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Original Article

Comparison of the effects of midazolam and dexmedetomidine on cognitive functions, anxiety and hemodynamics in fiber optic bronchoscopy

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Abstract

Aim: Fiber optic bronchoscopy (FB) is an invasive method used in the diagnosis and treatment of lung diseases. There are several different sedation guidelines for FB, all of which are used by different healthcare providers. We aimed to compare the sedative effects of midazolam and dexmedetomidine in FB, together with their effects on cognitive functions, hemodynamic parameters, and patient satisfaction and anxiety.

Material and Methods: The study includes a total of 80 randomly selected subjects aged ≥ 18 years. The subjects were divided into two groups: midazolam (n = 40) and dexmedetomidine (n = 40). We evaluated treatment outcomes using hemodynamic findings, the Mini-Mental State Examination, the State Anxiety Inventory, and a survey form.

Results: The two groups were not significantly different in terms of systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, and peripheral oxygen values. Patient and medical professional satisfaction levels were significantly higher in the dexmedetomidine group. The cognitive functions and anxiety levels both before and after the intervention were similar for the two groups.

Conclusion: We conclude that dexmedetomidine can be used safely for sedation in fiber optic bronchoscopy and is preferable to midazolam.

Keywords: Anxiety; bronchoscopy; dexmedetomidine; hemodynamics; midazolam

INTRODUCTION

Fiber optic bronchoscopy (FB) is an invasive method used in the diagnosis and treatment of lung diseases. Diagnostic bronchoscopy is used for bronchoalveolar lavage in foreign body aspirations, hemoptysis, tracheoesophageal fistula, airway tumors, tracheomalacia and infections (1,2). It can also be used for treatment purposes as in the resection of intraluminal tumors, stent applications, foreign body aspirations, endobronchial closure, and endolaryngeal and endobronchial balloon dilatations (1,2).

There are several different sedation guidelines for FB, all of which are used by different healthcare providers. These guidelines differ in whether to apply sedation and the methods of sedation, premedication and topical anesthesia (3). According to the American College of Chest Physicians (ACCP), sedation prior to FB helps with tolerance to the intervention and increases patient satisfaction (4). An ideal sedative should have minimal side effects, a small amount of inactive metabolites, should allow for quick recovery after the operation, and should not cause re-sedation (5). Drugs that can be used for sedation for bronchoscopy include topical anesthetics (cocaine, lidocaine, benzocaine, tetracaine), benzodiazepines (lorazepam, midazolam, diazepam), opiates (hydrocodone, alfentanil, fentanyl, remifentanil), propofol, ketamine, fospropofol and dexmedetomidine (3).

Among these, midazolam is commonly preferred for its short half-life, and its amnesic and anxiolytic potency, and sedative effect (6). However, both benzodiazepines and narcotic analgesics can cause hypoxia and decreased peripheral arterial saturation (7). Sedation-related deaths shortly after the administration of midazolam also bring forth the question of its safety (8,9).

Dexmedetomidine is a highly selective α2-agonist (10,11). It has analgesic, sedative, and anxiolytic properties. Healthcare providers have recently begun

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using dexmedetomidine for the sedation of mechanical ventilation patients in intensive care units (11). Dexmedetomidine is a relatively new drug, mainly preferred due to providing sedation without respiratory depression (11). Medical establishments have recently started to use it for sedation in bronchoscopy.

Currently, there is not a standard or optimal sedation protocol for bronchoscopy procedures. Researchers state that further studies are needed to evaluate the effects of new sedative options like dexmedetomidine in bronchoscopy (5). We aimed to compare the sedative effects of midazolam and dexmedetomidine in the context of FB, together with their effects on cognitive functions, hemodynamic parameters, and patient satisfaction and anxiety. "No clinical studies are available; which compare the use of two sedative agents during fiber optic bronchoscopy in Turkey. Therefore, we believe that our study will contribute to the information in the literature.

MATERIAL and METHODS

The study was conducted at Kars Harakani Public Hospital between January 2019 and January 2020. The study was granted ethical approval by the ethics committee of Kafkas University Faculty of Medicine. Each subject gave written consent to participate. The study was designed as a prospective, randomized, double-blind trial. There were a total of 80 subjects that were divided into two study groups. The subjects did not take alcohol or sedative drugs within 24 hours before the procedure. An assistant bronchoscopist conducted the anesthesia. The exclusion criteria were as follows: (a) mental retardation, (b) chronic alcohol use, (c) psychiatric treatment, (d) heart, liver and kidney diseases, (e) pregnancy, and (f) being allergic to midazolam or dexmedetomidine. FB patients were sedated with midazolam (group M) and dexmedetomidine (group D). Group D patients were given 1 µg/kg of dexmedetomidine 10 minutes before FB, with an infusion time of at least 10 minutes. The anesthesia was maintained at Ramsey sedation score 3. Group M patients were given 0.02 mg/kg of midazolam; the infusion time was at least 10 minutes. The anesthesia was maintained at Ramsey sedation score 3.

Patients' consciousness levels, vital signs (ECG, heart rate, peripheral oxygen saturation, non-invasive blood pressure) and sedation scores were recorded before and after the procedure. The patients' pre- and post-FB (10-, 30- and 60-minute after FB) heart rate, peripheral oxygen saturation, non-invasive blood pressure and mean arterial pressure were recorded. After the procedure, both the patients and the bronchoscopist were asked questions using the survey form. Recovery was evaluated according to the modified Aldrete's scoring system. After the modified Aldrete's score reached 10, the patients were asked about how they perceived the procedure (1: very difficult, 2: difficult, 3: easy), whether they would consent to the same procedure to be repeated in the future if required, and their degree of amnesia (1: I do not remember anything about the procedure, 2: I remember some parts of the procedure, 3: I clearly remember the entire procedure). The bronchoscopist that was blind to the used sedative was asked about the difficulty of that specific procedure (1: easy, 2: difficult) and whether the patient had coughed or swallowed during the treatment (1: no coughs or swallowing, 2: patient coughed and swallowed). All subjects were examined by a psychiatrist before and after the procedure using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), the Mini-Mental State Examination, and the State Anxiety Inventory. The results were statistically analyzed. The psychiatric evaluation scales were used only after the subjects had a modified Aldrete's score of 10, both before and after the procedure.

Examination Scales

Standardized Mini-Mental State Examination (SMMSE) This scale is one of the most commonly used tools to evaluate cognitive dysfunction. It evaluates a person's orientation to time and place, recall ability, short-term memory, arithmetic ability, language skills, and visual-spatial skills. The scale is scored over 30, where a low score reflects cognitive impairment (12). The scale was first developed by Folstein et al. (13), who reported high retest and inter-rater reliability. SMMSE was found to be correlated with routine clinical examination results and several neurological scales (14). The validity and reliability of the Turkish version were tested by Gungen et al. (15).

The State Anxiety Inventory (S-Anxiety): This four-point Likert-type scale was developed by Spielberger et al. in 1970 to determine the state of anxiety of a patient at a given time (16) (1: not at all, 2: somewhat, 3: moderately so, 4: very much so). The validity and reliability of the Turkish version were tested in 1977 (17). S-Anxiety is a highly sensitive tool for evaluating the variable emotional reactions. The total score obtained from both inventories ranges from 20 to 80 where a high score indicates a high anxiety level, and a low score indicates a low anxiety level.

Modified Aldrete's Scoring System

The modified Aldrete's Scoring System is used to determine the safety of removing patients from the postanesthesia care unit by evaluating postanesthetic recovery (18). This scoring system examines muscle activity, respiration, blood pressure, consciousness, and oxygen saturation. Each item is assigned a score between 0 and 2, and the highest possible total score is 10. Patients with a total score of 8 or higher can be safely discharged from the recovery room (19).

Statistical analysis

It was done using SPSS 20.0 statistical package program. Mean, Standard deviation, t-Student Test, Mann Whitney U Test and Chi-Square Test were used. Results were evaluated as significant at $p < 0.05$ level.

RESULTS

There were a total of 80 subjects divided into two groups: midazolam (group M, n = 40) and dexmedetomidine (group D, n= 40). The mean ages of groups M and D were

56.78 ± 12.08 and 60.28 ± 8.42 years, respectively (p > 0.05). There were 9 women and 31 men in Group M, and 9 women and 31 men in Group D (p > 0.05) (Table 1).

Systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, and peripheral oxygen saturation values of the two groups were measured a total of 4 times: before and 10, 30 and 60 minutes after the procedure. These findings were not significantly different for the two groups at any time (p > 0.05) (Table 2).

Table 1. Sociodemographic characteristics of the subjects

	Grup M (n=40)	Grup D (n=40)	p
Age(year) (Mean±Sd)	56.78±12.088	60.28±8.422	>0.05
Gender			
Male	31	31	>0.05
Female	**9**	**9**	

M; Midazolam, D; Dexmedetomidine, Mean±standart deviation (Mean±Sd), p<0.05

Table 2. Comparison of the study groups regarding systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, and peripheral oxygen saturation

	Grup M (n=40) Mean±Sd				Grup D (n=40) Mean±Sd			
	t_1	t_2	t_3	t_4	t_1	t_2	t_3	t_4
SBP	135.83±18.18	140.30±15.28	130.40±14.95	125.35±12.35	143.35±21.44	145.43±29.72	127.50±20.27	124.5+17.41
DBP	82.27±13.28	84.25±17.59	75.33±9.98	76.08±7.52	80.90±10.70	85±16.69	77.80±11.40	76.37±9.33
MAP	99.00±14.79	103.77±14.70	93.95±10.16	92.58±7.92	101.38±12.96	105.07±19.43	94.17±12.97	92.35±11.14
SpO2	91.05±10.22	94.58±3.33	94.65±4.42	94.50±2.47	93.33±4.59	92.95±6.69	94.13±2.95	92.65±6.61
HR	90.73±14.58	94.50±17.43	91.10±12.37	91.08±10.89	91.40±15.15	94.05±18.10	91.45±19.48	90.35±15.29

M; Midazolam, D; Dexmedetomidine, Mean±standart deviation (Mean±Sd), Systolic blood pressure (SKB), Diastolic blood pressure (DBP), Mean arterial pressure (MAP), Peripheral oxygen saturation (SpO2), Heart rate (HR), t_1 (Preoperative), t_2 (Postoperative10.minute), t_3 (Postoperative30. minute), t_4 (Postoperative60.minute), p<0.05*, There was no statistically significant difference between the two groups

Table 3. Comparison of the study groups regarding amnesia, evaluation of the procedure by the patient, the patient allowing a repeat procedure, the difficulty of the procedure as evaluated by the doctor, and cough and swallowing findings

	Grup M (n:40)	Grup D (n:40)	P
Amnesia Degree			
Don't remember anything	23	23	>0.05
Don't remember some things	16	16	
I remember everything	1	1	
Evaluation of the procedure by the patient			
So hard	14	2	**<0.01**
Hard	24	13	
Easy	2	25	
The patient allowing a repeat procedure			
Yes	17	28	**<0.05**
No	23	12	
The difficulty of the procedure as evaluated by the doctor			
Easy	12	27	**<0.05**
Hard	28	13	
Cough and swallowing			
Yes	10	28	**<0.01**
No	30	12	

M; Midazolam, D; Dexmedetomidine, p<0.05, p<0.01

Both the subjects and the bronchoscopist were asked about the difficulty of the procedure. We found that coughing and swallowing were significantly less common in the dexmedetomidine group ($p < 0.01$). Also, the bronchoscopist evaluated the procedure to be significantly easier in the dexmedetomidine group ($p < 0.05$). The subjects were asked whether they would allow the procedure to be repeated in the future, and it was found that group D patients were significantly more likely to allow a repeat intervention ($p <0.05$). Patients in the dexmedetomidine group found the procedure to be significantly more comfortable than the midazolam group ($p < 0.01$). The amnesia or side effect findings of the two groups were not significantly different ($p > 0.05$). In group D, there were 8 cases of hypotension and 5 cases of hypertension. In group M, there was 1 case of hypotension, 1 case of agitation, and 4 cases of hypertension. (Table 3)

All subjects were examined by a psychiatrist, where none of the subjects had a psychiatric disorder or abnormal cognitive functions. There was no statistically significant difference between the S-Anxiety scores, the Mini-Mental State Examination scores or the SMMSE subscale scores of the two groups ($p > 0.05$). (Table 4).

Table 4. . Comparison of the study groups regarding the Status Anxiety Inventory and the Mini Mental State Examination scores, and the Orientation, Recall Ability and Short-Term Memory subscores of MMSE

	Grup M (n:40) Mean±Sd		Grup D (n=40) Mean±Sd	
	Prior	After	Prior	After
SAI	33.23±8.71	33.63±6.90	36.10±9.53	34.05±6.26
MMSE	24.60±3.17	23.60±3.58	25.53±2.79	24.58±3.58
Orientation	9.07±1.20	8.95±1.19	9.33±1.04	9.15±1.42
Short-Term Memory	2.87±0.40	2.78±0.53	2.93±0.35	2.87±0.40
Recall Ability	2.20±0.79	1.95±0.59	2.20±0.68	2.20±0.68

M; Midazolam, D; Dexmedetomidine, Mean±standart deviation (Ort±Sd), Status Anxiety Inventory (SAI), Mini Mental State Examination (MMSE), p<0.05*, There was no statistically significant difference between the two groups

DISCUSSION

Bronchoscopy is most commonly performed under moderate sedation. Moderate sedation is the depression of the consciousness to a level that cardiac functions are maintained, the airway is patent, and the individuals can respond to verbal stimuli (3). Deep sedation includes the loss of reflexes where the patient only responds to painful stimuli. Deep sedation can disturb respiratory functions and airway patency (20). Sedation also aims to create an anxiolytic effect and amnesia. The ideal sedative agent will be fast-acting, have a short duration of action, and will not impair cardiovascular stability or cause respiratory depression whilst having analgesic and amnestic efficacy (5).

Different anesthetic agents have different degrees and durations of effect on central nervous system functions. It takes some time before the psychomotor functions are restored to their pre-intervention levels (21). Cognitive functions include higher brain functions such as consciousness, attention, learning, memory, perception, orientation, intelligence, action, emotion, dreaming, problem-solving, decision-making, speaking, reading, writing and calculating (22). The purpose of the postoperative evaluation of cognitive functions is to detect mental changes that occur after anesthesia and the intervention, and to evaluate recovery by determining residual effects of anesthesia (23). The examination of memory, perception, attention, other cognitive functions and psychomotor abilities are as important as the evaluation of respiratory and cardiovascular functions in determining recovery from anesthesia (24). Said cognitive functions can be evaluated with the Mini-Mental State Examination (25). Studies have shown that MMSE can distinguish healthy patients from patients with impaired cognitive function with high reliability and validity (25). In our study, the post-intervention MMSE scores of the two groups were not significantly different, which indicates that the cognitive functions of the two groups were similar. One study compared dexmedetomidine with remifentanil and found that dexmedetomidine had a significantly smaller impact on postoperative cognitive functions.

Most patients develop some degree of anxiety when waiting for an intervention after the initial diagnosis. The severity of this anxiety is associated with the diagnosis itself, the affected organ, the difficulty and risks of the intervention, as well as the predispositions of the individual. State anxiety is defined as the reaction of an individual to real or perceived danger at a given moment, which is influenced both by internal and external factors (26). We evaluated our subjects' anxiety levels using the State Anxiety Inventory (S-Anxiety). The two study groups were not significantly different in terms of anxiety scores. However, the pre- and post-intervention anxiety scores of group M were similar whereas the anxiety scores of group D had significantly decreased. Both dexmedetomidine and midazolam are reported to reduce anxiety when used for local anesthesia. We believe that the similar pre-

intervention S-Anxiety scores of the two groups support the accuracy of our evaluation of cognitive functions.

We evaluated intervention satisfaction by directing both the subjects and the physician certain questions. Our results indicate that dexmedetomidine allows for a more comfortable procedure, both for the patient and the physician, where the patients are more likely to allow a repeat intervention and less likely to cough and swallow during the procedure. Our findings are consistent with the literature.

The cardiovascular findings (systolic and diastolic blood pressures, heart rate, and mean arterial pressure) were not different for the two groups at any point before or after the intervention. Midazolam is commonly used for sedation in bronchoscopy interventions. We believe that dexmedetomidine can be a viable alternative.

We observed that peripheral oxygen saturation was normal in both groups, with a minimal increase after the procedure. This finding can be attributed to the more regular breathing that results from decreased anxiety.

Our study has some limitations. Bispectral Index scores can be used for monitoring the sedation depth during bronchoscopy. The depth of sedation was not monitored with the Bispectral Index and this can be a limitation for our study. The selection of the study sample from a single study site can be another limitation. One can suggest that large-scale and multi-center studies can yield more specific results.

CONCLUSION

We conclude that dexmedetomidine and midazolam are similar in their effects on cognitive functions, anxiety levels, and vital signs when used for sedation in bronchoscopy. However, dexmedetomidine was found to be superior in terms of patient and physician satisfaction. Midazolam is commonly used in bronchoscopy, and dexmedetomidine has recently started to be used for the same purpose. We found that dexmedetomidine can be used safely for sedation in bronchoscopy and can be preferable to midazolam.

Competing interests: The authors declare that they have no competing interest.

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