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# A Comparative Evaluation of Lorazepam and Midazolam in Bronchoscopic Premedication

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## SUMMARY

We designed a prospective study to evaluate the efficacy of lorazepam and midazolam in bronchoscopic premedication. Sixty patients were randomly assigned to use nothing (Group 0) or lorazepam (Group 1) or midazolam (Group 2) for sedation before bronchoscopy. In lorazepam group FEV<sub>1</sub>, FVC reduced significantly ( $p < 0.05$ ). A questionnaire assessing patients cooperation was completed immediately after the bronchoscopy by the bronchoscopist. Among three groups, there were not any statistically differences in cooperation of patients ( $p > 0.05$ ). A questionnaire included three questions was administered to the patients, immediately after the procedure and the following day. First question assessed the patients perception of the procedure as easy or difficult. With significant statistically difference, at 24 hours, more patients in midazolam group described the procedure as easy than in those other groups ( $p < 0.05$ ). There was no statistically significantly difference among groups when assessing agreement a repeated bronchoscopy with second question ( $p > 0.05$ ). Patients recollection of procedure was asked in the third question and at 24 hours the recalling of the procedure was less precise in midazolam group, than those of other groups ( $p < 0.05$ ). In conclusion, midazolam was found a useful agent for bronchoscopy with satisfactory amnestic effectiveness. It was observed that lorazepam reduced FEV<sub>1</sub> and FVC, so it had to be used carefully when bronchoscopy performed on patients with COPD.

**Key Words:** Bronchoscopy, premedication, sedation.

## ÖZET

### Bronkoskopi Sedasyonunda Midazolam ve Lorazepamın Karşılaştırılması

Bronkoskopi premedikasyonunda lorazepam ve midazolamın etkinliğini değerlendirmek amacıyla prospektif bir çalışma düzenledik. Altmış hastanın randomize olarak seçilen 20'sine, bronkoskopi öncesi sedasyon için ilaç verilmezken (Grup 0), 20'sine lorazepam (Grup 1), 20'sine midazolam (Grup 2) verildi. Lorazepam grubunda FEV<sub>1</sub> ve FVC, anlamlı olarak düştü ( $p < 0.05$ ). Hastanın işlem sırasındaki kooperasyonunu değerlendiren bir anket hemen bronkoskopi sonrasında bronkoskopist tarafından uygulandı. Kooperasyon açısından 3 grup arasında istatistiksel olarak farklılık yoktu ( $p > 0.05$ ). Üç soru içeren bir anket hemen işlem sonrasında ve sonraki gün hastalara uygulandı. İlk soruda hastanın işlemi nasıl algıladığı (zor, kolay) araştırıldı. Midazolam grubundaki hastaların çoğu 24 saat sonra istatistiksel olarak anlamlı farklılıkla işlemi diğer gruplardaki hastalardan daha kolay olarak tanımlamışlardı ( $p < 0.05$ ). İkinci soruda değerlendirilen bronkoskopinin tekrar yapılmasına onay açısından üç grup arasında anlamlı istatistiksel farklılık gözlenmedi ( $p > 0.05$ ). Üçüncü soruda hastanın

*işlemi hatırlayıp hatırlamadığı değerlendirildi ve 24 saat sonunda midazolam grubundaki hastaların işlemi diğer gruptakilerden daha az hatırladığı anlaşıldı ( $p < 0.05$ ). Sonuçta midazolam amnestik etkinliğinin fazla olması nedeniyle bronkoskopi için uygun bulundu. Lorazepamın FEV<sub>1</sub> ve FVC'yi düşürdüğü, dolayısıyla kronik obstrüktif akciğer hastalığı (KOAH) grubunda bronkoskopi yapılırken dikkatli olunması gerektiği belirtildi.*

**Anahtar Kelimeler:** Bronkoskopi, premedikasyon, sedasyon.

Flexible fiberoptic bronchoscopy (FFB) is an indispensable tool for the diagnosis of and therapy for pulmonary diseases (1). Performance of FFB causes anxiety in some of the patients. The main purpose of bronchoscopic premedication is to minimize secretion and anxiety of patients (1-3). But there are some controversies about premedication for FFB. Some investigators claim that premedication and sedation aren't essential for FFB (4). Other studies showed depressive effects of sedative drugs on respiratory system (5-7). In addition, sedative drugs increase the cost and prolong the duration of hospitalisation (8).

The purposes of our study are to evaluate the effects of lorazepam and midazolam on respiratory and cardiovascular systems, to make a comparison of lorazepam and midazolam for sedative and amnestic effectiveness.

#### MATERIALS and METHODS

Sixty patients hospitalized in the hospital of University of Ankara were recruited this study. Patient data recorded were age, gender, indication for FFB. Patients who had hepatic and renal insufficiency, those older than 80 years, subjects using benzodiazepine on a regular basis and intubated patients were excluded. The study protocol was approved by the university ethics committee and a consent form was obtained in each case.

Sixty patients were divided three groups randomly. Each group included 20 patients. Patients in the first group (Group 0) didn't use any sedative drugs for FFB. Lorazepam was given orally (2 mg), 75-90 minutes before the procedure to the second group (Group1). Midazolam was given intravenously (5 mg), 2 minutes before the procedure, to the third group (Group 2).

#### Procedure

Seven bronchoscopists performed the procedure randomly. All of the procedures were assisted

by the same experienced nurses. The route for the bronchoscopy (oral, nasal) and the diagnostic procedures were chosen by the bronchoscopist. A flexible fiberoptic bronchoscope (Olympus BF Type 1T20D) was used. Atropine was administered intramuscularly to all of the patients, 20 minutes before the procedure. Citanest (2%) was administered with a nebulizer prior to the bronchoscopy and during the procedure it was administered by bronchoscopic aspiration channel. Maximum dose was limited to 20 mL.

For each procedure, the route of insertion, duration of the procedure, diagnostic procedures which were performed and complications were recorded. Supplemental oxygen was administered by nasal cannula (2 L/min) to all of the patients.

#### Monitoring

Body temperature, pulse rate, blood pressure, arterial blood gas values, pulmonary function values (FEV<sub>1</sub>, FVC, MMF) were measured one hour before the procedure and 2-4 hours after the procedure. Arterial blood gas values were measured by Radiometer ABL 330. Pulmonary function test measurements performed by Vitalograph Alpha spirometer. During the procedure all patients were monitored with pulse oxymeter (Sensor Medics Fas Trac) and electrocardiographic monitor.

#### Measurements

A questionnaire assessing patients cooperation and cough control was completed immediately after the bronchoscopy by the bronchoscopist.

A questionnaire included three questions was administered to the patients, immediately after the procedure and the following day. First question assessed the patients perception of the procedure as "easy" or "difficult". The second asked if patients would agree to a second bronc-

hospocopy if believed necessary. The third question was about the patients recollection of the procedure as clear, indistinct or not at all.

### Statistics

For numeric data ANOVA was used to compare three groups. For nominal data chi-square test was used, Wilcoxon's test was used to compare pre and postprocedure variables.

### RESULTS

Sixty patients were included the study. 18 were female (30%), 42 were male (70%). Demographic data is found in Table 1. No statistically significant difference was found among three groups.

Bronchoscopic indications are listed in Table 2. The indications for bronchoscopy were similar for all groups.

There were 8 patients with chronic obstructive pulmonary disease (COPD), 1 coronary artery disease (CAD), 1 hypertension in control group (Group 0), 2 COPD, 1 CAD, 1 hypertension in lorazepam group (Group 1), 3 COPD, 1 bronchiectasis, 1 congestive heart failure in midazolam group (Group 2).

The most preferred insertion way of bronchoscope was oral route and was similar for all groups ( $p > 0.05$ ). Data was not shown.

The mean duration of the procedure was not different in the three groups ( $p > 0.05$ ) and was below 15 minutes. Data was not shown.

Mucosal biopsy, bronchial lavage, bronchoalveolar lavage were the most frequently performed procedures during FFB. There was not any statistically significant difference in the procedures

**Table 1. Patients demographic data.**

	Group 0 (n= 20)	Group 1 (n= 20)	Group 2 (n= 20)
Age (Mean $\pm$ SD)	59.350 $\pm$ 11.398	53.900 $\pm$ 12.268	54.050 $\pm$ 11.180
Sex			
Male	15	12	15
Female	5	8	5
Total	20	20	20

**Table 2. Indications for bronchoscopy.**

Indication	Group 0		Group 1		Group 2	
	Number	%	Number	%	Number	%
Mass	9	45	7	35	10	50
Pneumonia	1	5	2	10	1	5
Interstitial lung disease*	4	20	4	20	2	10
Hemoptysis	-	-	1	5	-	-
Pleural effusion	3	15	-	-	1	5
Cough	-	-	-	-	3	15
Pulmonary nodule	1	15	2	10	2	10
Atelectasis	-	-	2	10	-	-
Hilar abnormality	-	-	1	5	-	-
Cleaning of secretions	1	5	1	5	1	5
Abcess	1	5	-	-	-	-
Total	20	100	20	100	20	100

\* Interstitial lung disease: Idiopathic pulmonary fibrosis, sarkoidosis, lung involvement of romatoid arthritis

**Table 3. Pre and postprocedure body temperature, pulse rate, systolic and diastolic blood pressure values.**

	Group 0			Group 1			Group 2		
	Pre	Post	p	Pre	Post	p	Pre	Post	p
Body temp.	36.465 ± 0.507	36.665 ± 0.586	0.053	36.420 ± 0.263	36.530 ± 0.289	0.191	36.440 ± 0.482	36.365 ± 0.409	0.349
Pulse rate	95.300 ± 15.013	93.600 ± 119.321	0.433	95.500 ± 10.797	90.900 ± 17.075	0.070	91.700 ± 9.718	91.200 ± 10.807	0.808
Systolic blood pressure	130.250 ± 27.932	132.000 ± 22.501	0.113	126.750 ± 20.918	124.000 ± 26.438	0.414	126.500 ± 21.770	116.000 ± 13.822	0.030*
Diastolic blood pressure	82.000 ± 15.079	78.000 ± 13.992	0.191	82.750 ± 13.325	76.250 ± 11.796	0.028*	80.000 ± 11.698	73.500 ± 8.127	0.044*

\* p values showed significantly statistically difference

Pre: Preprocedure, Post: Postprocedure

**Table 4. Pre and postprocedure arterial blood gas values.**

	Group 0			Group 1			Group 2		
	Pre	Post	p	Pre	Post	p	Pre	Post	p
pO <sub>2</sub>	65.950 ± 14.993	63.850 ± 13.758	0.332	72.700 ± 11.411	72.000 ± 9.776	0.737	71.700 ± 15.114	73.100 ± 13.290	0.518
pCO <sub>2</sub>	39.650 ± 6.635	38.100 ± 6.537	0.386	40.800 ± 4.009	39.600 ± 3.235	0.142	38.950 ± 5.586	38.000 ± 3.479	0.279
SaO <sub>2</sub> (%)	90.400 ± 8.964	90.050 ± 9.605	0.605	93.300 ± 3.799	93.850 ± 2.368	0.623	93.200 ± 8.664	93.800 ± 2.984	0.477
pH	7.421 ± 0.035	7.424 ± 0.034	0.627	7.405 ± 0.380	7.420 ± 0.029	0.105	7.425 ± 0.042	7.424 ± 0.038	0.972

\* No statistically significant differences were found among all groups

Pre: Preprocedure, Post: Postprocedure

performed during FFB among three groups ( $p > 0.05$ ). Data was not shown.

In control group 1 patient with hypertension, 1 patient with hemorrhage abandoned the FFB. In lorazepam group, 1 patient with hypertension abandoned the FFB. In midazolam group 1 patient abandoned the FFB because of his inpatientce. The frequency of these complications was similar in all groups ( $p > 0.05$ ). Pulse rate, body temperature, arterial blood pressure are shown

in Table 3. In lorazepam group postbronchoscopic diastolic blood pressure was significantly lower than prebronchoscopic diastolic blood pressure ( $p = 0.028$ ). In midazolam group both postbronchoscopic systolic and diastolic blood pressure values were significantly lower than prebronchoscopic values ( $p = 0.030$ ,  $p = 0.044$ , respectively). But the comparison of three groups with ANOVA didn't show statistical difference ( $p > 0.05$ ).

**Table 5. Pre and postprocedure spirometric values.**

Spirometry (% Pred.)	Group 0			Group 1			Group 2		
	Pre	Post	p	Pre	Post	p	Pre	Post	p
FEV <sub>1</sub> (% Pred)	68.300 ± 24.242	69.800 ± 24.729	0.324	70.400 ± 22.779	67.350 ± 22.940	0.016*	75.950 ± 24.661	76.000 ± 27.419	0.466
FCV (% Pred)	71.950 ± 21.259	74.650 ± 21.318	0.121	76.900 ± 21.069	72.750 ± 21.031	0.021*	78.650 ± 24.807	81.550 ± 28.734	0.205
MMF	53.800 ± 28.567	55.300 ± 28.019	0.199	51.250 ± 29.790	49.450 ± 27.607	0.717	62.600 ± 30.403	56.250 ± 28.749	0.185

\* p values showed significant statistically difference with Wilcoxon's test

Pre: Preprocedure, Post: Postprocedure

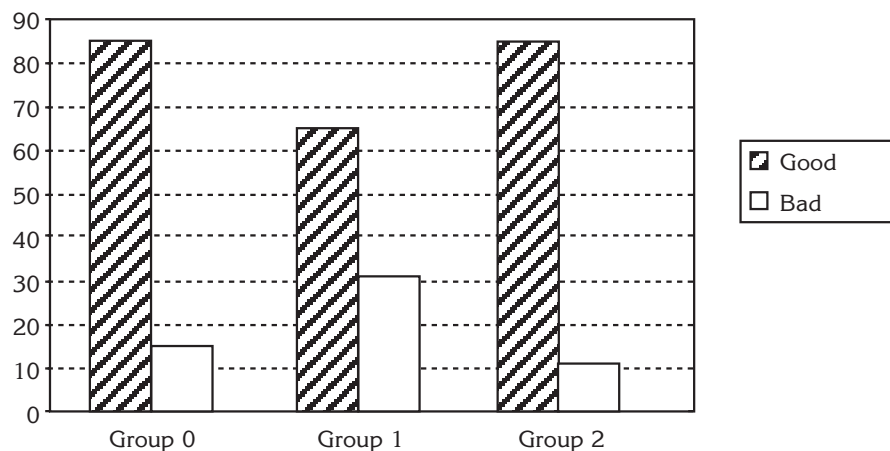
Arterial blood gas values are listed in Table 4. No statistically significant difference in arterial blood gas values found among all groups ( $p > 0.05$ ).

Spirometric values are shown in Table 5. There was a statistically significant decrease in postbronchoscopic FEV<sub>1</sub> and FVC values in lorazepam group with Wilcoxon's test ( $p = 0.016$ ,  $p = 0.028$ , respectively). But no statistically significant difference was found among all groups with ANOVA test ( $p > 0.05$ ).

Sinus cardiac rhythm was the most observed pattern in all groups. There was no statistically difference among three groups ( $p > 0.05$ ). Data was not shown.

During the FFB and different stages of FFB (vocal cords, carina, left and right main bronchus levels and during the performance of biopsy, lavage, BAL) oxygen saturation levels didn't show statistical difference ( $p > 0.05$ ). In all groups O<sub>2</sub> saturation levels were above 90%. Data was not shown. Cooperation of patients is shown in Figure 1. There was not any statistically significant difference in cooperation of patients among groups ( $p > 0.05$ ). Cough control is shown in Figure 2. Less cough control was observed in lorazepam group, but the difference was not statistically significant ( $p > 0.05$ ).

Patients perception of the procedure is shown in Figure 3. There was no statistically difference among three groups, immediately after the proce-

**Figure 1. Cooperation of patients.**

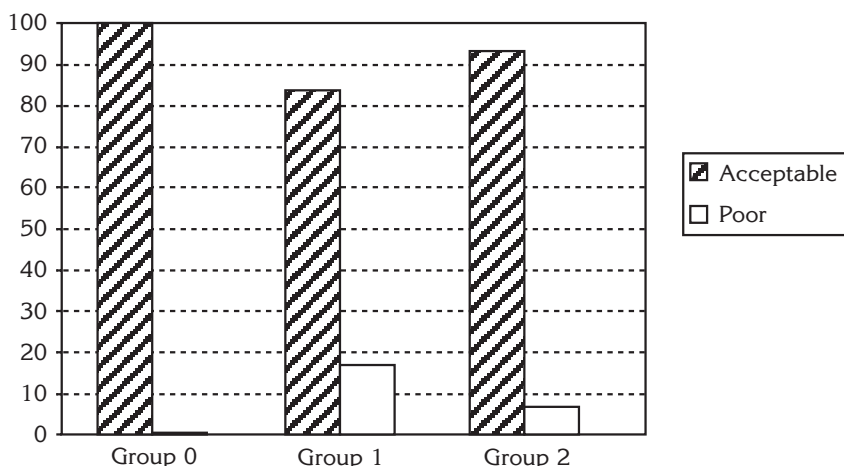


Figure 2. Cough control.

dure ( $p > 0.05$ ). At 24 hours in midazolam group more patients described the procedure as easy than in those other groups, the difference was statistically significant ( $p = 0.048$ ). There was no statistically significant difference among three groups when assessing agreement a repeated bronchoscopy ( $p > 0.05$ ). Data was not shown.

Patients recollection of the procedure is shown in Figure 4. At 24 hours the recalling of the procedure was less precise in midazolam group, than those of other groups ( $p = 0.00008$ ).

**DISCUSSION**

The studies evaluated the role of sedative drugs in bronchoscopic premedication showed diffe-

rent results. Some investigators proposed the sedative drugs for their anxiolytic effects and for their effects on facilitating the bronchoscopist's training (9). On the other hand, some investigators pointed out that sedative drugs caused respiratory depression and prolonged hospitalisation, increased the cost (4,8,10).

It was observed that like sedative drugs, prolongation of FFB duration and type of diagnostic procedures (TBLB etc.) reduced O<sub>2</sub> saturation during FFB. In a study included 167 patients, Stanopoulos et al reported that according to type of the procedure and to duration of procedure O<sub>2</sub> saturation level had reduced (11). So-

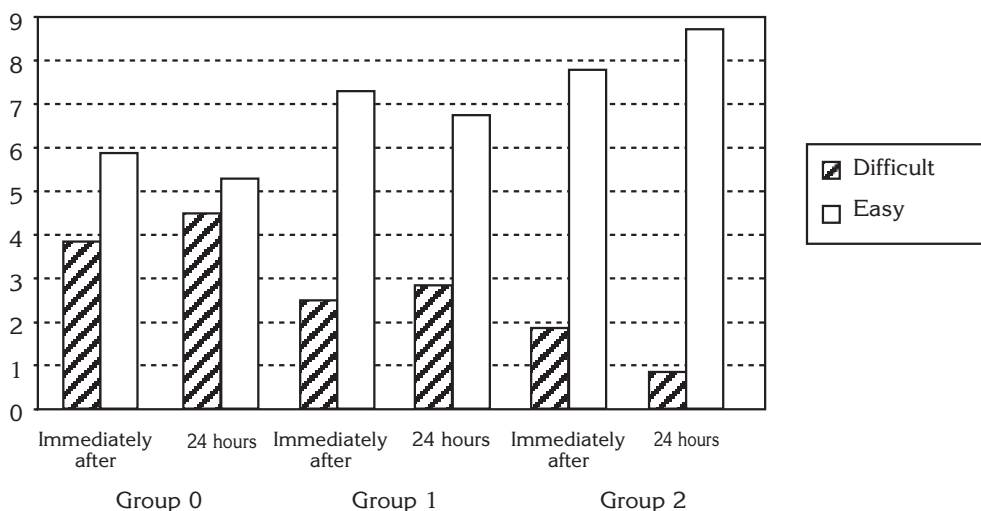


Figure 3. Perception of the procedure (Immediately after the procedure and the following day).

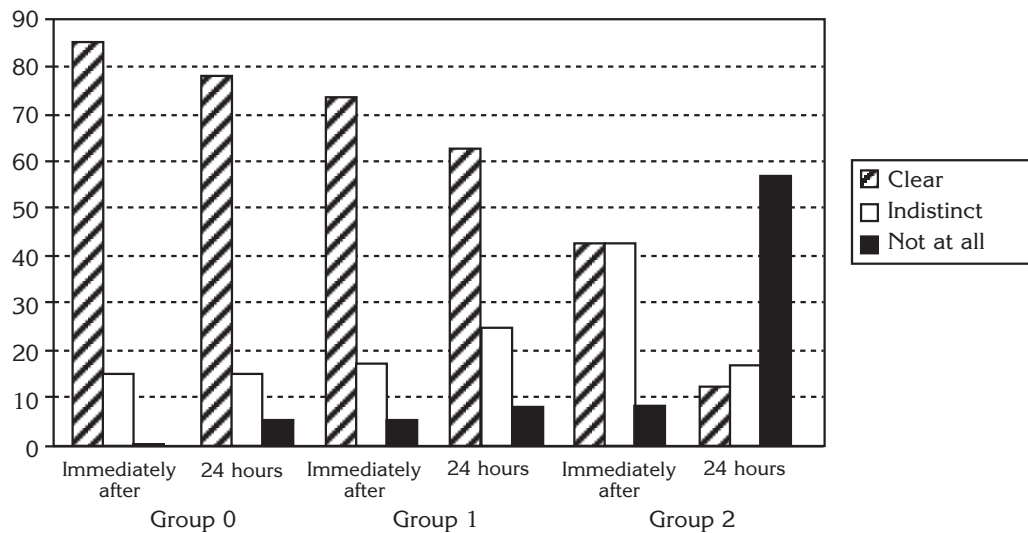


Figure 4. Recollection of the procedure.

me studies showed that benzodiazepines caused respiratory depression especially in patients who had COPD (12,13). In our study, we couldn't discuss the safety of using sedative drugs on COPD. Because most patients who had COPD were included in the control group.

In this study, we observed that 1 patient in control group, 1 patient in lorazepam group abandoned FFB because of hypertension. It was reported that midazolam was more effective than the other sedative agents for preventing intubation-induced hypertension. Boralessa et al suggested that midazolam was more effective than thiopentone (14). In our study, with a statistically significant difference, lower systolic and diastolic arterial blood pressure levels had been observed in midazolam group.

During FFB, pulmonary function tests could be deteriorated. Reasons for this deterioration are diminished airway area by bronchoscope, irritative effect of local anesthetic agent and the heat of lavage fluid (15). Peacock et al reported deterioration on FEV<sub>1</sub>, FVC, MMF and PIF during FFB, especially performed on normal subjects (16). In that study, it was also shown that sedative drugs didn't affect pulmonary function. We observed that FEV<sub>1</sub> and FVC significantly reduced in lorazepam group, in our study. Effects of benzodiazepines on respiratory system were

known to reduce the tonus of upper airway, to cause depression on respiratory control, to cause cough in rare cases (17,18). We observed lorazepam related cough (not statistically different) in our study. We suggested that the reasons of deterioration of FEV<sub>1</sub> and FVC related to lorazepam had to be investigated by further studies.

In our study, cooperation of patients didn't show statistical difference among three groups ( $p > 0.05$ ). Some investigators suggested that confidence between patient and bronchoscopist reduced the necessity of sedative drugs in FFB (9,15).

In this study, at 24 hours most patients in midazolam group described the procedure as easy ( $p = 0.048$ ). In addition, at 24 hours most patients in midazolam group didn't remember the procedure ( $p = 0.00008$ ). But agreement rate for repeated FFB was not statistically different among three groups ( $p > 0.05$ ).

In a randomized, double-blind, placebo-controlled study, Maltais et al reported that patients who were administered lorazepam before FFB, were recognizing the procedure as easy. In the same study most patients in lorazepam group had high agreement rates for repeated FFB and recalled less precise the procedure (16). In our study, we found midazolam had more amnesic effect than lorazepam. But there was no diffe-

rence in agreement rates for repeated FFB among three groups. So we suggested that negative influences between patients, lack of reliance between bronchoscopist and patient, affected the patients agreement on repeated FFB.

In conclusion, in hospitalised patients midazolam was found an useful agent for FFB with satisfactory amnestic effectiveness. In this study, midazolam didn't reduce O<sub>2</sub> saturation with clinical significance, so it could be used safely during FFB. It was observed that lorazepam reduced FEV<sub>1</sub> and FVC, so it had to be used carefully on COPD patients. Sedative drugs weren't seem essential for FFB performed in outpatients. Because there was no statistically difference among three groups for cooperation of patients. In addition performance of FFB without sedative drugs, reduces cost and decreases observation time after FFB.

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