Original Article

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Comparison of dexmedetomidine alone with dexmedetomidine and fentanyl during awake fiberoptic intubation in patients with difficult airway: a randomized clinical trial

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Background: Awake fiberoptic intubation (AFOI) is the procedure of choice for securing the airway in patients with a difficult airway when undergoing surgeries under general anesthesia. An ideal drug would not only provide conscious sedation but also maintain spontaneous ventilation, smooth intubation conditions, and stable hemodynamics. We compared the effects of dexmedetomidine alone and dexmedetomidine in combination with fentanyl at a dose lower than the standard dose for achieving conscious sedation during AFOI in difficult airway patients undergoing oral cancer and dental surgeries.

Methods: We included 68 adult patients undergoing AFOI. The patients were randomized in two groups, wherein Group D received intravenous dexmedetomidine 1 μg/kg and Group DF received dexmedetomidine 0.5 μg/kg and fentanyl 1 μg/kg. The outcomes measured were airway obstruction score, intubation scores, fiberoptic intubation comfort score, sedation score, and hemodynamic variables.

Results: Low-dose dexmedetomidine with fentanyl showed similar results as those with the standard dose of dexmedetomidine in terms of airway obstruction, vocal cord movement, degree of cough, degree of limb movements, and intubation comfort. However, the sedation achieved and incidence of hypotension and bradycardia were higher in Group D than in Group DF.

Conclusions: A low dose of dexmedetomidine–fentanyl provides satisfactory intubation conditions as those with a standard dose of dexmedetomidine in AFOI, thereby avoiding bradycardia, hypotension, and sedation.

Keywords: Airway Management; Awake; Dexmedetomidine; Fentanyl; Fiberoptic Endoscopy; Intubation.

INTRODUCTION

Awake fiberoptic intubation (AFOI) is the procedure of choice for securing the airway in patients with a difficult airway when undergoing surgeries under general anesthesia. Preparing patients for AFOI is an important step that includes anxiolysis, amnesia induction, attenuation of airway reflexes, minimal sedation, and maintaining patent airway and adequate ventilation. The drug used should be safe and easy to titrate with minimal adverse effects.

Benzodiazepines (diazepam and midazolam), opioids (morphine, fentanyl, and remifentanil), intravenous induction agents (ketamine and propofol), and alpha-2 agonists (clonidine and dexmedetomidine) have been

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used alone or in combination to achieve appropriate intubation conditions for AFOI [1]. However, these drugs have certain advantages and disadvantages.

Although midazolam offers minimal sedation with anxiolysis and amnesia, its dose requirement varies and has no effect on the airway reflexes. Fentanyl and remifentanyl reduce the discomfort during the passage of the bronchoscope through the vocal cords, maintaining cardiovascular stability; however, fentanyl induces dose-dependent respiratory depression [2,3]. Propofol exhibits prompt onset and offset of action with intense amnesia but is associated with respiratory depression and increased incidence of hypoxemia when used alone or in combination with another drug [4]. Moreover, at high doses, it causes loss of upper airway tone, causing difficulty in negotiation of the bronchoscope beyond the epiglottis, as well as apnea [5].

Dexmedetomidine is the agent of choice for many practitioners to achieve sedation in AFOI because of its advantages over the other drugs [1]. It produces profound sedation with easy arousability, without respiratory depression. Furthermore, it has the added advantage of having anxiolytic and analgesic properties. It decreases the salivary secretions, thereby allowing better visualization through the fiberscope [6]. However, it can result in cardiovascular depression causing bradycardia and hypotension [7].

These effects are generally temporary and can be successfully treated with atropine or ephedrine and volume infusions [7]; however, in some cases such as hypovolemic patients or those with fixed stroke volume, it can be deleterious.

Hence, our study aimed to find an ideal agent and its appropriate dose for conscious sedation. The goal is to achieve patent airway with spontaneous ventilation, patient's cooperation, and steady hemodynamics without triggering respiratory depression.

This study compared dexmedetomidine alone with low-dose dexmedetomidine and fentanyl in achieving conscious sedation during AFOI in difficult airway patients undergoing oral cancer and dental surgeries.

METHODS

This was a randomized placebo-controlled double-blind trial conducted in a tertiary health care hospital in eastern India. The study was approved by the Institutional Ethical Committee (DMR/IMS.SH/SOA/18032/2019) and was registered in the Clinical Trial Registry of India (CTRI/2021/03/0317640). The study period was 9 months from April to December 2021. All the procedures were conducted as per the revised ethical guidelines of the Declaration of Helsinki of 2013. Written informed consent was obtained from all patients.

This parallel, two-arm, double-blind study with a 1:1 allocation ratio included patients aged 18–65 years. We included patients with American Society of Anesthesiologists grades 1 and 2 undergoing oral cancer or dental surgeries, wherein difficult intubation is anticipated due to limited mouth opening (< two fingers), restriction of neck mobility, or lack of space for laryngoscopy. The exclusion criteria were pregnancy, alcohol/drug use, allergy to the drugs used in this study, cardiovascular abnormalities, severe neurological, hepatic, renal, or pulmonary diseases, and bleeding disorders.

All patients were subjected to a pre-anesthetic checkup. Metoclopramide 10 mg, ranitidine 50 mg, and glycopyrrolate 5 μg/kg were administered intravenously (IV) 30 min before the procedure. Lidocaine 4% (5 ml) nebulization was administered to select patients for 10 min. In the operation theater, the baseline hemodynamic parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation, and electrocardiogram findings were recorded.

The patients were randomly allocated to two groups in a 1:1 ratio. The drug solution was prepared by an anesthetic technician not involved in the study. Randomization was performed by a statistician using computer-generated random numbers, and the group allocation was concealed in an opaque envelope that was opened by the technician in the operating room.

One group received an IV infusion of dexmedeto-

Table 1. Demographic profile of the patients

	Group D	Group DF	P value
Age (years; mean ± SD)	38.97 ± 7.92	41.35 ± 5.92	0.17
Weight (kg; mean ± SD)	75.00 ± 11.9	71.65 ± 9.73	0.21
Gender (Male: Female)	19:15	17:17	0.42
ASA grading (Grade I: II)	17:17	15:19	0.81

ASA, American Society of Anesthesiologist; SD, standard deviation.

Table 2. Comparison of the vital parameters between the groups

Variables		Group D	Group DF	P value
HR (beats/min)	Baseline	88.00 ± 6.49	86.29 ± 7.07	0.30
	Post-Intubation	82.65 ± 6.66	87.62 ± 8.67	0.31
SBP (mmHg)	Baseline	121.97 ± 11.10	121.53 ± 12.71	0.88
	Post-Intubation	103.82 ± 11.97	107.21 ± 12.77	0.26
DBP (mmHg)	Baseline	79.94 ± 5.53	78.21 ± 7.06	0.26
	Post-Intubation	66.97 ± 6.37	69.76 ± 8.87	0.14
SPO_2 (%)	Baseline	99.03 ± 0.88	97.67 ± 1.36	0.78
	Post-Intubation	98.97 ± 0.90	97.38 ± 1.81	0.47

DBP, diastolic blood pressure; HR, Heart rate; SBP, systolic blood pressure; SPO_2, oxygen saturation.

midine 1 μg/kg diluted in normal saline to a total volume of 50 ml (Group D). The other group received an IV infusion of dexmedetomidine 0.5 μg/kg and fentanyl 1 μg/kg diluted in normal saline to a total volume of 50 ml (Group DF). All patients received the drug solutions as IV infusion for 10 min. Oxymetazoline (0.05%) nasal drops were administered in both the nostrils. A nasal pack soaked in lidocaine (2%) and adrenaline (1:200,000) was placed in the patent nostril. Airway manipulation was started immediately after the administration of the drugs. A lubricated flexo-metallic endotracheal tube, as appropriate for each patient, was loaded in the fiberoptic endoscope. Fiberoptic intubation was performed using the "spray as you go" (SAYGo) technique with 2% lidocaine with adrenaline (1:200,000) through the working channel. The scope was manipulated to visualize the vocal cords, and 2 ml of 2% lidocaine was sprayed. The scope was directed towards the vocal cords and then crossed beyond them. The carina of the trachea was identified to spray 2 ml of 2% lidocaine beyond it. The tube was then advanced over the scope to stay approximately 2 cm above the carina. After confirmation of the proper position of the tube using capnography, the cuff was inflated, and the endotracheal tube was secured in place.

The primary outcome evaluated was the airway obstruction score (1, absent; 2, requiring neck extension; and 3, requiring jaw thrust) [8]. The secondary outcome measurements were the hemodynamic variables such as HR, SBP, and DBP measured during baseline drug administration and post-intubation. The intubation score was evaluated according to the vocal cord movement, degree of coughing, and degree of limb movement on a four-level scale [8]. Furthermore, the intubation comfort score and Ramsay sedation score (RSS) were evaluated for both groups [8].

The observer anesthesiologist recorded the intubation and intubation comfort scores during the procedure. After endotracheal tube insertion, the HR, SBP, DBP, and mean arterial BP (MAP) were recorded. General anesthesia was induced after the airway was secured. Any adverse events of oxygen desaturation (< 90%), bradycardia (HR < 60 beats/min), or hypotension (SBP < 100 mmHg, DBP < 60 mmHg, and MAP < 65 mmHg) were recorded.

Episodes of bradycardia were treated by administering atropine 0.6 mg IV. Hypotensive episodes were managed by crystalloid infusion and IV ephedrine 6 mg. Hypoxia

Table 3. Comparison of outcome measure between the groups

Variables		Group D n (%)	Group DF n (%)	P value
Airway obstruction	No	32 (94.1)	33 (97.1)	0.18
	Relieved by neck extension	2 (5.8)	1 (2.9)	
	Requiring jaw thrust	0 (0)	0 (0)	
Vocal cord movement	Open	19 (55.9)	24 (70.6)	0.51
	Moving	12 (35.3)	9 (26.5)	
	Closing	2 (5.9)	1 (2.9)	
	Closed	1 (2.9)	0 (0)	
Degree of cough	None	12 (35.3)	13 (38.2)	1.00
	Slight	18 (52.9)	18 (52.9)	
	Moderate	3 (8.8)	2 (5.9)	
	Severe	0 (0)	1 (2.9)	
Degree of limb movements	None	10 (29.4)	12 (35.3)	0.87
	Slight	21 (61.8)	20 (58.8)	
	Moderate	3 (8.8)	2 (5.9)	
	Severe	0 (0)	0 (0)	
Degree of Intubation comfort	No reaction	9 (26.5)	13 (38.2)	0.57
	Slight grimacing	23 (67.6)	20 (58.8)	
	Heavy grimacing	2 (5.9)	1 (2.9)	
	Verbal objection	0 (0)	0 (0)	
	Defensive movement of head and hands	0 (0)	0 (0)	
Ramsay sedation score	1- anxious	0	0	0.001*
	2- cooperative	6 (17.6%)	1 (2.9%)	
	3- response to command	12 (35.3%)	27 (79.4%)	
	4- brisk response to glabellar tap	16 (47.1%)	6 (17.6%)	
	5- sluggish response to glabellar tap	0	0	
	6- no response	0	0	

was managed by oxygen insufflation through the oxygen port of the scope. If it persisted, then the endoscope was temporarily removed, followed by bag and mask ventilation with 100% oxygen.

1. Sample size calculation

The primary outcome assessed was the degree of airway obstruction. Liu et al. reported an incidence of 22% of airway obstruction with dexmedetomidine (1 μg/kg), while Hassan et al. reported an incidence of 6% with fentanyl and dexmedetomidine (1 μg/kg) [8,9]. The calculated sample size was 25 in each arm with a power of 80% and alpha error of 5%. We increased the sample size to 34, considering a nonresponse rate of 20% and dropout rate of 10%.

2. Statistical analysis

The data were analyzed using Statistical Product and Service Solutions statistic software (version 23) and Microsoft Office Excel 2019. The demographic data are expressed as means and standard deviations. Parametric data between the two groups were compared using an independent t-test and non-parametric data using Mann–Whitney U test. Categorical data were compared using chi-square test or Fisher's exact test. All analyses were two-tailed; P-values $\leq$ 0.05 were considered statistically significant.

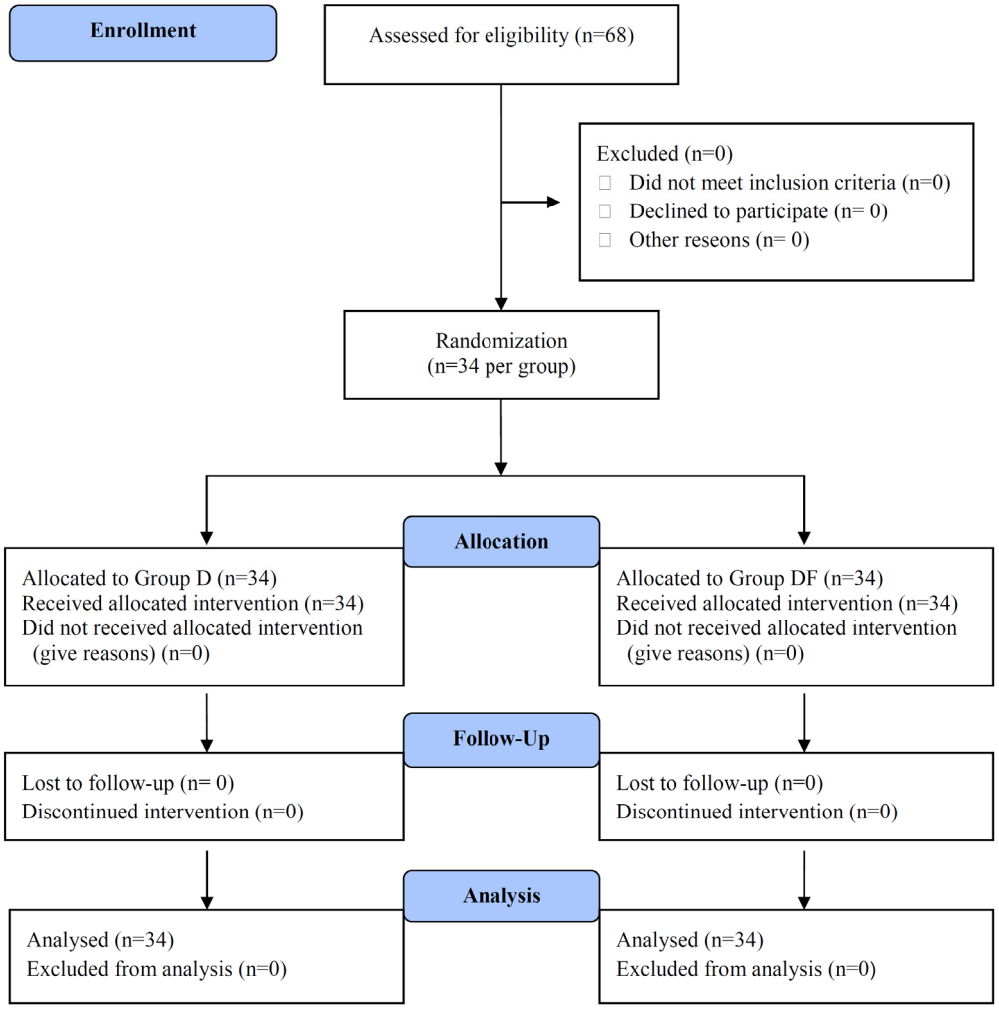

Fig. 1. CONSORT flow chart of the study. CONSORT, consolidated standards of reporting trials; n, number.

Table 4. Comparison of complications between the groups

Variables	Group D	Group DF	P value
Bradycardia	18 (52.9%)	6 (17.6%)	0.005*
Hypotension	16 (47.1%)	6 (17.6%)	0.02*

*, P value ≤ 0.05

RESULTS

In total, 68 patients completed the study (Fig. 1). No staistically significant differences were observed in the baseline data between the two groups (Table 1). Moreover, there were no significant differences in the vital parameters measured at baseline or post-intubation between the two groups (Table 2). Low-dose dexmedetomidine with fentanyl showed similar results as those with the standard dose of dexmedetomidine in terms of airway obstruction, vocal cord movement, degree of cough, degree of limb movements, and intubation comfort (P > 0.05; Table 3). None of the patients needed jaw thrust for relieving the airway obstruction in either group. The sedation achieved was higher in Group D than in Group DF as per the RSS (Table 3). No patient in either group showed RSS of 1 or ≥ 5.

The incidence of bradycardia was 52.9% and 17.6% in Group D and Group DF, respectively. Among them,

the proportion of patients requiring administration of IV atropine 0.6 mg was higher in Group D than in Group DF (22.22% vs. 1.2%). Similarly, the incidence of hypotension was higher in Group D than in Group DF (47.1% vs. 17.6%). However, no significant episodes of oxygen desaturation <90% were observed in either group (Table 4).

DISCUSSION

Our study found that the addition of low-dose fentanyl (1 μg/kg) to a low dose of dexmedetomidine (0.5 μg/kg) resulted in similar intubation conditions as those with the standard dose of dexmedetomidine (1 μg/kg), albeit with lesser side effects. The standard dose of dexmedetomidine (1 μg/kg) is associated with an increased risk of moderate or deep sedation, bradycardia, and hypotension.

Dexmedetomidine acts primarily on the locus ceruleus, a pontine nucleus, to inhibit the norepinephrine production in response to anxiety and stress. Hence, it induces efficient sedation with arousable and cooperative patients without any airway obstruction [10]. Cabrini et al. analyzed different drugs used in AFOI in difficult intubation cases and found that dexmedetomidine showed fewer desaturation episodes when compared to opioids such as propofol or midazolam [11]. Yadav et al. compared the combination of dexmedetomidine (1 μg/kg) and midazolam with that of fentanyl (2 μg/kg) and midazolam and reported that the former provides better intubation conditions with more stable hemodynamic parameters [12]. Hassan et al. studied the effects of the different doses of dexmedetomidine alone or in combination with fentanyl on sedation during AFOI in oral cancer surgery patients [8]. They found that either dexmedetomidine (2 μg/kg) or dexmedetomidine (1 μg/kg) in combination with fentanyl (1 μg/kg) produces a significant undesirable increase in the incidence of airway obstruction when compared with dexmedetomidine (1 μg/kg) administered alone. Based on these findings, we selected a comparatively low dose of dexmedetomidine (0.5 μg/kg) with fentanyl (1 μg/kg) and found that it was safer in AFOI, with a reduced incidence of airway obstruction. All the other parameters, such as vocal cord movement, degree of cough, degree of limb movements, and intubation comfort, were similar to those observed with dexmedetomidine (1 μg/kg) and dexmedetomidine (0.5 μg/kg) with fentanyl (1 μg/kg). Hassan et al. found that although the degree of limb movements was much less with dexmedetomidine (2 μg/kg), the incidence of airway obstruction was high [8]. The selected dose of dexmedetomidine for AFOI should be high enough to reduce airway reflexes but low enough to prevent airway relaxation and collapse. This can also be achieved by combining it with fentanyl to reduce the dose, which not only decreases the risk of airway obstruction but also creates optimum intubation conditions.

Chu et al. compared a low dose of fentanyl (1 μg/kg) with the standard dose of dexmedetomidine (1 μg/kg) and found a better tolerance to intubation with dexmedetomidine [13]. We found that when dexmedetomidine (0.5 μg/kg) was added to fentanyl (1 μg/kg), the results were similar to those with dexmedetomidine (1 μg/kg) in terms of intubation tolerance. Mondal et al. compared dexmedetomidine (1 μg/kg) with fentanyl (2 μg/kg) and found that fentanyl caused more airway obstruction at this dose and consequent oxygen desaturation, whereas dexmedetomidine had better tolerance to intubation as it showed lower cough scores [10]. We combined low doses of dexmedetomidine (0.5 μg/kg) and fentanyl (1 μg/kg) to avoid respiratory depression and found that this combination showed similar intubation conditions as those with dexmedetomidine (1 μg/kg) with respect to cough reduction. This implies that fentanyl and dexmedetomidine in low doses act synergistically to produce favorable intubation conditions in AFOI with reduced complications.

Flexible fiberoptic intubation is associated with hemodynamic responses leading to increased HR and BP [14]. Dexmedetomidine 0.5 μg/kg with fentanyl 1 μg/kg attenuated the hemodynamic responses to intubation in

AFOI, which was comparable to that of the other study group. However, the degree of reduction in the hemodynamic parameters, such as bradycardia and hypotension, with 1 μg/kg dexmedetomidine was more significant than that with the other drug combination. The effectiveness of dexmedetomidine 0.5 μg/kg in AFOI was assessed in the study by Sharma et al., who found it to be effective in combination for airway blocks during AFOI [15]. They assessed the level of sedation using the Observer's Assessment of Alertness/Sedation scale. The scores with 1 μg/kg of dexmedetomidine were significantly lower than those with 0.5 μg/kg of dexmedetomidine, indicating a higher level of sedation achieved with higher dose of dexmedetomidine. Our study showed a similar observation. We used the SAYGo technique for selectively anesthetizing the airway, which is an appropriate choice in most AFOI cases [16,17].

Our study had certain limitations. The individual drug impact in the postoperative period was not recorded, which should be evaluated in future studies. This was a single-center study, and a multi-centric study could give results of higher precision. Our study was limited to patients with a difficult airway undergoing oral cancer and dental surgeries. Nevertheless, this study paves a path for studies on different doses of dexmedetomidine, such as 0.25 and 0.75 μg/kg, to understand the best combination and dose that can be used safely. Similarly, varying doses of fentanyl, such as 1.5 or 0.5 μg/kg, should also be assessed.

This study showed that a low dose of dexmedetomidine –fentanyl provides satisfactory intubation conditions in AFOI as those with the standard dose of dexmedetomidine, thereby avoiding bradycardia, hypotension, and sedation.

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AUTHOR CONTRIBUTIONS

Ranjita Acharya: Conceptualization, Investigation, Supervision
Bhavna Sriramka: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing
Priyangshu Koushik: Data curation, Investigation, Methodology, Project administration, Writing – original draft

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REFERENCES

1. Johnston KD, Rai MR. Conscious sedation for awake fibreoptic intubation: a review of the literature. Can J Anaesth 2013; 60: 584-99.
2. Stoeckel H, Schüttler J, Magnussen H, Hengstmann JH. Plasma fentanyl concentrations and the occurrence of respiratory depression in volunteers. Br J Anaesth 1982; 54: 1087-95.
3. Mildh L, Taittonen M, Leino K, Kirvelä O. The effect of low-dose ketamine on fentanyl-induced respiratory depression. Anaesthesia 1998; 53: 965-70.
4. Lallo A, Billard V, Bourgain JL. A comparison of propofol and remifentanil target-controlled infusions to facilitate fiberoptic nasotracheal intubation. Anesth Analg 2009; 108: 852-7.
5. Bailey PL, Pace NL, Ashburn MA, Moll JW, East KA, Stanley TH. Frequent hypoxemia and apnea after sedation with midazolam and fentanyl. Anesthesiology 1990; 73: 826-30.
6. Alfieri A, Passavanti MB, Franco S Di, Sansone P, Vosa P, Coppolino F, et al. Dexmedetomidine in the Management of Awake Fiberoptic Intubation. Open Anesth J 2019; 13: 1-5.
7. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: a novel sedative-analgesic agent. Proc (Bayl Univ Med Cent) 2001; 14: 13-21.
8. Hassan ME, Mahran E. Evaluation of different doses of dexmedetomidine alone versus the combination of

dexmedetomidine and fentanyl in sedation during awake fiberoptic intubation in oral cancer surgery patients: a prospective, randomized, double-blind clinical trial. Saudi J Anaesth 2017; 11: 196-202.

9. Liu HH, Zhou T, Wei JQ, Ma WH. Comparison between remifentanil and dexmedetomidine for sedation during modified awake fiberoptic intubation. Exp Ther Med 2015; 9: 1259-64.
10. Mondal S, Ghosh S, Bhattacharya S, Choudhury B, Mallick S, Prasad A. Comparison between dexmedetomidine and fentanyl on intubation conditions during awake fiberoptic bronchoscopy: a randomized double-blind prospective study. J Anaesthesiol Clin Pharmacol 2015; 31: 212-6.
11. Cabrini L, Baiardo Redaelli M, Ball L, Filippini M, Fominskiy E, Pintaudi M, et al. Awake fiberoptic intubation protocols in the operating room for anticipated difficult airway: a systematic review and meta-analysis of randomized controlled trials. Anesth Analg 2019; 128: 971-80.
12. A randomized controlled study comparing dexmedetomidine-midazolam with fentanyl-midazolam for sedation during awake fiberoptic intubation in anticipated difficult airway. Anesth Essays Res 2020; 14: 271-6.
13. Chu KS, Wang FY, Hsu HT, Lu IC, Wang HM, Tsai CJ. The effectiveness of dexmedetomidine infusion for sedating oral cancer patients undergoing awake fibreoptic nasal intubation. Eur J Anaesthesiol 2010; 27: 36-40.
14. Adachi YU, Suzuki K, Obata Y, Doi M, Sato S. Is the hemodynamic response to nasotracheal fiberoptic bronchoscopy less than that following orotracheal bronchoscopy? Anesth Analg 2007; 105: 543-4.
15. Sharma J, Purohit S, Bhatia S, Kalra P, Sharma M, Meena R. Awake orotracheal fibre-optic intubation: comparison of two different doses of dexmedetomidine on intubation conditions in patients undergoing cervical spine surgery. Indian J Anaesth 2017; 61: 811-7.
16. Nebulisation versus spray-as-you-go airway topical anaesthesia in patients with temporomandibular joint ankylosis using 2% lignocaine. J Maxillofac Oral Surg 2015; 14: 398-402.
17. Xue FS, Liu HP, He N, Xu YC, Yang QY, Liao X, et al. Spray-as-you-go airway topical anesthesia in patients with a difficult airway: a randomized, double-blind comparison of 2% and 4% lidocaine. Anesth Analg 2009; 108: 536-43.