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

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Abstract: Topical anaesthesia 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, spraying the oropharynx with lignocaine spray, Injecting lignocaine by piercing cricothyroid membrane. Nebulization of lidocaine in airways gives very satisfying anesthesia comparable to oral spraying with significant low plasma levels of the drug. Nebulization of lignocaine with midazolam gives good results than using only lignocaine without sedation. Nebulization of lignocaine 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 fibroptic 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, 60 study cases were given nebulization. With lignocaine & 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 lignocaine diluted in 4 ml of normal saline by nebulization for 15 minutes, before bronchoscopy, control patients had lignocaine oral 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 lignocaine 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 install 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 fibrooptic bronchoscopy. They have less discomfort & procedure is uneventful. The drug Medizolam 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 Midozolam 0.2 mg/kg IV gives good sedation [35]. The dose of Midizolam can be increased after 2 min by increments of 1 mg 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. Lignocaine is safe analgesic compared to cocaine [37]. Oropharynx can be safely anesthesied 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 Medizolam 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) Endobronchial 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 semirectum 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 doses 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 2 to 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.

**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

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

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

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Lidocaine Group</th>
<th>Placebo Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchial washings</td>
<td>52(87)</td>
<td>40(80)</td>
<td>92(84)</td>
</tr>
<tr>
<td>Bronchial brushing</td>
<td>32(53)</td>
<td>30(60)</td>
<td>62(54)</td>
</tr>
<tr>
<td>Endobronchial biopsy</td>
<td>32(53)</td>
<td>20(40)</td>
<td>52(47)</td>
</tr>
<tr>
<td>BAL</td>
<td>8(13)</td>
<td>10(20)</td>
<td>18(16)</td>
</tr>
</tbody>
</table>

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 122 mm 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. Midozolam 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 80 mm in study group and 84 mm in control group the P values is 0.932. Both control and study group had midozolam injection so not much of fluctuation of blood pressure. The diastolic blood pressure after the procedures are 70 mm in study group 80 mm 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.

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

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

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Lidocaine Group (n=60)</th>
<th>Placebo Group (n=50)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough score physicians, VAS (0-10)</td>
<td>1.5 (0-10)</td>
<td>4(0-10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cough score patients, VAS (0-10)</td>
<td>1.5(0-10)</td>
<td>3.75(0-10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Discomfor score patients, VAS (0-10)</td>
<td>2(0-10)</td>
<td>2(0-10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Supplemental lidocaine dose, mg</td>
<td>58(13)</td>
<td>157(44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total lidocaine dose, mg</td>
<td>218(41)</td>
<td>157(44.4)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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
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 then 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 note. Patient s 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 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 transcricoidal and bronchoscopic injection. The transcricoid 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 transcricoid injection group. Webb et al.; compared transcricoid injection of lignocaine to spraying the drug though bronchoscope “sprays as you go” technique. The required supplemental lidocaine dose was higher in the transcricoid injection group compared to the “sprays as you go” group.

Although effective, transcricoid administration of the lidocaine has not been widely used. The main reason seems to be sent to be procedure is unpleasant. Moreover, transcricoid 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 fibro optic 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 crico thyroid membrane which is a laborious process and very uncomfortable patients. Nebulised lignocaine with midazolam sedation before bronchoscopy is safe they undergo bronchoscopy they have less cough, stable vital parameters, less discomfort during and after procedure.

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