Comparison of Fiberoptic Bronchoscopy with Midazolam-based Anesthesia and Lidocaine-based Anesthesia

Mohamadreza Rafiei¹, Mahmod Karimi², Vahid Ziae³, Seid Ali Zargar^{4*}

¹Associate Professor of Anesthesiology, AJA University of Medical Sciences, Tehran, Iran.
²Lung Specialist, Assistant Professor, AJA University of Medical Sciences, Tehran, Iran.
³Assistant Professor of Anesthesiology, Azad University of Najafabad, Isfahan, Iran.
^{4*}Internal Medicine Specialist, AJA University of Medical Sciences, Tehran, Iran.
Email: nilufarabi33@yahoo.com

Abstract: Introduction: Bronchoscopy is one of the essential methods for diagnosing lung diseases that is associated with many different uncomfortable complications for patients. The aim of this study was to compare fiberoptic bronchoscopy with midazolam-based anesthesia and lidocaine-based anesthesia.

Materials and Methods: The present study is a double-blind clinical trial study that was performed on patients who underwent bronchoscopy from 2017to 2018. Midazolam-based anesthesia was compared with lidocaine-based anesthesia, and then the data were analyzed using SPSS software version 21.

Results: 140 patients were studied (mean age total 61.4 years) and among them 52.14% were male and 47.86% were female. Half of the Individuals received midazolam and half of them received lidocaine. The use of lidocaine has been much more satisfactory for physicians and patients, in comparison with midazolam. Complications of bronchoscopy (nausea, decreased arterial blood oxygen saturation, sore throat, cough, and need for intubation) and the duration of bronchoscopy were lower in those who received lidocaine than in those who received midazolam.

Conclusion: The use of lidocaine in bronchoscopy reduced complications such as nausea, sore throat, cough, intubation, duration of bronchoscopy, and decreased arterial blood oxygen saturation, and was associated with increased patient and physician satisfaction. Lidocaine can be an appropriate alternative medicine for use in bronchoscopy.

Keywords: Bronchoscopy, Midazolam, Lidocaine, Anesthesia.

1. INTRODUCTION

Bronchoscopy is one of the useful methods for diagnosing lung diseases, which is performed under different levels of anesthesia [1, 2]. Although bronchoscopy is generally a short procedure, it is inherently uncomfortable for patients and the use of sedation and local anesthesia during this procedure is recommended [3]. Bronchoscopy may be associated with complications such as intrabronchial hemorrhage, bronchospasm, and pneumothorax, or fever, sore throat, and cough [2]. Complications have made physician and patient satisfaction as important issue in performing an ideal bronchoscopy [4]. For this purpose, various methods of anesthesia, including general anesthesia, local anesthesia, and MAC (conscious sedation), have been used [5]. Various drugs such as midazolam, intravenous anesthetics (propofol-etomidate), different opioids, and inhaled anesthetics (isoflurane and desflurane) or a mixture of them have been used for fiberoptic bronchoscopy [6]. Inhaled anesthetics have side effects such as air pollution and the use of a mixture or combination of them can lead to severe respiratory depression [4, 7].Sedatives reduce anxiety and pain and cause anterograde amnesia. Among the agents used for local anesthesia, lidocaine is the most widely used medication due to its safety and favorable pharmacokinetic properties [8]. Lidocaine is available in various formulations and can be delivered to the respiratory tract using various modes (spray, nebulization, trachea injection, bronchoscopic injection, etc.); In general, several articles have reported the effectiveness of lidocaine in bronchoscopy at different levels [9-13]. On the other hand, midazolam has also shown effective results in reducing side effects [14].

Recognizing the effectiveness of anesthetic drugs can be effective in reducing complications and increasing patient satisfaction. Numerous studies have compared the differences between methods and drugs used in anesthesia for bronchoscopy, and among them, different results have been reported about the superiority and side effects of each method and medication [15, 16].

The use of new drugs or new drug combinations, which have minimal hemodynamic and respiratory complications and simultaneously lead to the greatest satisfaction of the physician and patient, appears to be very necessary. Therefore, the present study compares a common method of anesthesia in bronchoscopy, namely midazolam-based anesthesia, and a new method of anesthesia, which is lidocaine-based anesthesia, and also, tries to select the most appropriate method for fiberoptic bronchoscopy.

2. MATERIALS AND METHODS

Study Design

This clinical trial study was performed on patients who were candidates for elective fiberoptic bronchoscopy who referred to the pulmonary clinic of Imam Reza Hospital in 2017 and 2018. Patients who met the inclusion criteria and consciously signed the written consent form to participate in the research project were included in the study. The present study has been approved by the ethics committee of the Army University of Medical Sciences with the ID of IR.AJAUMS.REC.1398.022 and the test code of IRCT20110103005536N8.

Inclusion and Exclusion Criteria

Inclusion criteria were male and female patients aged 18 to 80 years and with ASA I-II scores, who have referred for fiberoptic bronchoscopy under general anesthesia since the plan was approved and entered the study with satisfaction. Exclusion criteria were people with a history of sore throat and lung disease with 90% O2sat (hypoxemia), people with 40%> EF<, HR<50, PB<90 mmHg hypotension, grade II and III heart conduction blocks, GCS \leq 8, patients with carotid sinus syndrome, MI or angina pectoris, hepatic and renal failure, pregnant or lactating women, and people with a long history of taking antipsychotic or sedative drugs.

Method

For all patients, after being placed on the operating room bed, complete hemodynamic monitoring including barometer, pulse oximeter, and EKG was performed and 5 mg/kg of normal saline was infused as a preloaded fluid. Also, 1 ml (equivalent to 50 micrograms) of the short-acting intravenous fentanyl was prescribed for all patients.

Patients were divided into two groups (randomly using simple black and white cards), namely, the midazolam-based group (70 people) and the lidocaine-based group (70 people). In the midazolam group, 3 mg equivalent to 3 ml of midazolam was injected intravenously, and the volume was increased to 5 cc by adding 2 cc of distilled water. After the fiberoptic

bronchoscope entered the patient's mouth and before passing through the vocal cords, distilled water was poured on the vocal cords by a syringe with a volume of 5 cc (through the fluid entry spot in the bronchoscope). Then, after passing the bronchoscope through the vocal cords, a syringe with a volume of 5 cc of distilled water was poured into the patient's trachea (tracheobronchial tree). In the lidocaine group, a syringe containing 5 cc of lidocaine (100% lidocaine 2%) was injected intravenously. After the fiberoptic bronchoscope was inserted into the patient's mouth and before passing through the vocal cords, a syringe with a volume of 5 cc containing lidocaine 2% was poured on the vocal cords (through the entrance of fluid in the bronchoscope). Then, after passing the bronchoscope through the vocal cords, a syringe with a volume of 5 cc containing lidocaine 2% was poured into the patient's trachea (tracheobronchial tree). The two groups were examined in terms of research variables.

Variables and Data Collection

Variables such as age, sex, bronchoscopy complications, type of basic drug, physician satisfaction, patient satisfaction, and duration of bronchoscopy were examined. The obtained information was collected and recorded in a checklist that included all the variables required for the study. The satisfaction of physician and patient was measured by a 5-point scale (no, probably no, not sure, probably yes, definitely). In order to measure patient satisfaction, the tools of patients undergoing bronchoscopy, which had been used in previous studies, were used [17]. It should be noted that during the study, the patients and the data collector did not have any information about the distribution of samples. Lastly, the obtained data were statistically analyzed.

Data Analysis

Frequency and percentage were used to express qualitative variables. Chi-square and Mann-Whitney U tests were used to evaluate the variables. SPSS-v21 software was used for analysis and P<0.05 was considered significant.

3. RESULTS

The study population included 140 people, of which 52.14% were male and 47.86% were female. The mean age was 61.48 years in the midazolam group and 61.32 years in the lidocaine group. The mean age of the total patients was 61.40 with a standard deviation of 9.28. Half of the patients received lidocaine for anesthesia and the other half received midazolam.

	Mean	Standard deviation	
Age	61.40	9.28	
Gender	Percentage	Frequency	
Male	52.14	73	
Female	47.86	67	
Total	100	140	

Table 1: Frequency Distribution of Patients' Gender and Age

Decreased arterial blood oxygen saturation was seen in 46 cases, of which 35 were in the midazolam group and 11 were in the lidocaine group; the two groups were significantly different in terms of arterial blood oxygen saturation. The total number of patients with nausea was 33, of which 22 were in the midazolam group and 11 in the lidocaine group; the

two groups were significantly different in terms of nausea. In total, 33 patients had sore throat, of which 24 were related to the midazolam group and 9 were related to the lidocaine group; the two groups were significantly different in terms of sore throat. The total number of patients with cough was 33 cases, of which 24 received midazolam and 9 of them received lidocaine; the two groups were significantly different in terms of cough. The need for intubation was seen in a total of 9 cases, all of which were in the midazolam group, and none of the people who used lidocaine needed intubation. The two groups were significantly different in terms of cough were significantly different in terms of the people who used lidocaine needed intubation. The two groups were significantly different in terms of number of the people who used lidocaine needed intubation.

		Type of received anesthetic		Total	P value
		Lidocaine	Midazolam		
	Yes	11	35	46	
Decreased arterial blood oxygen saturation	No	59	35	94	0.017
	Total	70	70	140	
	Have	11	22	33	
Nausea	Have not	59	48	107	0.028
	Total	70	70	140	
Sore throat	Have	9	24	33	
	Have not	61	46	107	0.043
	Total	70	70	140	
	Have	9	24	33	
Cough	Have not	61	46	107	0.043
	Total	70	70	140	
	Have	0	9	9	
Need for intubation	Have not	70	61	131	< 0.0001
	Total	70	70	140	

Table 2: Frequency of Bronchoscopy Complications based on the Type of Received Anesthetic

According to Figure 1, the physician's satisfaction with lidocaine was high and moderate and the satisfaction with midazolam was low and moderate. In total, 48 people expressed high satisfaction and 22 people expressed moderate satisfaction, among the physicians who used lidocaine as an anesthetic. There was a significant difference between the two groups of physicians in terms of the rate of satisfaction (p <0.0001). Patients' satisfaction with lidocaine was high in 33 cases, moderate in 29 cases, and low in 3 cases, and satisfaction with midazolam was low in 42 cases, moderate in 27 cases, and high in only 1 case. There was a significant difference between the two groups of patients in terms of the rate of satisfaction (p <0.0001).

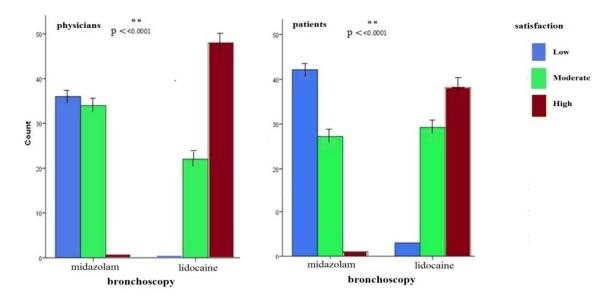


Figure 1: The Rate of Satisfaction for Physicians and Patients based on the Type of Received Anesthetic

The duration of bronchoscopy in patients who received lidocaine was shorter than in those who received midazolam so that bronchoscopy lasted 15 minutes in 42 of the 70 people who received lidocaine. According to Table 3, the two groups were significantly different in terms of time spent (p < 0.0001).

		Type of received		Frequency	P value
		anesthetic			
		Lidocaine	Midazolam		
Duration of	15 minutes	42	8	50	< 0.0001
bronchoscopy	15-20 minutes	26	34	60	
	More than 20	2	28	30	
	minutes				
	Total	70	70	140	

Table 3: Duration of Bronchoscopy based on the Type of Received Anesthetic

4. **DISCUSSION**

The present study showed that the use of lidocaine in bronchoscopy reduced nausea, sore throat, cough, intubation, duration of bronchoscopy, and hypoxemia, and increased patient and physician satisfaction, and had a significant difference compared to midazolam. Similar studies have shown that the use of an appropriate percentage of lidocaine in bronchoscopy reduces pain, reduces the need for intubation, reduces the duration of bronchoscopy, reduces hypoxemia, and increases patient satisfaction [12, 18, 19]. In this regard, Sorasitrungsakun et al. compared the effect of lidocaine 2% solution and lidocaine 2% viscous on improving discomfort and satisfaction in patients undergoing bronchoscopy and showed that lidocaine 2% solution had well results [20]. Madan et al. found that the addition of a percentage of lidocaine was effective in increasing patient satisfaction [19].Studies by Gu et al. In 2019 have shown that inhalation of dexmedetomidine-lidocaine is effective in reducing complications of bronchoscopy [18]. Findings of a study by Dreher in 2016 showed that

injection of lidocaine could be a safe method that is effective in reducing complications and increasing patient satisfaction [21].Regarding the effectiveness of midazolam, in a study conducted by Marco Contoli et al. in 2013, it was found that administration of midazolam at a dose of 0.7 mg/kg in patients undergoing bronchoscopy, increases tolerance and satisfaction of patients without inducing side effects [14]; however, in our study, the effectiveness of lidocaine was higher.

To date, no study was conducted on the comparison of lidocaine and midazolam in fiberoptic bronchoscopy, but similar studies have examined midazolam administration in different cases. In a study by Yang Gao et al., It was found that although dexmedetomidine alone is suitable for inducing anesthesia and maintaining its continuity in patients undergoing bronchoscopy, its administration in combination with midazolam has reduced side effects, increased the satisfaction of physician, and facilitated patient recovery [22]. In another study, it was found that intravenous administration of Dexmedetomidine at a dose of 1 microgram/kg, ten minutes before bronchoscopy, resulted in greater patient satisfaction and better tolerance than intravenous administration of midazolam, however, patients using Dexmedetomidine needed accurate monitoring [15]. In our study, a reduction in side effects was observed following the use of lidocaine, and it was found that the use of lidocaine leads to major satisfaction among patients and physicians compared to midazolam; but the findings show that combining lidocaine with midazolam can achieve better results. In 2020, Koulelidis et al. performed a study on the comparison of the lidocaine method with lidocaine + midazolam. In the lidocaine + midazolam group, significant differences in pain reduction were observed; they stated that the use of midazolam with lidocaine reduced respiratory side effects and improved patient satisfaction in this group. In a study conducted by Xiujing Dang et al. in 2017, it was found that co-administration of dexmedetomidine and sufentanil, in addition to shortening the duration of anesthesia, decreased the patient's movements during the procedure and reduced the occurrence of tachycardia during and after the procedure. In this method, the hemodynamic profile of the patients was more stable and the need for complementary sedatives was also reduced; whereas, in our study, the use of lidocaine showed similar properties to concomitant administration of dexmedetomidine and sufentanil. therefore, lidocaine can be used as an alternative to the above-mentioned combination, due to its availability, fewer complications, and ease of use [23]. In general, topical administration of lidocaine during bronchoscopy is widely used and is recommended according to current guidelines [2, 4, 24]. However, there are still some concerns about the use of lidocaine, considering its side effects such as cardiac arrhythmia, seizures, or impaired pulmonary function [25-27]; accordingly, it is important to pay attention to the doses of lidocaine; also, other findings indicate that the use of nebulizers can be effective in reducing the dose and increasing the efficacy of the drug [28, 29]

In 2017, a study by Toblas Muller et al., which examined the combination of fentanylpropofol and midazolam in candidate patients for flexible bronchoscopy, found that induction of triple anesthesia (a combination of three drugs; Fentanyl-propofol and midazolam) have been shown to be completely safe in performing flexible bronchoscopy and was associated with reducing the dose of prescribed sedatives [30];In the present study, lidocaine alone has the properties of inducing triple anesthesia, so the use of this drug can be preferred to the mentioned combination.

The British thoracic society has recommended protocols to reduce complications and increase patients' comfort [2]. Numerous studies have evaluated appropriate anesthesia methods for bronchoscopy and suggested the use of different anesthetic drugs, and all of them have shown different levels of satisfaction, however, a standard protocol that can provide a 100% rate of satisfaction for physicians and patients has not been presented so far [29, 31-34].

In summary, the findings of the present study showed that the use of lidocaine induced a higher rate of satisfaction for physicians and patients compared to the use of midazolam. Also, the complications of bronchoscopy (nausea, decreased arterial oxygen saturation, sore throat, cough, and need for intubation) were lower during bronchoscopy in the lidocaine group.

One of the limitations of the present research was the lack of cooperation between patients and staff to follow up and examine patients, which was removed with the necessary coordination. One of the strengths of the present study was the appropriate sample size, which was effective in the accuracy of the results and another outcome of this study was that the information needed for future research projects as well as the necessary evidence for choosing a more appropriate method of anesthesia in bronchoscopy was provided, especially in people with debilitating diseases.

5. CONCLUSION

Decreased need for intubation, reduced duration of bronchoscopy, reduced hypoxemia, and increased satisfaction, as well as fewer side effects in the lidocaine-based group, indicated that lidocaine was more effective than midazolam; according to this finding, it can be concluded that lidocaine is a suitable alternative drug for use in bronchoscopy. Also, conduction of similar research on a larger scale and examination of these cases in other age groups is recommended.

6. REFERENCES

- [1] Du Rand IA, Barber PV, Goldring J, Lewis RA, Mandal S, Munavvar M, Rintoul RC, Shah PL, Singh S, Slade MG, et al. Summary of the British Thoracic Society guidelines for advanced diagnostic and therapeutic flexible bronchoscopy in adults. *Thorax*. 2011; 66(11): 1014-1015. doi:10.1136/thoraxjnl-2011-201052
- [2] Du Rand IA, Blaikley J, Booton R, Chaudhuri N, Gupta V, Khalid S, Mandal S, Martin J, Mills J, Navani N, et al. British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults: accredited by NICE. *Thorax.* 2013; 68 Suppl 1:i1-i44. doi:10.1136/thoraxjnl-2013-203618
- [3] McCambridge AJ, Boesch RP, Mullon JJ. Sedation in Bronchoscopy: A Review. *Clinics in chest medicine*. 2018; 39(1): 65-77. doi:10.1016/j.ccm.2017.09.004
- [4] Wahidi MM, Jain P, Jantz M, Lee P, Mackensen GB, Barbour SY, Lamb C, Silvestri GA. American College of Chest Physicians consensus statement on the use of topical anesthesia, analgesia, and sedation during flexible bronchoscopy in adult patients. *Chest.* 2011; 140(5): 1342-1350. doi:10.1378/chest.10-3361
- [5] Chadha M, Kulshrestha M, Biyani A. Anaesthesia for bronchoscopy. *Indian J Anaesth*. 2015; 59(9): 565-573. doi:10.4103/0019-5049.165851
- [6] Abdelmalak B, Khanna A, Tetzlaff J. Fospropofol, a new sedative anesthetic, and its utility in the perioperative period. *Curr Pharm Des.* 2012; 18(38): 6241-652. doi:10.2174/138161212803832308
- [7] Bauer TL, Berkheim DB. Bronchoscopy: Diagnostic and Therapeutic for Non-Small Cell Lung Cancer. *Surgical oncology clinics of North America*. 2016; 25(3): 481-491. doi:10.1016/j.soc.2016.02.009
- [8] Foster WM, Hurewitz AN. Aerosolized lidocaine reduces dose of topical anesthetic for bronchoscopy. *The American review of respiratory disease*. 1992; 146(2): 520-522. doi:10.1164/ajrccm/146.2.520

- [9] Graham DR, Hay JG, Clague J, Nisar M, Earis JE. Comparison of three different methods used to achieve local anesthesia for fiberoptic bronchoscopy. *Chest.* 1992; 102(3): 704-707. doi:10.1378/chest.102.3.704
- [10] Stolz D, Chhajed PN, Leuppi J, Pflimlin E, Tamm M. Nebulized lidocaine for flexible bronchoscopy: a randomized, double-blind, placebo-controlled trial. *Chest.* 2005; 128(3): 1756-1760. doi:10.1378/chest.128.3.1756
- [11] Charalampidou S, Harris E, Chummun K, Hawksworth R, Cullen JP, Lane SJ. Evaluation of the efficacy of nebulised lignocaine as adjunctive local anaesthesia for fibreoptic bronchoscopy: a randomised, placebo-controlled study. *Irish medical journal*. 2006; 99(1): 8-10.
- [12] Dhooria S, Chaudhary S, Ram B, Sehgal IS, Muthu V, Prasad KT, Aggarwal AN, Agarwal R. A Randomized Trial of Nebulized Lignocaine, Lignocaine Spray, or Their Combination for Topical Anesthesia During Diagnostic Flexible Bronchoscopy. *Chest*. 2020; 157(1): 198-204. doi:10.1016/j.chest.2019.06.018
- [13] Poletti V, Casoni GL, Gurioli C, Ryu JH, Tomassetti S. Lung cryobiopsies: a paradigm shift in diagnostic bronchoscopy? *Respirology*. 2014; 19(5): 645-654. doi:10.1111/resp.12309
- [14] Contoli M, Gnesini G, Artioli D, Ravenna C, Sferra S, Romanazzi C, Marangoni E, Guzzinati I, Pasquini C, Papi A, et al. Midazolam in flexible bronchoscopy premedication: effects on patient-related and procedure-related outcomes. *Journal of bronchology & interventional pulmonology*. 2013; 20(3): 232-240. doi:10.1097/LBR.0b013e3182a10b7a
- [15] Goneppanavar U, Magazine R, Periyadka Janardhana B, Krishna Achar S. Intravenous Dexmedetomidine Provides Superior Patient Comfort and Tolerance Compared to Intravenous Midazolam in Patients Undergoing Flexible Bronchoscopy. *Pulmonary medicine*. 2015; 2015: 727530. doi:10.1155/2015/727530
- [16] Matsumoto T, Otsuka K, Kato R, Shimizu R, Otoshi T, Fujimoto D, Kawamura T, Tamai K, Nagata K, Otsuka K, et al. Evaluation of discomfort and tolerability to bronchoscopy according to different sedation procedures with midazolam. *Experimental and therapeutic medicine*. 2015; 10(2): 659-664. doi:10.3892/etm.2015.2547
- [17] Hirose T, Okuda K, Ishida H, Sugiyama T, Kusumoto S, Nakashima M, Yamaoka T, Adachi M. Patient satisfaction with sedation for flexible bronchoscopy. *Respirology*. 2008; 13(5): 722-727. doi:10.1111/j.1440-1843.2008.01311.x
- [18] Gu W, Xu M, Lu H, Huang Q, Wu J. Nebulized dexmedetomidine-lidocaine inhalation as a premedication for flexible bronchoscopy: a randomized trial. *Journal of thoracic disease*. 2019; 11(11): 4663-4670. doi:10.21037/jtd.2019.10.59
- [19] Madan K, Mittal S, Gupta N, Biswal SK, Tiwari P, Hadda V, Mohan A, Guleria R. The Cricothyroid versus Spray-As-You-Go Method for Topical Anesthesia during Flexible Bronchoscopy: The CRISP Randomized Clinical Trial. *Respiration; international review* of thoracic diseases. 2019; 98(5): 440-446. doi:10.1159/000501563
- [20] Kongpolprom N, Ailachamroon D, Wongmanee K. A Comparison of 2% lidocaine viscous versus 2% lidocaine solution for improving discomfort and satisfaction in patients undergoing flexible bronchoscopy. *Eur Respiratory Soc*; 2017.
- [21] Dreher M, Cornelissen CG, Reddemann MA, Müller A, Hübel C, Müller T. Nebulized versus Standard Local Application of Lidocaine during Flexible Bronchoscopy: A Randomized Controlled Trial. *Respiration; international review of thoracic diseases*. 2016; 92(4): 266-273. doi:10.1159/000449135
- [22] Gao Y, Kang K, Liu H, Jia L, Tang R, Zhang X, Wang H, Yu K. Effect of dexmedetomidine and midazolam for flexible fiberoptic bronchoscopy in intensive care

- [23] Dang X, Hu W, Yang Z, Su S. Dexmedetomidine plus sufentanil for pediatric flexible bronchoscopy: A retrospective clinical trial. *Oncotarget*. 2017; 8(25): 41256-41264. doi:10.18632/oncotarget.17169
- [24] Koulelidis A, Anevlavis S, Nikitidis N, Pappas P, Ntolios P, Karkabounas A, Boti V, Steiropoulos P, Karpathiou G, Eleftheriadis S, et al. Local Anesthesia Thoracoscopy with versus without Midazolam: A Randomized Controlled Trial. *Respiration; international review of thoracic diseases*. 2020; 99(9): 789-799. doi:10.1159/000509761
- [25] Wu FL, Razzaghi A, Souney PF. Seizure after lidocaine for bronchoscopy: case report and review of the use of lidocaine in airway anesthesia. *Pharmacotherapy*. 1993; 13(1): 72-78.
- [26] Peacock AJ, Benson-Mitchell R, Godfrey R. Effect of fibreoptic bronchoscopy on pulmonary function. *Thorax*. 1990; 45(1): 38-41. doi:10.1136/thx.45.1.38
- [27] Mittal S, Mohan A, Madan K. Ventricular Tachycardia and Cardiovascular Collapse following Flexible Bronchoscopy: Lidocaine Cardiotoxicity. *Journal of bronchology & interventional pulmonology*. 2018; 25(2): e24-e6. doi:10.1097/lbr.00000000000448
- [28] Pirlich N, Lohse JA, Schmidtmann I, Didion N, Piepho T, Noppens RR. A comparison of the Enk Fiberoptic Atomizer Set(TM) with boluses of topical anaesthesia for awake fibreoptic intubation. *Anaesthesia*. 2016; 71(7): 814-822. doi:10.1111/anae.13496
- [29] 29.Müller T, Cornelissen C, Dreher M. Nebulization versus standard application for topical anaesthesia during flexible bronchoscopy under moderate sedation - a randomized controlled trial. *Respiratory research*. 2018; 19(1): 227. doi:10.1186/s12931-018-0926-5
- [30] Müller T, Thümmel K, Cornelissen CG, Krüger S, Dreher M. Analogosedation during flexible bronchoscopy using a combination of midazolam, propofol and fentanyl A retrospective analysis. *PLoS One.* 2017; 12(4): e0175394. doi:10.1371/journal.pone.0175394
- [31] Ibrahim E, Sultan W, Helal S, Abo-Elwafa H, Abdelaziz A. Pregabalin and dexmedetomidine conscious sedation for flexible bronchoscopy: a randomized doubleblind controlled study. *Minerva anestesiologica*. 2019; 85(5): 487-493. doi:10.23736/s0375-9393.18.12685-x
- [32] Riachy M, Khayat G, Ibrahim I, Aoun Z, Dabar G, Bazarbachi T, Khalil N, Habr B. A randomized double-blind controlled trial comparing three sedation regimens during flexible bronchoscopy: Dexmedetomidine, alfentanil and lidocaine. *The clinical respiratory journal*. 2018; 12(4): 1407-1415. doi:10.1111/crj.12669
- [33] Zhang H, Fang B, Zhou W. The efficacy of dexmedetomidine-remifentanil versus dexmedetomidine-propofol in children undergoing flexible bronchoscopy: A retrospective trial. *Medicine (Baltimore)*. 2017; 96(1): e5815. doi:10.1097/md.00000000005815
- [34] Li X, Wang X, Jin S, Zhang D, Li Y. The safety and efficacy of dexmedetomidineremifentanil in children undergoing flexible bronchoscopy: A retrospective dose-finding trial. *Medicine (Baltimore)*. 2017; 96(11): e6383. doi:10.1097/md.00000000006383