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Conscious sedation with midazolam and dezocine for diagnostic flexible bronchoscopy

X.-K. CHEN[1], Y.-P. ZHOU[1], X. ZHANG[2], L.-P. XIA[1], A.-F. LI[1], H. LIU[1], H.-Q. YU[1]

[1]Deparment of Respiratory Diseases, Affiliated Futian People's Hospital of Guangdong Medical College, Shenzhen, Guangdong, P.R. China
[2]Anesthesiology, Affiliated Futian People's Hospital of Guangdong Medical College, Shenzhen, Guangdong, P.R. China

Xiao-Ke Chen and Yi-Ping Zhou contributed equally to this work

Abstract. – OBJECTIVE: This study aimed to assess the benefits and risks of conscious sedation with midazolam and dezocine in diagnostic flexible bronchoscopy (FB).

PATIENTS AND METHODS: This prospective case control study enrolled 40 non-sedated and 40 sedated subjects who underwent diagnostic FB. All received the standard upper airway preparation, while sedated subjects received midazolam and dezocine for conscious sedation. Subject discomforts during FB were assessed using the verbal analogue score (VAS, 0-10 scale). Willingness to return was assessed as five scales to monitor subject's satisfaction level. Safety profiles throughout the procedures were also assessed.

RESULTS: Anterograde amnesia existed in 75.0% sedated subjects. Compared to non-sedated subjects, sedated ones expressed less discomfort, with lower VAS scores regarding scope insertion (4 [0-10] vs. 0 [0-4], $p < 0.001$), cough (5.5 [0-10] vs. 0 [0-4], $p < 0.001$), dyspnea (3.5 [0-10] vs. 0 [0-4], $p < 0.001$), pain (3 [0-10] vs. 0 [0-5], $p < 0.001$), and global tolerance of the procedures (5.5 [1-10] vs. 0 [0-5], $p < 0.001$). More sedated subjects expressed willingness to return (90.0% vs. 30.0%, $p < 0.001$). Sedated subjects had no more hypoxemic episodes during the procedure (7.5% vs. 5.0%, $p > 0.99$), which were all transient and not life-threatening.

CONCLUSIONS: Conscious sedation with midazolam and dezocine reduces discomforts, improves satisfaction level, and carries no significantly risks in subjects undergoing diagnostic FB.

Key Words:
Conscious sedation, Flexible bronchoscopy, Midazolam, Dezocine.

Introduction

Flexible bronchoscopy (FB) plays an important role in the diagnosis and treatment of pulmonary diseases. While FB is an extremely safe procedure as long as some basic precautions are taken, patients undergoing FB may experience cough, shortness of breath, sore nose, sore throat, or other discomfort. More than half of the patients express fear of the discomfort they may have during this procedure[1]. Current British Thoracic Society (BTS) guidelines suggest that sedation should be offered to all patients undergoing diagnostic FB, except for those with contraindications. Sedation may reduce patient's discomfort level, and make the procedure easier for the bronchoscopist to perform and, thereby, the patient is more willing to accept a repeat procedure (if necessary)[2]. A study done in Malaysia reported that 80% of patients preferred to be sedated[3]. Sedation in FB is widely used in Europe and in the USA. However, it is not a daily routine practice in China, and most of the FB performed is under local anesthesia without sedation. This study aimed to assess the benefits and risks of conscious sedation with midazolam and dezocine in FB.

Patients and Methods

Patients

During January 2013 to June 2013, subjects who were willing to receive intravenous conscious sedation when undergoing diagnosis FB, were evaluated for enrollment. The study was approved by the Institutional Ethics Committee and each subject gave written consent to participate. We included 80 subjects who underwent FB. They were randomly assigned to two groups (40 subjects in each group): Sedatives (received intravenous midazolam and dezocine) and Non-sedatives (only local anesthesia). Exclusion criteria were: inability or refusal to give informed

Corresponding Author: Xiaoke Chen, MD; e-mail: xiaokechengd@163.com

consent, intubation, respiratory failure, intolerance or allergy to the study drug. Subjects younger than 18 years of age, pregnant and nursing women were excluded as well.

Pulse oximetric results were recorded continuously during the procedure and automated noninvasive blood pressure monitoring was performed every 5 mins. A standard three-lead electrocardiography machine monitored the heart rate and rhythm. Supplemental oxygen was administered via nasal prongs if SPO_2 decreased to less than 90%.

Sedation Procedure

Topical anesthesia was achieved by applying the lidocaine gel into one nostril and giving lidocaine 2% solution down the bronchoscope with the spray-as you-go technique. Subjects in the control group received only lidocaine for upper airway preparation. In the study group, subjects received 2.5-5 mg dezocine and 1-3mg midazolam intravenously, according to age and body weight. Dezocine was injected 10 mins before the examination while midazolam was injected immediately prior to FB. After FB insertion, right above the vorcal clord, subsequent boluses of 1-2 mg midazolam were administered if the subject was not sufficiently sedated.

Evaluation and Score

Subject's discomfort level during FB were assessed using the verbal analogue score (VAS), ranging from the lowest point (0, no bother) to the highest point (10, worst intolerable level). The scored was given based on the following aspects: bronchoscopy insertion, cough, dyspnea, pain and global tolerance of the entire procedure. Willingness to return for a second FB if needed was evaluated as a five-scale question (i.e., definitely would, probably would, unsure, probably not, and definitely not). Non-sedated subjects were asked the same questions right before hospital discharge.

Statistical Analysis

All statistical analyses were performed using Statistical Package for the Social Science for windows version 17.0 (SPSS Inc., Chicago, IL, USA). Numeric and categorical parameters were analyzed by Chi-square. Age, weight, and procedure time were presented as mean ± standard deviation (SD). Mann-Whitney U test was used for analysis of VAS, presented as the median (range). $p < 0.05$ was considered to indicate a statistical significant difference.

Results

Subject characteristics of both groups were comparable based on age, gender, weight, ASA physical status, lung function, rates of hypertension and coronary heart disease (Table I). There

Table I. Patient Characteristics, Insertion route and Bronchoscopic Procedures.

	Non-sedatives (n = 40)	Sedatives (n = 40)	*p*-value
Patient characteristics			
Male, n (%)	24 (60.0%)	26 (65.0%)	0.817
Age (mean ± SD)	56.0 ± 11.4	57.5 ± 10.6	0.544
Weight (mean ± SD), kg	58.1 ± 12.1	59.2 ± 10.4	0.664
ASA ≤ 2, n (%)	22 (55.0%)	24 (60.0%)	0.821
FEV1% predicted	62.3 ± 14.5	60.2 ± 13.5	0.505
FVC% predicted	65.2 ± 17.4	63.3 ± 16.6	0.619
Hypertension	10 (25.0%)	12 (30.0%)	0.802
Coronary heart disease	5 (12.5%)	6 (15.0%)	> .99
Insertion route			
Nasal	38 (95.0%)	36 (90.0%)	0.671
Oral	2 (5.0%)	4 (10.0%)	0.671
Procedures during FB, n (%)			
Bronchial biopsy	18 (45.0%)	19 (47.5%)	> .99
Bronchial washing	20 (50.0%)	21 (52.5%)	> .99
Bronchial brushing	15 (37.5%)	20 (40.0%)	0.367
Bronchoalveolar lavage	20 (50.0%)	22 (55.0%)	0.823

Abbreviations: ASA: American Society of Anesthesia physical status classification.

Table II. Procedure Time, Hemodynamic parameters, Post-bronchial Discomfort, and Willingness to Return.

	Non-sedatives (n = 40)	Sedatives (n = 40)	*p*-value
Procedure time (min)	14.2 ± 6.5	13.1 ± 5.5	0.460
Hemodynamic parameters			
MAX Heart rate	110.2 ± 11.5	100.1 ± 8.7	< 0.001
Systolic BP (mmHg)	145.1 ± 20.3	132.2 ± 16.5	0.002
Diastolic BP (mmHg)	87.3 ± 12.5	80.2 ± 9.2	0.006
Hypoxemia ($SPO_2 \leq 90\%$)	3 (7.5%)	4 (10.0%)	> .99
Post-bronchial discomfort			
Throat pain	15 (37.5%)	14 (35.0%)	> .99
Cough	20 (50.0%)	18 (45.0%)	0.823
Dyspnea	10 (25.0%)	2 (5.0%)	0.028
Malaise	5 (12.5%)	6 (15.0%)	1.000
Dizziness	3 (7.5%)	4 (10.0%)	1.000
Nose pain	6 (15.0%)	4 (10.0%)	0.735
Willing to return, n (%)			
Definitely would	12 (30.0%)	36 (90.0%)	< 0.001
Definitely would or probably would	24 (60%)	39 (96%)	< 0.001

was no significantly difference between the two groups in both insertion routes and procedures during FB.

The procedure time and post-bronchial discomfort level were similar in both groups, while hemodynamic parameters, such as maxium heart rate, systolic and diastolic BP, were more stable in the sedatives group (Table II). Subjects who received systemic sedation had lower VAS scores than those who received local anesthesia in terms of scope insertion, cough, dyspnea, pain, and global tolerance of the whole procedure (Table III). The average recovery times were 10.2±8.5 mins. The average induction dose of midazolam was 3.0±1.2 mg. Anterograde amnesia existed in 75.0% sedated subjects. Compared to the sedated subjects during FB, fewer non-sedated subjects expressed a definite intent to return for repeated bronchoscopy if needed.

Discussion

The British Thoracic Society guidelines recommend that sedation should be offered to patients where there is no contraindication, and also suggest that sedatives should be used in incremental doses to achieve adequate sedation and amnesia[2]. The present study showed that compared to local anesthesia, conscious sedation with midazolam and dezocine during FB, resulted in less patient discomfort in terms of scope insertion, cough, dyspnea, and pain as well as less post-bronchoscopy dyspnea. It also offered better tolerance and higher rates of willingness to return for a second FB if needed. In regard of safety, there were less hypertension or tachydardia events in sedated subjects. Patient's satisfaction level with sedation for FB was accessed based on the willingness to return: the rate was 90.0% for definitely would and 96.0% for definitely would or probably

Table III. Verbal Analogue Scale (VAS) Scores Made by the Patients

	Non-sedatives (n = 40)	Sedatives (n = 40)	*p*-value
Scope insertion	4 [0-10]	0 [0-5]	<0.001
Cough	5.5 [0-10]	0 [0-4]	<0.001
Dyspnea	3.5 [0-10]	0 [0-5]	<0.001
Pain	3 [0-10]	0 [0-5]	<0.001
Global tolerance of the procedures	5.5 [1-10]	0 [0-5]	<0.001

*Score 0 represented no bother while 10 represented the worst intolerable level.

would, which was at the higher rate range in the previous literatures. In a recent Japanese study, 65.8% of patients undergoing FB reported that they were willing to return for a repeat FB if necessary[4], while in a Taiwan study, 70.5% sedated patients expressed willingness to return[5]. The high patient satisfaction may be due to the high anterograde amnesia rate, which existed in 75.0% sedated patients.

In our study, the mean midazolam dose administered for conscious sedation during bronchoscopy was 0.05 mg/kg, which was at the lower dose range in the reported literatures[2]. We believe that this is likely due to the beneficial combined effect of midazolam and dezocine. Dezocine is an opioid mixed agonist-antagonist. In laboratory animals dezocine produces less respiratory depression compared to morphine[6] and dezocine has a ceiling to its analgesic and respiratory depressant effect[7]. In China, the prescription of dezocine is more common than any other narcotics for its little side effect. A combination of a benzodiazepine and narcotic has been widely used[5,7-9]. Combining the amnesic effects of a benzodiazepine with the analgesic and antitussive effects of a narcotic is rational. Unfortunately, such combination may be associated with more arterial desaturation and CO_2 retention than using midazolam alone[2]. In the present study we combined midazolam with dezocine as sedatives, which caused no more hypoxemic episodes. It might be due to the fact that the combinated narcotic is dezocine, and midazolam was given step by step, in which total amount was less compare to that reported in the previous literatures[2,10]. The least amount of midazolam in a subject was 1 mg, 0.025 mg/kg.

In some subjects, scope was not inserted into vocal cord until extra midazolam was administered to get enough conscious sedation, which might require 1-2 mins. However, the operation duration was not prolonged, for the hard insertion episodes to be reduced significantly. After general anesthesia, in some subjects, wallowing tongue may appeared, epiglottis was in the way covering the vocal cords and it was hard to raise. Going through the sideway or using a pillow under shoulder and back to achieve hypsokinesis of head, may improve the success rate. And yet for one subject with epiglottis covering the vocal cords, despite of using all the methods mentioned above, the epiglottis was still in the way and the vocal cords could not be exposed. At last, the epiglottis was raised by a direct laryngoscopy to expose the vocal cords, and then FB was inserted. Guan et al[11] reported that for the fiberoptic intubation management of the difficult airway in general anaesthesia patients, the success rate was only 33%. Considering the individual difference of sedatives effect, it is import to calculate the dose of midazolam.

A 60 years old subject smoking 20 cigarettes a day for 30 years, has been coughing for two months. Chest CT result was negative. The subject only accepted FB when it was performed with conscious sedation. The FB result showed squamous cell carcinoma in left lower lobe. Lung cancer is the most common cause of cancer deaths worldwide. It has been reported that nearly 800,000 Chinese men died of lung cancer in 1998[12]. Most lung cancer is in advanced stage when first diagnosed. Low-dose CT has been used for detecting lung cancer. 74% of the lung cancers are central lung cancer, which can be missed by CT at the early stage. However, early central lung cancer can be detected by FB, especially by autofluorescence bronchoscopy[13,14]. Due to the discomfort that it may cause, some patients may refuse FB, which can result in delay diagnosis.

Conclusions

The present study revealed that conscious sedation with proper dose of midazolam and dezocine reduces discomforts, improves satisfaction level, and carries no significantly risks in patients undergoing FB, which may decrease the mortality of lung cancer by increasing the early diagnostic efficiency.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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