

## Original Research Article

## Role of Nebulised Lignocaine With Midazolam In Flexible Bronchoscopy in Reducing Patient Cough , Discomfort & Study the Side Effects of Nebulised Lignocaine in Patients Undergoing Fibro Optic Bronchoscopy Scope

Dr. K Ramesh Kumar<sup>1</sup>, Dr. K. Subhakar<sup>2</sup>, Dr. M. Madhusudan Reddy<sup>3</sup>

<sup>1</sup>Associate professor of TB &Respiratory diseases, Osmania medical college, Hyderabad

<sup>2</sup>Professor of TB & Respiratory diseases, Osmania Medical College, Hyderabad

<sup>3</sup>Pulmonologist, Hyderabad

### \*Corresponding author

Dr. K Ramesh Kumar

Email: [drrameshkumar2007@gmail.com](mailto:drrameshkumar2007@gmail.com)

**Abstract:** Topical anesthesia for flexible bronchoscopy can be achieved in several ways like administration of an anesthetic agents by injecting through cricothyroid membrane, by giving drug lignocaine through Nebulization, 3}administering the drug through oral spray. Nebulization of lidocaine can achieve very satisfying anesthesia comparable to oral spraying with significant low plasma levels of the drug. Nebulization of lidocaine with midazolam gives good results than using only lidocaine without sedation. Nebulization of lidocaine gives effective analgesia & the dose of conscious sedation is significantly reduced. So we studied the effect of nebulized lignocaine with midazolam as sedation in 60 patients needing bronchoscopy and compared them to 50 patients who underwent fiberoptic bronchoscopy with oral spray of lignocaine and midazolam as sedation. This is a study of 110 patients undergoing bronchoscopy were subjected to conscious sedation& local anaesthesia in Govt general hospital Osmania medical college for a period of two years. Patients were in the age group of 25 to 75 years. After obtaining consent, 60study cases were given nebulization. With lidocaine & sedation with midazolam. Control group had bronchoscopy with oral spray of drug lignocaine and midazolam given for sedation .All patients had Intravenous lines, pulse oximetry monitoring of saturations, serial recordings of their blood pressure, pulse, respiratory rate were noted. All patients received supplemental oxygen through oral mask at the rate of 1-2 liters per minute. In study group, patients had 4 ml of lidocaine diluted in 4 ml of normal saline by nebulization for 15 minutes, beforebronchoscopy,control patients had lidocaineoral spraying before bronchoscopy. After the procedure patients perception of discomfort ,their severity of cough ,were analyzed ,discomfort status was perceived by administration of visual analog scale, heart rate, breathing patterns, blood pressure and continuous pulse oximetry readings in both groups are compared. Patients undergoing bronchoscopy after nebulization with lignocaine have less intensity of cough, they tolerate the procedure better than placebo group, experience less discomfort during bronchoscopy. Oxygen saturation is well maintained in study group. These patients needed less dose of midazolam for conscious sedation. Statistical analysis was performed by calculating mean, P Value. Standard Deviation , Anova For Cough Score By Patients & Physicians, Anova For Discomfort Score ,Anova For Total Lignocaine Dose in both groups. Nebulised lignocaine with midazolam sedation before bronchoscopy is safe .These patients undergo bronchoscopy procedure better than control group. They have less cough .stable vital parameters, less discomfort during and after procedure.

**Keywords:** bronchoscopy, nebulization, sedation

### INTRODUCTION:

Topical anaesthesia for flexible fibro optic bronchoscopy can be achieved in many ways [1]. It can be achieved by A nebulization of lignocaine in airways [B] spraying the oropharynx with lignocaine spray, Injecting lignocaine by piercing cricothyroid membrane

[2, 3]. It can also be given through the bronchoscope “spray as you go” [4].

Lignocaine has better safety profile [4, 5] and is commonly used. The side effects of lidocaine are more if plasma levels exceed 5 mg /lt in patients with

abnormal liver function or 8 mgs in normal individuals. The drug at toxic doses can cause arrhythmias. Cardiorespiratory arrest & rarely death [6, 8]. The dose of lidocaine nebulization is small and safe for bronchoscopy though it may be little more than oral spraying [10]. It gives good anesthesia to the airways [11,12]. Nebulization can instill the drug directly in to airways and also fewer doses is needed for an aesthetic effect of airways, The dose used is far below optimal levels & is very safe, patients undergoing fibroptic bronchoscopy. They have less discomfort & procedure is uneventful. The drug Midazolam given IV has good sedation and increases effect of lidocaine [16, 17]. Patient need to be fasting for two to three hours before FOB and Midazolam 0.2.mg/kg IV gives good sedation [35]. The dose of Midazolam can be increased after 2 min by increments of 1mg per /Min [29, 30]. Sedation with midazolam and nebulised lignocaine, patients tolerate fibroptic bronchoscopy better than patients on lignocaine spray with sedation. Lignocaine nebulization is more comfortable than injecting lignocaine through cricothyroid membrane. Lidocaine is safe analgesic compared to cocaine [37]. Oropharynx can be safely anesthetized by 10 percent lidocaine spray [41]. In additional 2 percent lidocaine liquid can be instilled [42, 43]. pulse oximetry is a sensitive detector of hypoventilation [33]. FOB is safe procedure and experienced hands with appropriate sedation and analgesia [51]. Complications like bleeding occur in rare cases of uraemic, liver abnormalities & immunosuppressed patients [60].

Good selection of patients with nebulized lidocaine and sedation with Midazolam before bronchoscopy, FOB is safe and gives highly rewarding. These patients have less cough and discomfort after the bronchoscopy with stable heart rate & good hemodynamic stability [64, 65].

#### **Indications for Bronchoscopy**

- 1) Patients suffering from lung cancer
- 2) Endo bronchial tuberculosis
- 3) Bronchoalveolar lavage for ILD
- 4) Bronchial Washings in Bronchiectasis, Lung Abscess

#### **Contra indications**

1. refractory hypoxia
2. unstable cardiopulmonary status
3. Patients with arrhythmias
4. Patients with altered sensorium.
5. Patients with bleeding diathesis

#### **MATERIALS AND METHODS**

##### **Patients:**

This study was done in Government General and Chest Hospital, Osmania medical college Hyderabad, A total of 110 patients of aged between 22 to 75 were selected for the study. Intubated patients, Patients with other systemic diseases, pregnant women and children were not included in this trial. After obtaining written informed consent, 110 consecutive patients undergoing diagnostic flexible bronchoscopy were prospectively randomized to receive either nebulized 4% lidocaine or placebo in double – blind fashion. 60 patients in study group and 50 in control group

##### **Study Design: prospective study**

Bronchoscopies were performed trans nasally with the patient in the semirecumbent position. Pulse Oximetry was recorded continuously during the procedure, and automated noninvasive BP was monitored every 5 min. supplemental oxygen was offered at 2-4 lts/min via nasal cannula to all patients. In case of desaturation < 90 % oxygen delivery was increased to 6L/min.

After randomization ,Study group patients had received 4 ml of 4% lidocaine (160 mg of lidocaine) of 4 ml of saline as placebo delivered by nebulization over 15 min immediately before bronchoscopy. Control group received Nasal anesthesia by spraying 10% lidocaine in the nasopharynx and oropharynx (two times). vocal cords were sprayed with 4 % lignocaine. Lignocaine administered through the bronchoscope was defined as supplemental lidocaine. Bronchoscopists were advised to instill 2 ml aliquots of 2% lidocaine over the vocal cords, at the carina and both right and left main bronchi. All does of supplemental local anesthesia required as judged by the bronchoscopist were recorded for each patient.

All patients received 2 mg IV Midazolam immediately before flexible followed by further 1 –to 2 mg intermittent boluses during the procedure at the discretion of the bronchoscopist. The total doses of Midazolam were documented. Diagnostic bronchoscopic procedures were performed depending on the clinical setting. At the end of the procedure, bronchoscopists noted their perception of indicated greater frequency of cough. Patients were enquired about cough, discomfort in throat. Later 2to 3 hrs after bronchoscopy, patients were asked to record both their perception of cough, discomfort related to the procedure on a 10 cm VAS(VISUAL ASSESSMENT SCORE), where 0 = no discomfort or cough , and 10= greater

levels of discomfort or incessant cough. BP and heart rate were also measured in both study and control group

- Heart rate at the time of reevaluation
- Duration of procedure

**PROFORMA**

1. Name
2. Age /Sex
3. Indication for FOB
4. Procedures during FOB
5. Variables

- Initial O2 saturation
- Initial Blood Pressure
- Initial Heart rate
- Highest Heart rate
- Lowest O2 saturation
- Maximum O2 flow, lit / min
- Blood pressure and the end of procedure
- Time to reevaluation (hr)
- Blood pressure at the time of reevaluation

1) Outcome Parameters:

- Cough score (VAS) - (0-10)
  - By physicians
  - By patients
- Discomfort score (VAS) – (0 -10)
  - By Patients
    - Supplemental lidocaine dose (mg)
    - Total lidocaine dose (mg)
    - Midazolam dose (mg)

**RESULTS**

Patient characteristics are presented in Table. 1. All examinations could be completed as planned. There were no significant differences in age, gender, and indication for bronchoscopy between both groups.

**Table 1: Patients Characteristics**

Characteristics	Lidocaine Group (n=60)	Placebo Group (n=50)	Total(n=110)
Age, yr	(25-75)	(22-73)	(22-75)
Male /female gender, No.	42/18	38/12	88/30
Indication for flexible bronchoscopy			
Tumor diagnosis /staging	42(71)	35(70)	77(70)
Interstitial lung disease	5(8)	3(6)	8(7)
Infection	6(10)	7(14)	13(12)
Hemoptysis	7(11)	5(10)	12(11)

Data are presented as mean (range) or No. (%) unless otherwise indicated. Sex ratio in study group 30% females &70% males. In control group 37%

females,67% males Distribution of different invasive bronchoscopic procedures performed were also similar in both groups (Table2).

**Table 2: Invasive procedures performed in Both Groups**

Procedures	Lidocaine Group	Placebo Group	Total
Bronchial washings	52(87)	40(80)	92(84)
Bronchial brushing	32(53)	30(60)	62(54)
Endobronchial biopsy	32(53)	20(40)	52(47)
BAL	8(13)	10(20)	18(16)

Data are presented as No. (%)

The most common procedures were bronchial washings in 92 cases (84%), followed by bronchial brushings in 60 cases (56%), endobronchial biopsy in 52 cases (47%), and BAL in 18(16%) cases, respectively. In 52 cases (47%),endobronchial biopsy

and bronchial washings was performed, either alone or in combination.Hemodynamic findings before, during, and after bronchoscopy for both groups are illustrated in Table 3

Most of the patients in the study group had a systolic blood pressure of 122mm and in the control group 120. The Blood pressure fluctuation in study group was minimal and stable. The heart rate variation was only 10 beats during the procedure. Oxygen saturation was maintained in study group. The diastolic pressure in study group 80 mm. Midazolam was given in both groups and had good sedation. Table showing the various parameters of blood pressure in study and control group, so the fluctuations in both group were not significant. They had stable BP readings due to sedation. Mean systolic blood pressure in study group is 122 mm and while in control group was 120 mm. The p value variations in systolic blood pressure 0.743. The diastolic blood pressures are 80mm in study group and 84mm in control group the P values is 0.932. Both

control and study group had medazolam injection so not much of fluctuation of blood pressure. The diastolic blood pressure after the procedures are 70mm in study group 80mm in control group, P value is 0.129. The nebulization of lignocaine leads to less throat irritation and, cough in study group. The p value for cough, discomfort score was significant when both groups are compared. The standard deviation of systolic blood pressure in the study group is 4 and control group is also 4. The standard deviation in diastolic group is 1.6 and control group is 2.6 before the procedure. The standard deviation after bronchoscopy in the study group is 3 for systolic blood pressure and 3.2 in the control group. The standard deviation for diastolic blood pressure in the study group 2.3 and control group is 1.5.

**Table 3: Hemodynamic findings before, during, and After Bronchoscopy in the study and Placebo Groups.**

Variables	Lidocaine (n=60)	Group (n=50)	Placebo Group P Value
Initial oxygen saturation ,	% 96.7 (3.0)	96.7(2.8)	0.689
Initial systolic/	122	120	0.743
Initial heart rate, beats / min	82(18)	84(16)	0.640
Highest heart rate, beats / min	92(20)	92(18)	0.334
Lowest oxygen flow, L /min	92.9(11.8)	93.6(4.7)	0.468
Maximum oxygen flow, L /min	4.5(0.5)	4.7(0.5)	0.139
Duration of the procedure, min	16(9.9)	18(10)	0.285
Diastolic Blood pressure	80	84	0.932
Time to reevaluation, min	168(13)	172(12)	0.877
Diastolic / reevaluation, Mm Hg	74	80	0.129
Heart rate at reevaluation	80(12)	80(12)	0.836
Midazolam dose(mg)	3.5(1.2)	4.0(1.4)	0.236

Data are presented as mean (SD) or No.

Oxygen requirement was 4.5 + 0.5 L/ min and 4.7 + 0.5 L/ min, in the Study and placebo groups, respectively (p = 0.139). The lowest oxygen saturation during the procedure was 92.9 + 11.8 % and 93.6 + 4.7 % in the lidocaine and placebo groups, respectively (p= 0.468). These cases of oxygen desaturations < 90%

were noted in the lidocaine group, as compared to six cases in the placebo group (p= 0.319). The total Midazolam dose in lidocaine group and placebo groups are 3.5+ 1.2 and 4.0 + 1.4 mg respectively (p =0.236). Cough scores for physicians and patients as well as the discomfort score for patients are shown in Table 4.

**Table 4: Outcome parameters in Both Randomized Groups**

Parameters (n=60)	Lidocaine Group (n=50)	Placebo Group	P Value
Cough score physicians, VAS	1.5 (0- 10)	4(0-10)	< 0.001
Cough score patients, VAS	1.5( 0-10)	3.75( 0-10)	< 0.001
Discomfort score patients, VAS	2(0-10)	2(0-10)	<0.001
Supplemental lidocaine dose, mg	58(13)	157(44)	<0.001
Total lidocaine dose, mg	218(41)	157(44.4)	<0.001

Data are presented as median or mean (SD). There was a statistical significance between both groups

in regard to cough score evaluated by the physician (p< 0.001). There is also a significant difference in

discomfort score of the patient ( $p < 0.001$ ) between the two groups. Both cough and discomfort lidocaine was  $58 \pm 13$  mg in the lidocaine group as compared to  $157 \pm 44$  mg in the placebo group ( $p < 0.001$ ). Accordingly mean total lidocaine dose required in the lidocaine group was  $218 \pm 41$  mg, and was higher than the total dose required in the placebo group ( $157 \pm 44.4$  mg) ( $p < 0.001$ )

## DISCUSSION

This study demonstrates a benefit of nebulized lidocaine in reducing the total dose of topical anesthetic administered for flexible bronchoscopy in patients receiving conscious sedation with midazolam. The amount of supplemental lidocaine received by study group is little higher than lidocaine in the placebo group. The administration of aerosolized lidocaine by nebulization was in the therapeutic levels of the drug, even though marginally higher than control group. The side effects of lidocaine drug noted were negligible except dryness of mouth and difficult in swallowing. There were no arrhythmias nor did convulsion noted. Patients tolerated bronchoscopy well. They had less cough discomfort than control group during the FOB and during recovery. There was no significant changes in heart rate, systolic blood pressure, diastolic pressure in both groups because both received equal amounts of sedation with midazolam. There was no statistical significance in p value, mean and standard deviation of the hemodynamic profile.

Many studies were performed utilizing either lidocaine alone or a combination with a benzodiazepine. In one of these studies, Gove *et al.* [69] reported a reduction in the duration of the procedure with nebulized lidocaine, both alone and combined with IV diazepam. However, midazolam has replaced diazepam in most centers due to its shorter duration of action compared to diazepam and is now by far the most common sedative used during bronchoscopy.

Isaac *et al.* [13] compared three different methods of local anesthesia, including nebulization, and transcrioidal and bronchoscopic injection. The transcrioidal method produced better working conditions than nebulization, although both techniques were satisfactory. In another study with a similar design, all patients in the nebulized group required supplemental local anesthesia, compared to few patients in the transcrioidal injection group. Webb *et al.*; compared transcrioidal injection of lignocaine to spraying the drug through bronchoscope – “sprays as you go” technique. The required supplemental lidocaine dose was higher in

the transcrioidal injection group compared to the “sprays as you go” group.

Although effective, transcrioidal administration of the lidocaine has not been widely used. The main reason seems to be that the procedure is unpleasant. Moreover, transcrioidal puncture may be unacceptable in some patients, if coagulation abnormalities are presented and also very apprehensive patients. Foster and Hurewitz demonstrated a reduction of supplemental lidocaine doses required for flexible bronchoscopy if nebulized lidocaine was previously administered. Despite the fact that the results were statistically significant, it is difficult to judge the clinical relevance of this finding, particularly due to the small number of patients in each group ( $n=5$  and  $n=9$ , respectively). One possible limitation of this study is that tolerability may have been overestimated 2 h after the procedure because of the amnesic effect of midazolam. According to several previous studies, wake up time for conscious sedation with benzodiazepine is 35 to 60 min and discharge time is 75 to 120 min after the procedure. We therefore believe that it is fair to assume that patients were able to estimate their discomfort during flexible bronchoscopy 2 h after the procedure.

## SUMMARY AND CONCLUSION

The aim of present study was to evaluate the role of nebulized lidocaine in flexible fiber optic bronchoscopy in patients with midazolam sedation in reducing patients cough, discomfort and supplemental lidocaine. The study was done in 110 patients undergoing diagnostic flexible bronchoscopy by double blind prospective randomization to receive either nebulized 4% lidocaine or placebo. Nebulization of lidocaine with IV midazolam was effective pre anesthetic medication for fiberoptic bronchoscopy. The dose of lidocaine is within the optimal levels and patients had no discomfort. Their saturations were well maintained and a post procedure was uneventful. It is an effective means of anesthesia to patients undergoing bronchoscopy. It is as effective as giving the drug by puncturing the cricothyroid membrane which is a laborious process and very uncomfortable patients. Nebulized lignocaine with midazolam sedation before bronchoscopy is safe. They undergo bronchoscopy. They have less cough. Stable vital parameters, less discomfort during and after procedure.

## REFERENCES

1. Gupta H, Dai L, Datta G, Garber DW, Grenett H, Li Y, Mishra V, Palgunachari MN, Handattu S, Gianturco SH, Bradley WA. Inhibition of lipopolysaccharide-induced inflammatory

- responses by an apolipoprotein AI mimetic peptide. *Circulation research*. 2005 Aug 5;97(3):236-43.
2. British Thoracic Society guidelines on diagnostic flexible bronchoscopy, *Thorax* 2001;56(suppl) :i1 – i21
  3. Keane D, McNicholas WT. Comparison of nebulized and sprayed topical anaesthesia for fiberoptic bronchoscopy. *European Respiratory Journal*. 1992 Oct 1;5(9):1123-5.
  4. Sanderson DR. Lignocaine for topical anesthesia in fiberoptic bronchoscopy. *Respiration*. 2000 Feb 24;67(1):9-10.
  5. Teale C, Gomes PJ, Muers MF, Pearson SB. Local anaesthesia for fiberoptic bronchoscopy: comparison between intratracheal cocaine and lignocaine. *Respiratory medicine*. 1990 Sep 1;84(5):407-8.
  6. Day RO, Chalmers DR, Williams KM, Campbell TJ. The death of a healthy volunteer in a human research project: implications for Australian clinical research. *The Medical journal of Australia*. 1998 May;168(9):449-51.
  7. Wu FL, Razzaghi A, Souney PF. Seizure after lidocaine for bronchoscopy: case report and review of the use of lidocaine in airway anesthesia. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*. 1993 Jan 2;13(1):72-8.
  8. Ritchie JM, Greene NM. Local anesthetics In: Hardman JG, Limbird LE, and Gliman AG, eds. *Goodman and Gliman's the pharmacological basic of therapeutics*. 8<sup>th</sup>ed. New York, Ny: Pergamon, 2000: 320-322
  9. Sutherland AD, Santamaria JD, Nana A. Patient comfort and plasma lignocaine concentrations during fiberoptic bronchoscopy. *Anaesthesia and intensive care*. 1985 Nov;13(4):370-4.
  10. Milman N, Laub M, Munch EP, Angelo HR. Serum concentrations of lignocaine and its metabolite mono methyl glycinexylidide during fibre-optic bronchoscopy in local anaesthesia. *Respiratory medicine*. 1998 Jan 1;92(1):40-3.
  11. Eyres RL, Bishop W, Oppenheim RC, Brown TC, Chalon J. Plasma lignocaine concentrations following topical laryngeal application. *Survey of Anesthesiology*. 1983 Dec 1;27(6):372.
  12. Korttila K, Tarkkanen J, Tarkkanen L. Comparison of laryngotracheal and ultrasonic nebulizer administration of lidocaine in local anaesthesia for bronchoscopy. *Acta anaesthesiologica Scandinavica*. 1981 Apr 1;25(2):161-5.
  13. Isaac PA, Barry JE, Vaughan RS, Rosen M. A jet nebuliser for delivery of topical anaesthesia to the respiratory tract A comparison with cricothyroid puncture and direct spraying for fiberoptic bronchoscopy. *Anaesthesia*. 1990 Jan 1;45(1):46-8.
  14. Foster WM, Hurewitz AN. Aerosolized Lidocaine Reduces Dose of Topical Anesthetic for Bronchoscopy1-3. *Am Rev Respir Dis*. 1992;146:520-2.
  15. Gjonaj ST, Lowenthal DB, Dozor AJ. Nebulized lidocaine administered to infants and children undergoing flexible bronchoscopy. *Chest*. 1997 Dec 31;112(6):1665-9.
  16. Pickles J, Jeffrey M, Datta A, Jeffrey AA. Is preparation for bronchoscopy optimal? *European Respiratory Journal*. 2003 Aug 1;22(2):203-6.
  17. Stolz D, Chhajed PN, Leuppi JD, Brutsche M, Pflimlin E, Tamm M. Cough suppression during flexible bronchoscopy using combined sedation with midazolam and hydrocodone: a randomised, double blind, placebo controlled trial. *Thorax*. 2004 Sep 1;59(9):773-6.
  18. Ikeda S. Flexible bronchofiberscope. *Ann OtolRhinolLarygol* 1970; 79;916
  19. Benumof JL. Management of the difficult adult airway. With special emphasis on awake tracheal intubation. *Anesthesiology*. 1991 Dec;75(6):1087-110.
  20. Nicolai T. Pediatric bronchoscopy. *Pediatric pulmonology*. 2001 Feb 1;31(2):150-64.
  21. American Society of Anesthesiologists. A report by the American Society of anesthesiologist's task force on preoperative fasting: practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration; application to healthy patient's undergoing elective procedures. *Anesthesiology*, 1999; 90:896
  22. Poi PJ, Chuah SY, Srinivas P, Liam CK. Common fears of patients undergoing bronchoscopy. *European Respiratory Journal*. 1998 May 1;11(5):1147-9.
  23. Rees PJ, Hay JG, Weeb JR. Premedication for fiberoptic bronchoscopy. *Thorax* 1983; 38:624-627
  24. Macfarlane JT, STORR A, Ward MJ, Smith WR. Safety, usefulness and acceptability of fiberoptic bronchoscopy in the elderly. *Age and ageing*. 1981 Jan 1;10(2):127-31.
  25. Williams TJ, Nicoulet I, Coleman E, McAlaney C. Safety and patient acceptability of intravenous midazolam for fibre optic bronchoscopy. *Respiratory medicine*. 1994 Apr 1;88(4):305-7.
  26. Maltais F, Laberge F, Laviolette M. A randomized, double-blind, placebo-controlled study of lorazepam as premedication for bronchoscopy. *Chest*. 1996 May 31;109(5):1195-8.

27. Benzodiazepines .In: Stoelting RK. Pharmacology and physiology in Anesthetic practice 3<sup>rd</sup>ed. New York: Lippincott –raven: 1999:128-131.
28. Bailey PL, Pace NL, Ashburn MA, Moll JW, East KA, Stanley TH. Frequent hypoxemia and apnea after sedation with midazolam and fentanyl. *Anesthesiology*. 1990 Nov;73(5):826-30.
29. Benzodiazepines. In: Stoelting RK Pharmacology and physiology in Anesthetic practice. 3<sup>rd</sup>ed. New York: Lippincott –Raven: 1999:133.
30. Benzodiazepines. In: Stoelting RK Pharmacology and physiology in Anesthetic practice. 3<sup>rd</sup> New York: Lippincott-Raven 1999:13-137.
31. Rosow CE, Moss J, Philbin DM. et al. Histamine release during morphine and fentanyl anesthesia. *Anesthesiology* 1982;56:93.
32. Noorily AD, Noorily SH, Otto RA. Cocaine, lidocaine, and tetracaine: which is best for topical nasal anesthesia? *Anesthesia & Analgesia*. 1995 Oct 1;81(4):724-7.
33. American Society of Anesthesiologists. A report by the American Society of anesthesiologist's task force on preoperative fasting: practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patient's undergoing elective procedure. *Anesthesiology* 2002; 96:1004-1017.
34. Dundee JW, Collier PS, Carlisle RJ, Harper KW. Prolonged midazolam elimination half-life. *British journal of clinical pharmacology*. 1986 Apr 1;21(4):425-9.
35. Korttila K, Tarkkanen J. Comparison of diazepam and midazolam for sedation during local anaesthesia for bronchoscopy. *British journal of anaesthesia*. 1985 Jun 1;57(6):581-6.
36. Crawford M, Pollock J, Anderson K, Glavin RJ, MacIntyre D, Vernon D. Comparison of midazolam with propofol for sedation in outpatient bronchoscopy. *British journal of anaesthesia*. 1993 Apr 1;70(4):419-22.
37. Teale C, Gomes PJ, Muers MF, Pearson SB. Local anaesthesia for fiberoptic bronchoscopy: comparison between intratracheal cocaine and lignocaine. *Respiratory medicine*. 1990 Sep 1;84(5):407-8.
38. Webb AR, Woodhead MA, Dalton HR, Grigg JA, Millard FJ. Topical nasal anaesthesia for fiberoptic bronchoscopy: patients' preference for lignocaine gel. *Thorax*. 1989 Aug 1;44(8):674-5.
39. Efthimiou J, Higenbottam T, Holt D, Cochrane GM. Plasma concentrations of lignocaine during fiberoptic bronchoscopy. *Thorax*. 1982 Jan 1;37(1):68-71.
40. Randell T, Yli-Hankala A, Valli H, Lindgren L. Topical anaesthesia of the nasal mucosa for fiberoptic airway endoscopy. *British journal of anaesthesia*. 1992 Feb 1;68(2):164-7.
41. Isaac PA, Barry JE, Vaughan RS, Rosen M. A jet nebuliser for delivery of topical anaesthesia to the respiratory tract A comparison with cricothyroid puncture and direct spraying for fiberoptic bronchoscopy. *Anaesthesia*. 1990 Jan 1;45(1):46-8.
42. Webb AR, Fernando SS, Dalton HR, Arrowsmith JE, Woodhead MA, Cummin AR. Local anaesthesia for fiberoptic bronchoscopy: transcricoid injection or the " spray as you go" technique?. *Thorax*. 1990 Jun 1;45(6):474-7.
43. 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 Sep 30;102(3):704-7.
44. Roffe C, Smith MJ, Basran GS. Anticholinergic premedication for fiberoptic bronchoscopy. *Monaldi archives for chest disease= Archivio Monaldi per le malattie del torace/Fondazione clinica del lavoro, IRCCS [and] Istituto di clinica fisiologica e malattie apparato respiratorio, Universita di Napoli, Secondo ateneo*. 1994 Apr;49(2):101-6.
45. Woodcock A, Campbell I, Collins JV, Hanson P, Harvey J, Corris P, Johnston ID. Bronchoscopy and infection control. *The Lancet*. 1989 Jul 29;334(8657):270-1.
46. Langmack EL, Martin RJ, Pak J, Kraft M. Serum lidocaine concentrations in asthmatics undergoing research bronchoscopy. *CHEST Journal*. 2000 Apr 1;117(4):1055-60.
47. Matsushima Y, Jones RL, King EG, Moysa G, Alton JD. Alterations in pulmonary mechanics and gas exchange during routine fiberoptic bronchoscopy. *Chest*. 1984 Aug 31;86(2):184-8.
48. Miner JR, Heegaard W, Plummer D. End-tidal carbon dioxide monitoring during procedural sedation. *Academic Emergency Medicine*. 2002 Apr 1;9(4):275-80.
49. Lindholm CE, Oilman B, Snyder JV, Millen EG, Grenvik A. Cardiorespiratory Effects of Flexible Fiberoptic Bronchoscopy in Critically III Patients. *Chest*. 1978 Oct 31;74(4):362-8.
50. Miner JR, Heegaard W, Plummer D. End-tidal carbon dioxide monitoring during procedural sedation. *Academic Emergency Medicine*. 2002 Apr 1;9(4):275-80.
51. Zavala DC. Diagnostic fiber optic bronchoscopy: techniques and result of biopsy in 600 patients. *Chest* 1975; 68:12-19

52. Cradle W, Smiddy J, Elliott R, Complications of fiber optic bronchoscopy. *Am Rev Respir Dis* 1974; 109:67-72
53. Suratt PM, Smiddy JF, Gruber B. Deaths and complications associated with fiberoptic bronchoscopy. *Chest*. 1976 Jun 30;69(6):747-51.
54. Simpson FG, Arnold AG, Purvis A, Belfield PW, Muers MF, Cooke NJ. Postal survey of bronchoscopic practice by physicians in the United Kingdom. *Thorax*. 1986 Apr 1;41(4):311-7.
55. Dreisin RB, Albert RK, Talley PA, Kryger MH, Scoggin CH, Zwillich CW. Flexible fiberoptic bronchoscopy in the teaching hospital: yield and complications. *Chest*. 1978 Aug 31;74(2):144-9.
56. Pereira W, Kovnat DM, Snider GL. A prospective cooperative study of complications following flexible fiberoptic bronchoscopy. *Chest*. 1978 Jun 30; 73(6):813-6.
57. Pue C, Pacht E. Complications of fiber optic bronchoscopy at university hospital. *Chest* 1995 ; 107:430-432
58. Zavala DC. Complications following fiber optic bronchoscopy. *Chest* 1978 ;73:783-785
59. Hanson RR, Zavala DC, Rhodes M, Keim LW, Smith JD. Transbronchial Biopsy Via Flexible Fiberoptic Bronchoscope: Results in 164 Patients 1, 2. *American Review of Respiratory Disease*. 1976 Jul;114(1):67-72.
60. Sutherland AD, Santamaria JD, Nana A. Patient comfort and plasma lignocaine concentrations during fibreoptic bronchoscopy. *Anaesthesia and intensive care*. 1985 Nov;13(4):370-4.
61. Milman N, Laub M, Munch EP, Angelo HR. Serum concentrations of lignocaine and its metabolite monoethylglycinexylidide during fibre-optic bronchoscopy in local anaesthesia. *Respiratory medicine*. 1998 Jan 1;92(1):40-3.
62. Albertini R, Harrel JH, Moser KM. Letter: Hypoxemia during fiberoptic bronchoscopy. *Chest*. 1974 Jan;65(1):117-8.
63. Carr -Hill RA. The measurement of patient satisfaction. *GastrointestEndosc* 1994; 40:119-120
64. Staniszewska S, Ahmed A. Patient expectations and satisfaction with health care. *Nursing Standard* 1998; 12:34-38.
65. Chapman A. Current theory and practice: a study of pre-operative fasting. *Nursing Standard*. 1996 Jan 24;10(18):33-6.
66. Chhajed PN, Glanville AR. Management of hypoxemia during flexible bronchoscopy. *Clinics in chest medicine*. 2003 Sep 30;24(3):511-6.
67. 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 Sep 30;102(3):704-7.
68. Gove RI, Wiggins J, Stableforth DE. A study of the use of ultrasonically nebulized lignocaine for local anaesthesia during fibreoptic bronchoscopy. *British journal of diseases of the chest*. 1985 Jan 1;79:49-59.
69. Webb AR, Fernando SS, Dalton HR, Arrowsmith JE, Woodhead MA, Cummin AR. Local anaesthesia for fibreoptic bronchoscopy: transcricoid injection or the " spray as you go" technique?. *Thorax*. 1990 Jun 1;45(6):474-7.
70. Kristensen MS, Milman N, Jarnvig IL. Pulse oximetry at fibre-optic bronchoscopy in local anaesthesia: indication for postbronchoscopy oxygen supplementation? *Respiratory medicine*. 1998 Mar 1;92(3):432-7.