tongue and hypopharynx were sprayed with lidocaine 10% (60 mg). The nostril with the least resistance during nasal packing was chosen for nasal intubation.

Fiber-optic intubation was commenced once the dexmedetomidine infusion ended or when the propofol infusion target concentration at the effect site (C_e) had equilibrated with the plasma concentration (C_p). A fiber-optic scope (Olympus ENF XP 4.5 mm; Olympus, Tokyo, Japan) was loaded with a 7.0 mm tracheal tube for male patients or 6.5 mm tube for females. Once the glottic structures were identified, 2 ml lidocaine 2% was sprayed directly onto the glottis through the working channel of the fiber-optic scope. Another 2 ml lidocaine 2% was then sprayed below the vocal cords.

The primary outcome measurements were as follows: (i) Intubation scores as assessed by vocal cord movement (1 = open, 2 = moving, 3 = closing, and 4 = closed), coughing (1 = none, 2 = slight, 3 = moderate, and 4 = severe), and limb movement (1 = none, 2 = slight, 3 = moderate, and 4 = severe) and (ii) patient tolerance as assessed by a 5-point fiber-optic intubation comfort score (1 = no reaction, 2 = slight grimacing, 3 = heavy grimacing, 4 = verbal objection, and 5 = defensive movement of head or hands)[13] and a 3-point score assessed immediately after nasotracheal intubation (1 = cooperative, 2 = restless/minimal resistance, and 3 = severe resistance/general anesthesia required immediately). Once tracheal intubation was complete and the nasotracheal tube was secured, general anesthesia was administrated.

Other parameters assessed in relation to awake fiber-optic intubation included: Conscious level using state entropy values; an airway obstruction score (1 = patent airway, 2 = airway obstruction relieved by neck extension, and 3 = airway obstruction requiring jaw retraction); consumption of the study drugs; final C_e for the propofol group; and

intubation time (time taken from inserting the fiber-optic scope to confirmation of nasotracheal intubation).

A post-operative visit was undertaken the day after operation during which the level of recall (memory of pre-anesthetic preparations, topical anesthesia, endoscopy, and intubation), adverse events (hoarseness and sore throat), and satisfaction score (1 = excellent, 2 = good, 3 = fair, and 4 = poor) were assessed.

Statistical analysis was carried using paired *t*-tests for numerical data and Mann–Whitney U-tests for ordinal data. Fisher's exact test was used for non-continuous data with non-normal distribution. The SPSS 10.0 statistical software package (SPSS Inc., Chicago, IL, USA) was used for all analyses and $P < 0.05$ was considered statistically significant.

RESULTS

A total of 40 patients were enrolled into the study. There were no differences between the baseline data of the two groups [Table 1]. Data collected during fiber-optic intubation are shown in Table 2.

All patients underwent successful fiber-optic intubation. The dexmedetomidine group had more favorable intubation scores for vocal cord opening than did the propofol group. However, the intubation scores for cough and movement did not differ significantly between groups [Table 2]. One patient in the propofol group showed severe movement during the procedure and suffered from upper airway obstruction after increasing the propofol infusion to the maximal target concentration of 5 μg/ml. This patient developed transient hypoxia, with the lowest recorded oxygen saturation 80% (baseline 97%). Facemask ventilation with 100% oxygen rapidly resolved the situation. Another patient, in the dexmedetomidine group, exhibited gross limb movement during the procedure, but this was not associated with any airway obstruction. Administration of a 30 mg propofol bolus was used to rescue the situation. Both underwent successful intubation and recovered uneventfully. Their data were analyzed on an "intention to treat" basis. Satisfactory intubation scores (without severe limb movement) were observed in the remaining 19 of the 20 patients in each group.

With respect to patient tolerance, the lowest median (IQR [range]) comfort score during the procedure was 2 (1–2 [1–4]) for the dexmedetomidine group and 3 (2–4 [2–5]) for the propofol group ($p = 0.027$). The post-intubation scores were 1 (1–2 [1–2]) for the dexmedetomidine group and 2 (2–2 [1–3]) for the propofol group ($P = 0.014$), illustrating that the procedure was better tolerated using a dexmedetomidine infusion.

Sedation was deeper in the propofol group at intubation (significantly lower state entropy value) compared to the dexmedetomidine group [Table 2]. Airway obstruction occurred more frequently in the propofol group than in the dexmedetomidine group [Table 3]. There were no episodes of airway obstruction or hypoxia in the dexmedetomidine group.

Anesthetic parameters including drug consumption and final target concentrations are also shown in Table 2. Intubation time and hemodynamic support did not differ significantly between the two groups [Table 3].

Table 1: Characteristics of patients receiving dexmedetomidine or propofol during awake intubation. Data are expressed as mean (SD) or numbers

Group	Dexmedetomidine group (n=20)	Propofol group (n=20)
Gender; M:F	19:1	19:1
Age; years	55.7 (9.0)	54.4 (6.8)
Weight; kg	65.5 (12.2)	69.5 (11.9)
Height; cm	165.9 (6.5)	166.9 (7.7)
BMI; kg.m−2	23.8 (3.9)	24.9 (3.8)
ASA status; 1/2/3	(1/7/12)	(0/6/14)
Interincisor distance; mm	13.3 (7.5)	12.9 (10.2)
Previous oral surgery	10	9

Table 2: Measurements made during fiber-optic intubation in patients receiving dexmedetomidine or propofol during awake intubation. Data are expressed as mean (SD) or number

Group	Dexmedetomidine group (n=20)	Propofol group (n=20)	P-value
Success	20	20	1
Intubation scores			
Vocal cord movement; 1/2/3/4	16/4/0/0	9/7/4/0	0.03
Cough; 1/2/3/4	8/9/3/0	7/6/5/2	0.37
Movement; 1/2/3/4	12/6/1/1	7/5/7/1	0.12
Intubation time (min)	3.8 (1.1)	3.5 (1.7)	0.48
Final target concentration Ce (μg.ml−1)	NA	3.6 (0.6)	–
Drug requirements	65.5 (12.2) μg	131 (42) mg	–
State entropy at intubation	88.2 (2.5)	66.5 (6.4)	<0.001

Table 3: Adverse events and satisfaction data in patients receiving dexmedetomidine or propofol during awake intubation. Data are expressed as median (IQR [range]) or number (proportion)

Group	Dexmedetomidine group (n=20)	Propofol group (n=20)	P-value
Airway obstruction score; 1/2/3	(20/0/0)	(12/7/1)	0.007
Hypoxia	0	1 (5%)	0.31
Temporary hemodynamic support			
Atropine	2 (10%)	0	0.15
Ephedrine	1 (5%)	0	0.31
Hoarseness	4 (50%)	4 (20%)	1
Sore throat	2 (10%)	5 (25%)	0.21
Satisfaction score (1–4)	1 (1–2 [1–3])	1 (1–2 [1–3])	0.48

HR and mean arterial pressure at three time points are shown in Figures 1 and 2. Baseline HR and mean arterial pressure did not differ significantly between groups and there were no episodes of severe bradycardia (<40 beats/min). Compared with baseline, the HR decreased significantly in the dexmedetomidine group at the end of the drug infusion; this was not seen in the propofol group [Figure 1]. Intubation resulted in a mean increase of 1 (10.4) and 14 (12.3) beats/min in HR in the dexmedetomidine group and the propofol group, respectively ($P < 0.003$). The change in mean arterial pressure in response to intubation did not differ significantly between the two groups from baseline (an increase of 3.6 [15.6] mmHg in the dexmedetomidine group and a decrease of 1.5 [16.3] in the propofol group [$P = 0.26$]) [Figure 2].

The recall of topical anesthesia, endoscopy, and intubation was generally higher in the dexmedetomidine group (75%, 50%, and 5%, respectively) compared with the propofol group (20%, 5%, and 0%, respectively) ($P < 0.001$, $P < 0.002$, and $P = 0.3$, respectively). In total, 15 patients recalled the endoscopy while 25 patients did not. Increased recall did not seem to be associated with increased limb movement ($P = 0.17$) or comfort score ($P = 0.1$). Post-operative adverse events and patient satisfaction did not differ significantly between the two groups [Table 3].

DISCUSSION

The primary outcomes of the study show that both dexmedetomidine and propofol TCI provide satisfactory conditions for fiber-optic intubation with limited adverse effects for almost 95% of the patients. Dexmedetomidine has been shown to offer adequate conscious sedation for the fiber-optic intubation of patients with anticipated difficult airways.[8,9,11,14] Abdelmalak *et al*.[8] reported a series of successful awake fiber-optic intubations using dexmedetomidine for sedation in patients with difficult airways caused by a subglottic mass, a thyroid tumor causing tracheal compression, a nasopharyngeal tumor causing obstructive sleep apnea, and morbid obesity with sleep apnea. Dexmedetomidine can be used as either the sole agent or an adjuvant to facilitate awake intubation in patients with anticipated difficult airways.[9,11,14] However, there are limited double-blind randomized controlled trials comparing the drug's effectiveness with other techniques. Propofol is widely used in anesthetic practice to facilitate tracheal intubation and recent developments in propofol delivery using TCI offer reliable techniques for providing safe sedation. Hence, this study aimed to compare the effectiveness of sedation provided by either dexmedetomidine or propofol TCI.

It is possible that the target C_e of propofol TCI might influence the intubation conditions. In our results, propofol TCI aiming for a target C_e of 3.6 μg/ml provided conditions for fiber-optic intubation that was comparable with those provided using dexmedetomidine but with less favorable patient tolerance and a higher degree of airway obstruction. Lallo *et al*.[1] reported that both propofol TCI (C_e = 3.9 μg/ml) and remifentanil TCI (C_e = 2.4 ng/ml) provided good intubating conditions and patient comfort. Aiming for a lower C_e using propofol TCI can result in worse intubating conditions than those provided using remifentanil. Rai *et al*.[2] reported that remifentanil TCI (C_e = 3.2 ng/ml) provided better conditions for fiber-optic intubation when compared with propofol TCI (C_e = 1.3 μg/ml). Patient comfort is also an important issue during fiber-optic intubation. When placing the tracheal tube, patients should be relaxed and comfortable in order that the anesthetist can confirm the tube's position and perform general anesthesia under controlled conditions. In our study, patients in the dexmedetomidine group showed better tolerance as assessed by less limb movement during fiber-optic intubation. Most patients (19/20) in the dexmedetomidine group were cooperative and able to open their eyes to command immediately after nasotracheal intubation. Not surprisingly, none of the patients in the propofol group could respond to command, and all of them needed general anesthesia immediately after nasotracheal intubation.

Airway obstruction occurred more frequently in the propofol group than the dexmedetomidine group. During

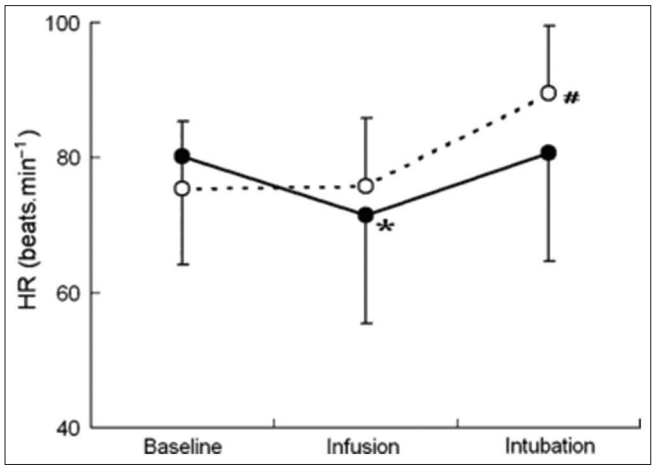

Figure 1: Open in figure viewer PowerPoint. Changes in heart rate in patients receiving dexmedetomidine (▲) or propofol (△) during fiber-optic intubation. Three time points were used for analyzing hemodynamic parameters: (i) Baseline = pre-anesthetic preparation; (ii) infusion = end of study drug infusion; and (iii) intubation = immediately after tracheal intubation. *$P < 0.001$ between groups; #$P < 0.05$ between groups

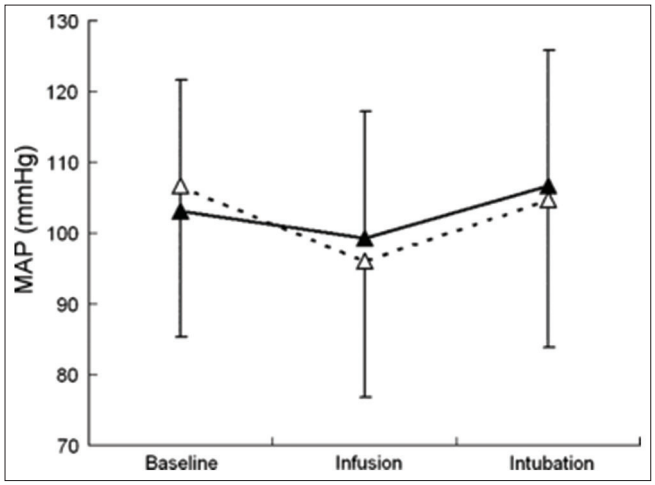

Figure 2: Open in figure viewer PowerPoint. Changes in mean arterial blood pressure in patients receiving dexmedetomidine (▲) or propofol (△) during fiber-optic intubation. Three time points were used for analyzing hemodynamic parameters: (i) Baseline = pre-anesthetic preparation; (ii) infusion = end of study drug infusion; and (iii) intubation = immediately after tracheal intubation. There was no significant difference between the two groups at each time point

management of the difficult airway, it is safest to keep patients breathing spontaneously until an alternative artificial airway is established. Dexmedetomidine activates the postsynaptic α_2-adrenergic receptors in the locus coeruleus and induces sedation by activation of the endogenous sleep-promoting pathway. Moreover, it has sedative, analgesic, anxiolytic, and antisialagogue properties without predisposing to airway obstruction and respiratory depression.[15,16]

With respect to hemodynamic stability, dexmedetomidine showed more favorable characteristics than propofol in our study. There was no significant difference in the change of mean arterial pressures during intubation for both the dexmedetomidine and propofol groups. Dexmedetomidine has been reported to prevent the hemodynamic responses to tracheal intubation more effectively than esmolol.[17] Its use was associated with a decrease in blood pressure and HR which might result from a decrease in noradrenaline release, a decrease in centrally mediated sympathetic tone and an increase in vagal activity.[18,19] Dexmedetomidine infusion may cause adverse effects such as hypotension, hypertension, nausea, bradycardia, atrial fibrillation, and hypoxia.[20,21] In our study, dexmedetomidine infusion induced bradycardia in two patients and hypotension in one patient. Both symptoms were easily managed with atropine, adrenaline, or intravenous fluid administration. None of the patients developed atrial arrhythmia or hypoxia.

Recall of topical anesthesia and endoscopy was more frequent in the dexmedetomidine group than in the propofol group. This is concordant with the significantly lower state entropy values in the propofol group, indicating higher sedation levels. In this study, propofol TCI (aiming for a C_e of 3.6 μg/ml) resulted in 20% recall for endoscopy and 5% recall for intubation. These results differ from those of some previous studies.[1,2] Amnesia induced by dexmedetomidine has also been reported. Two different doses (0.2 and 0.6 μg/kg/h) of dexmedetomidine infusion resulted in approximately 50% of the patients having impairment of their memory.[7] The study results revealed that a loading dose of dexmedetomidine (1 μg/kg/h) resulted in 50% of patients recalling the endoscopy and 5% recalling intubation.

CONCLUSION

Dexmedetomidine apart from satisfactory intubating conditions offers better patient tolerance, better preservation of a patent airway and spontaneous ventilation, and a reduced hemodynamic response to intubation than propofol infusion. These properties make it a useful drug for providing conscious sedation.

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