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Effect of Multiple Doses of Dexmedetomidine for Moderate Sedation Facilitating Intubation during Nasotracheal Fiberoptic Laryngoscope in Awake Patients-A Randomized Prospective Study

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Abstract

Background: Nasal fiberoptic intubation in fully conscious patients is the gold standard technique of choice in known difficult airway as cervical instability, limited mouth opening and any facial defects. The usage of an ideal sedation agent with a perfect dose or regimen securing stability of hemodynamic conditions and optimizing the intubating condition at the same time is an indispensable demand for awake fiberoptic intubation.

Aim: To detect variant efficiency of different doses of dexmedetomidine used for conscious sedation facilitating intubation by using nasotracheal fiberoptic laryngoscope in awake patients.

Methods: The study was performed in a prospective, blinded, randomized manner to compare the effect of different loading and maintenance doses of dexmedetomidine during awake fiberoptic intubation on 40 patients of both sexes aged between 20 and 60 years with ASA grade I or II enrolled for elective surgery. Patients randomly divided into two groups; 20 for each. All patients received 50 mcg Fentanyl and 2 mg Midazolam at premedication room, before transfer to operating room. Group I patients received I.V. Dexmedetomidine 1 mcg/kg as a bolus dose slowly over ten minutes then 0.7 mcg/kg/h as maintenance dose throughout the fiberoptic manipulation. Group II patients received I.V. Dexmedetomidine 0.7 mcg/kg as a bolus dose slowly over ten minutes then 0.2 mcg/kg/h as a maintenance dose throughout the technique. Primary outcomes were assessment of sedation level of each patient by Alertness and Sedation Scale (AA/S). Patient's reaction to insertion of tracheal tube that could be also assessed during Pre-oxygenation, both fiberscope placement and endotracheal placement (at 1, 2, 3, 4, 5 min interval) and if the patients were feeling comfort or distressing .This comfort scale for each patient was estimated by addition of seven comfort items at each time point, the total score was 35. Patient tolerance also was assessed on the basis of 5 point fiber optic index (FOI) score. Secondary outcomes were hemodynamic categories as heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure, oxygen saturation and end tidal capnography during Pre-oxygenation, both fiberoptic placement and endotracheal insertion (at 1, 2, 3, 4, 5 min interval) and any side effects were also explored.

Results: All patients in both groups underwent fiberoptic intubation with no differences statistically among two groups demographically, heart rate, systolic, diastolic and mean blood pressure. There were statistically differences among two groups as regard to SPO_2, $PACO_2$ and OAA/S scale only at 3, 4 and 5 min during endotracheal tube placement. No side effects were observed.

Conclusion: We concluded that dexmedetomidine especially with loading 1 µg/kg and higher maintenance dose 0.7 µg/kg/h were more suitable for fiberoptic intubation with better patient tolerance, patient comfort, patient satisfaction, good sedation and preserved upper airway with spontaneous breathing.

Keywords: Dexmedetomidine; Fiberoptic intubation; Comfort scale value; Alertness/Sedation scale

Introduction

Nasal fiberoptic intubation in fully conscious patients is the gold standard technique of choice in known or anticipated difficult airway as cervical instability, limited mouth opening and any facial defects [1]. Awake fiberoptic intubation was processed under sedation with or without topical anesthesia. The usage of an ideal sedation agent with a perfect dose or regimen securing stability of hemodynamic conditions and optimizing the intubating condition at the same time were an indispensable demand for awake fiberoptic intubation. Many sedation agents can be used as fentanyl, midazolam, propofol, dexmedetomidine and remifentanyl [2,3].

Remifentanyl has many advantages as an ultra-short acting opioid, underwent a rapid metabolism by blood and tissues [4], but has many drawbacks as respiratory depression, less effective anxiolytic, rapid clearance, hemodynamic instability, muscle rigidity, nausea and pruritus with high doses. Previous studies had shown the efficiency and efficacy of remifentanyl as an intravenous adjuvant to local anesthesia for managing pain and patient's discomfort during many surgeries [5,6].

Others used propofol for conscious sedation during fiberoptic intubation, with advantages of short acting, rapid clearance, dose related sedation time and dose related amnesia. While had some unwanted effects as respiratory depression and hemodynamic instability [7].

In this study, our aim was to compare variant efficiency of multiple doses of dexmedetomidine (loading and maintenance) used for sedating and suppressing upper airway reflexes in awake patients during nasotracheal fiberoptic intubation. The effects of two different doses of dexmedetomidine on patient's comfort, sedation, hemodynamic variability and patient tolerance to intubation were compared. Dexmedetomidine (precede, Pfizer, USA) selective α_2 agonist with shorter duration of action, its elimination half-life was 2 h and metabolized in the liver. It has privileges of good sedation, analgesic effects, suppressing upper airway reflexes, no respiratory depression like others and rapid recovery after discontinuation of administration [8].

Patients and Methods

After approval of the departmental ethics committee, written and informed consent obtained, the study was conducted at Aswan University Hospital for 6 months from May 2017 to October 2017. We studied on 40 adult patients of either gender aged from 20-60 years whose were scheduled to underwent elective cervical disc surgery under general anesthesia and extension of head wasn't allowed and assumed to be a hazardous for patients. Prospective randomized comp arative study enrolled on patients with ASA physical status I and II. Patients with obesity >30% above the ideal body weight were excluded from the study.

Also, patients refusal, patients with gastro esophageal reflux, uncontrolled hypertension, ischemic heart diseases, diabetic, asthmatic, severe bradycardia or any type of A-V block on ECG, coagulopathy, hepatic, renal dysfunction, thrombocytopenia, long term use of benzodiazepines or antidepressant drugs, any neurological disorders or mental retardation, pregnancy, nasal polyps, history of allergy to any used medication, any apparent airway abnormalities with Mallampati score more than III [7], thyro-mental distance less than 6 cm and history of laryngeal or pharyngeal surgeries all were excluded from our study. Patients should be fasted 6-8 h before surgery.

Electrocardiography (ECG), complete blood count, coagulation profile, hepatic and renal functions were evaluated for every patient. In operating room, an intravenous cannula was secured, basic monitors were applied 5-lead ECG, pulse oximetery, non-invasive blood pressure and radial artery cannulation in non-dependent hand that was done under local anesthesia only for arterial blood samples for blood gases analysis and samples were drawn before and after every 2 min throughout airway manipulation.

All patients were premedicated with 2 mg midazolam and 50 mcg fentanyl. Also all patients were received atropine sulphate 0.01-0.02 mg/kg IV to avoid bradycardia that may occur during procedure and to dry the salivary secretion. Before we started airway manipulation, all patients informed about the instruction and his entire role during procedure. Patients received topical anesthesia for all airway passages using lidocaine pump spray 10%. The nasal mucosa of both nostrils was prepared with a vasoconstriction agents as oxymetazoline spray and Xylocaine jelly 2% (lidocaine hydrochloride 30 g, AstraZeneca AB, Sweden).

Patients were randomly assigned to the following study groups using a sealed envelope technique:

Group I: 20 patients received I.V. dexmedetomidine 1 mcg/kg as a bolus dose slowly over ten min then 0.7 mcg/kg/h as a maintenance dose by a syringe pump.

Group II: 20 patients received dexmedetomidine 0.7 mcg/kg as a bolus dose slowly over ten min then 0.2 mcg/kg/h as a maintenance dose by syringe pump.

Solution of dexmedetomidine reconstituted to a concentration of 100 mcg/ml, prepared and administered by assistant investigator. Both nostrils were intubated with nasopharyngeal tubes (swept with lidocaine jelly 2%) of different sizes and one nostril was selected for intubation, the other nostril was conserved for oxygen supply (2-3 l/min).The biggest tube was left in place for one minute. After removal of the nasopharyngeal tube, a nasal endotracheal tube (7 to 7.5 mm diameter in male, 6-6.5 mm diameter in female), was guided into place with the bronchoscope.

After localization of the laryngeal and epiglottal region, 3 ml of lidocaine 2% was applied on the supraglottic region through the side channel of the bronchoscope. Additionally lidocaine 2% about 3 ml was added to be applied on vocal cords immediately before passage. After successful entry of the tube in between the vocal cords and after the assurance of the carina, the tube was inserted to about 3 cm above the carina and the cuff inflated. Once intubation proceeded in both groups and tube was secured. Propofol 2 mg/kg I.V. was given to start general anesthesia and maintained the mechanical ventilation of the patients.

Study design

Primary outcomes were assessment of sedation level of each patient by Alertness and Sedation Scale (AA/S) Table 1 [9]. AA/S was determined before taken any medications and during airway manipulation every two minutes, one day postoperatively, another investigator who was unaware to study also evaluated patient's reaction to insertion of tracheal tube that could be assessed during Pre-oxygenation, both fiberscope placement and endotracheal placement (at 1, 2, 3, 4, 5 min interval) and if the patients were feeling comfort or distressing Table 2.

This comfort scale for each patient was estimated by addition of seven comfort items at each time point, the total score was 35. Patient tolerance [10] also was assessed by a blind investigator to study groups on the basis of 5 point fiber optic index (FOI) score:1 represents No response, 2=light grimacing, 3=sever grimacing, 4=oral objection, 5=defensive movement of head, hands and feet.

Secondary outcomes were hemodynamic categories as heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure, oxygen saturation and end tidal capnography during pre-oxygenation, both fiberoptic placement and endotracheal insertion (1, 2, 3, 4, 5 min interval) and any side effects were also explored.

Responsiveness	Speech	Facial expression	Eyes	Score level
Respond readily to name and spoken in normally tone	Normal	Normal	Clear, no ptosis	5 (alert)
Lethargic response to name and spoken in normal tone	Mild slowing or thickening	Mild relaxation	Glazed or mild ptosis(less than half of eye)	4
Responds only after name is called loudly and/or repeatedly	Slurring or prominent slowing	Marked relaxation (slack jaw)	Glazed and marked ptosis (half the eye or more)	3
Responds only after mild prodding or shaking	Few recognizable words	--	--	2
Does not respond to mild prodding or shaking	--	--	--	1 (deep sleep)
Sum score: 20-18=alert, 17-15=light sedation, 14-11= heavy sedation, under 10=unable to cooperate.				

Table 1: The observer's Assessment of Alertness/Sedation Scale (Assessment categories).

Parameter	1	2	3	4	5
Alertness	Deeply asleep	Lightly asleep	Drowsy	Fully awake and alert	Hyper alert
Calmness	Calm	Slightly anxious	Anxious	Very anxious	Panicky
Respiratory response	No coughing and no spontaneous respiration	Spontaneous respiration	Occasional cough	Coughing regularly	Frequent coughing or choking
Crying	Quiet breathing, no crying	Sobbing or gasping	Moaning	Crying	Screaming
Physical movement	No movement	Frequent slight movement	Vigorous movement limited to the extremities	Vigorous movements including torso and head	Occasional slight movement
Muscle movement	Muscles totally relaxed, no muscle movement	Reduced muscle tone	Normal muscle tone	Increased muscle tone and flexing of fingers and toes	Extreme muscle rigidity and flexing of fingers and toes
Facial tension	Facial muscle totally relaxed	No facial tension evident	Tension evident through facial muscle	Facial muscle contorted	Grimacing

Table 2: Comfort Scale, as modified by Ambuel et al.

Power of study

The sample size was calculated using Epi-Info Software statistical package created by World Health Organization Atlanta, Georgia, USA version 2002.

The sample size was calculated at number equal 20, the criteria used were 95% significance level and 80% power. Based on this study on 40 patients, 20 in each group were required to detect a statistically significant difference between groups in our primary outcome parameters (Figure 1).

Statistical analysis

The full detailed form is: SPSS 20, IBM, and Armonk, NY, United States of America.

Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

- A one-way analysis of variance (ANOVA) when comparing between more than two means.
- Chi-square (X^2) test of significance was used in order to compare proportions between two qualitative parameters.

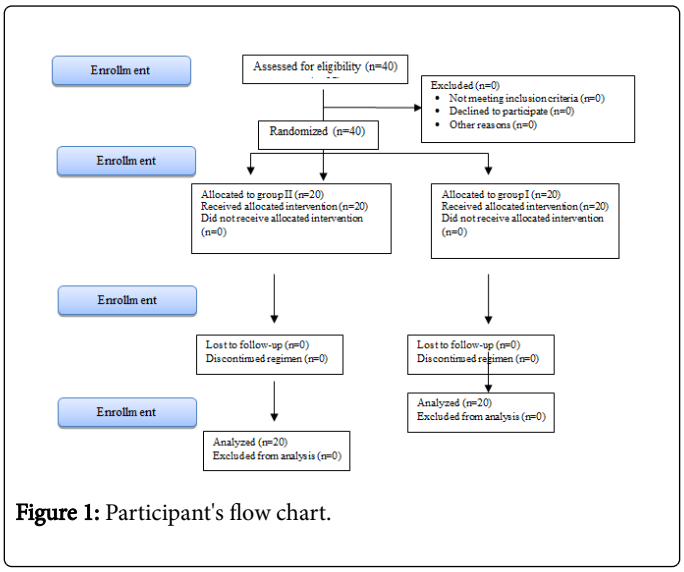

Figure 1: Participant's flow chart.

Results

All patients in both groups passed nasal fiberoptic intubation successfully. There was no significant difference demographically among two groups as regarding to age, sex, weight and height Table 3. There was some variability in hemodynamic parameters among two groups as the heart rate reduced in group I more than group II from baseline up to 5 min during endotracheal intubation but this variability was insignificant among two groups Figure 2.

Also the systolic, diastolic and mean arterial blood pressure were much reduced from baseline up to 5 min of endotracheal tube placement in group I more than group II but without any significant differences among both groups Table 4.

The mean SpO_2 was significantly lower in group I in comparison to group II from baseline, Pre-oxygenation, fiberscope insertion and up to 2 min of endotracheal tube insertion but without significant differences among them but at 3, 4 and 5 min interval of intubation, SpO_2 was much lower in group I as compared to group II with significant differences among two groups Figure 3. With consider to $PaCO_2$ was minimal increased in group I more than group II from baseline up to 2 min of endotracheal intubation with no significant differences between groups, while at 3, 4 and 5 min interval of endotracheal intubation $PaCO_2$ was much increased in group I than group II with significant differences among two groups Figure 4.

Total comfort scale were lower in group I (the patients were more sedating and calm) during fiberoptic insertion and tracheal tube insertion as compared to patients in group II with significant differences among two groups Table 5 and Figure 5.

Patients in groups II had high five point fiberoptic index score conflicting better patients' tolerance in group I than in group II with significant differences among two groups Table 6 and Figure 5.

According to the Observer's Assessment of Alertness/Sedation scale, sedation was sufficient in all groups and all patients were being able to cooperate during manipulation.

The score more than 10 with no significant differences between two groups from baseline up to 2 min of endotracheal tube placement, while at 3, 4 and 5 min interval of endotracheal tube placement, patients in groups 1 more sedated than group II with significance differences among two groups Figure 6.

No detectable side effects were detected in both groups, no apnea or bradypnea (respiratory rate less than 10 breaths/min) or bradycardia or any side effects from medications could be detected.

		Group I (n=20)	Group II (n=20)	p value
Age	Mean ± SD	41.73 ± 6.12	39.87 ± 5.87	0.333
Sex	Male (%)	8 (40%)	9 (45%)	0.749
	Female (%)	12 (60%)	11 (55%)	
Weight	Mean ± SD	63.45 ± 4.56	61.96 ± 4.72	0.316
Height	Mean ± SD	164.9 ± 9.8	163.7 ± 8.6	0.623

Table 3: Demographic data among group I and group II.

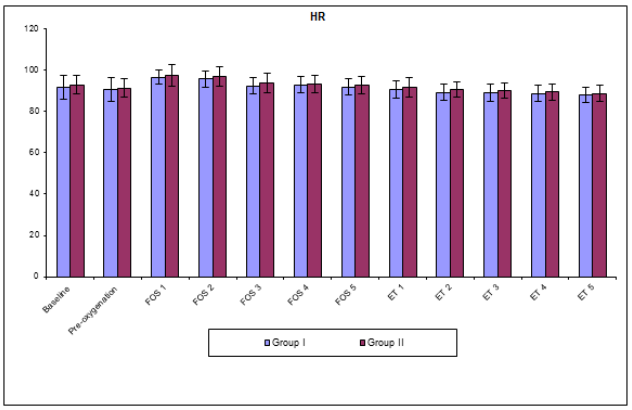

Figure 2: Comparison of heart rate baseline, during pre-oxygenation, fiberscope and endotracheal intubation among group I and group II.

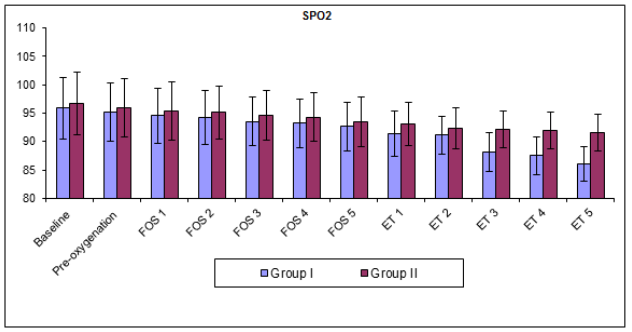

Figure 3: Comparison of saturation (SpO_2%) baseline, during Pre-oxygenation, fiberscope and endotracheal tube placement among group I and group II.

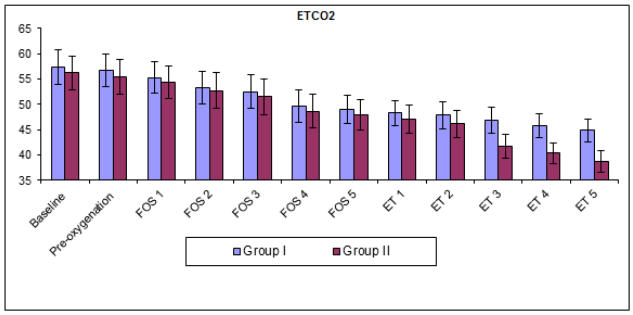

Figure 4: Comparison of $PaCO_2$ baseline, during Pre-oxygenation, fiberscope and endotracheal tube placement among group I and group II.

Mean arterial blood pressure	Group I (n=20)	Group II (n=20)	p value
Baseline	97.14 ± 5.25	98.21 ± 5.34	0.414

Pre-oxygenation	98.24 ± 5.47	99.25 ± 5.23	0.554
FOS 1	102.32 ± 5.84	103.35 ± 5.97	0.584
FOS2	103.84 ± 5.47	104.15 ± 5.27	0.856
FOS 3	101.36 ± 4.98	102.24 ± 4.26	0.552
FOS 4	99.58 ± 5.32	101.36 ± 5.17	0.290
FOS 5	99.14 ± 5.08	101.37 ± 5.13	0.175
ET 1	98.52 ± 4.59	99.57 ± 4.60	0.474
ET 2	98.12 ± 4.18	99.21 ± 4.72	0.444
ET 3	97.52 ± 4.52	98.47 ± 4.36	0.503
ET 4	97.02 ± 4.12	97.94 ± 4.52	0.505
ET 5	96.35 ± 4.19	97.85 ± 3.99	0.254

Table 4: Comparison of mean blood pressure baseline, during Pre-oxygenation, fiberscope and endotracheal intubation among group I and group II.

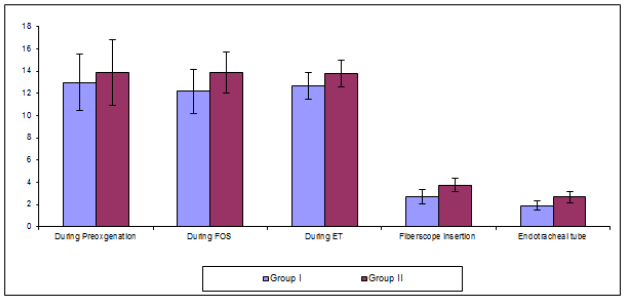

Figure 5: Comparison of total comfort scale (time interval) and patient's tolerance based on 5 point fiberoptic index score among group I and group II.

Total comfort scale		Group I (n=20)	Group II (n=20)	p value
During Pre-oxygenation	Mean ± SD	12.97 ± 2.54	13.84 ± 2.97	0.326
During FOS	Mean ± SD	12.18 ± 1.97	13.86 ± 1.84	0.008*
During ET	Mean ± SD	12.67 ± 1.17	13.74 ± 1.21	0.007*

Table 5: Comparison of total comfort scale (time interval) during Pre-oxygenation, fiberscope and endotracheal tube placement among group I and group II.

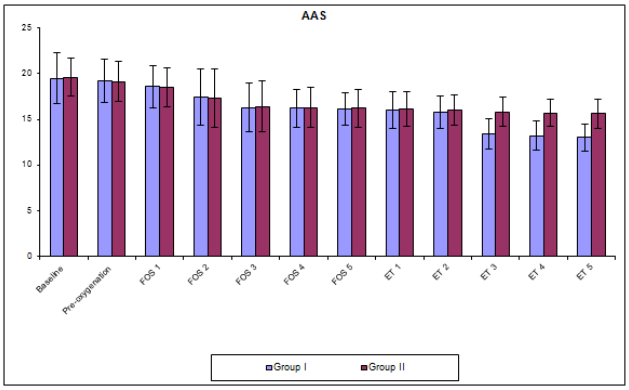

Figure 6: The observer's Assessment of Alertness/Sedation Scale (Assessment categories).

Patient's tolerance		Group I (n=20)	Group II (n=20)	p value
Fiberscope insertion	Mean ± SD	2.69 ± 0.65	3.74 ± 0.59	0.001*
Endotracheal tube	Mean ± SD	1.89 ± 0.42	2.68 ± 0.51	0.001*

Table 6: Comparison of patient's tolerance based on 5 point fiberoptic index score during fiberscope insertion and endotracheal tube placement among group I and group II.

Discussion

Many studies evaluated the use of dexmedetomidine for sedating the patients with anticipated difficult intubation for any reason, for which they underwent nasal fiberoptic intubation, but few compared the two different dose regimen of dexmedetomidine for fiberoptic uses. Our study approved that when we used dexmedetomidine in different two doses regimen for facilitating the intubation in awake patients, one group had loading dose 1 mcg/kg body weight and high maintenance dose 0.7 mcg/kg/h while the other group had loading 0.7 mcg/kg body weight and low maintenance dose 0.2 mcg/kg/h. there were wide variation among groups and also inside the main group.

As the patients in group of high maintenance dose showed marked decrease in heart rate, systolic, diastolic, mean blood pressure, decrease in SpO_2 and increase in $PaCO_2$ and the patients became more sedated and calm (total comfort scale better with this group), also patients had good tolerance during fiberoptic and endotracheal tube placement than the other group of low maintenance dose. Dexmedetomidine decreases blood pressure and heart rate either through peripheral or central mediated action. It's α_2-agonists reducing the release of norepinephine. It stimulates central presynaptic α2 receptor resulting in decreased noradrenaline release which in turn causes hypotension and bradycardia [11-14].

The study showed that fiberoptic intubation was much suitable, smooth and with no unwanted events when dexmedetomidine was used. All patients had been intubated successfully intubated from the first attempt. Our primary outcome measures, fiberoptic insertion, intubation condition, patients comfort and patients tolerances were

improved with higher dose of dexmedetomidine. It had sedative, analgesic and anxiolytic properties, with no drawbacks on the respiration. They sustained hemodynamic and sympathoadrenal stability by suppressing the circulating catecholamines. It can be used either as the sole agent or an adjuvant to ease awake intubation in patients with anticipated difficult airways [15-18]. Many medications like fentanyl, midazolam, ketamine, propofol and remifentanil were used to ease fiberoptic intubation, but dexmedetomidine had many privileges to make it suitable for use during fiberoptic intubation [19].

Our study were supported by study of Abdelmalak et al. reported a series of passed fiberoptic intubations successfully using dexmedetomidine for sedation in awake patients with difficult airway [20].

Total comfort scores were less in Group I (they were more calm) during FOS and tracheal intubation in comparison to group II. Group II had high five points FOI scores reflecting better patient tolerance in group I. These findings were similar to that of a study by Rodrigues AJ et al., Rolo R et al. and Dhasmana S et al. who documented that midazolam and fentanyl, provide better intubating circumstances, patient comfort and tolerance in fiberoptic bronchoscopy [21-23]. In our study, improved conditions were observed using dexmedetomidine due to its analgesic and sedative effects [24].

Also, in our study, patients of the dexmedetomidine assumed better intubating circumstances and maintained hemodynamic stability, which was similar to study done by Yavacaoglu et al. who reported that dexmedetomidine prevented the hemodynamic alterations to tracheal intubation more effectively than esmolol [25]. Falkman H et al. assumed that propofol shows more homogeneous satisfaction score [26].There were variations found in heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure among the two groups but it was statistically insignificant. These findings are similar to the studies conducted by Falkman H et al., Crawford M et al. and Clarkson K et al., who found statistically insignificant difference in hemodynamics parameters among propofol and midazolam groups during fiberoptic laryngoscopy [26-28]. However, a study assumed by Grendelmeier P et al. on propofol and midazolam as sedative agents concluded that patients received propofol showed more profound hypotension [29]. Chu et al. assumed that a loading dose 1 μg/kg of intravenous dexmedetomidine provided conscious sedation without airway obstruction or respiratory depression for fiberoptic intubation which was the same with our study [30]. Dexmedetomidine assumed privileges of adequate sedation without narcotic-induced respiratory depression. Spontaneous ventilation has the clear advantage of prevention of apnea during bronchoscopy [31]. Oxygen saturation was significantly lower in Group I compared to Group II during FOS and endotracheal intubation placement. These findings were similar to study by Grandelmeir P et al. who assumed study on comparative assessment of propofol and midazolam as sedative agents in 90 consecutive patients enrolling for medical thoracoscopy and observed that patients randomized to propofol group detected more hypoxia [29]. Also, Tsai CJ et al. approved in their comparative study that airway obstruction and hypoxia are frequently detected in propofol group than dexmedetomidine group [32].

We concluded that, dexmedetomidine provides optimum sedation without compromising airway or hemodynamic instability with better patient tolerance and satisfaction for awake fiberoptic intubation especially with higher loading and maintenance doses. It also preserves patient arousability for neurological assessment after intubation.

Conclusion

Dexmedetomidine has the attraction of prevention of respiratory depression or obstructive breathing during sedation and its sympatholytic effects should help deliver stable blood pressure and heart rate. The use of dexmedetomidine especially with loading 1 μg/kg and higher maintenance dose 0.7 μg/kg/h were preferable than loading 0.7 μg/kg and low maintenance dose 0.2 μg/kg/h as higher maintenance dose were more suitable for fiberoptic intubation with better patient tolerance, patient comfort, patient satisfaction and good sedation.

Limitations of the study

The patients study was small and a larger trial detecting dexmedetomidine with other agents were warranted approving greater differences in these agents.

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Conflict of Interest: No conflict of interest.

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