Randomized-controlled Trial to Study the Equivalence of 1% Versus 2% Lignocaine in Cough Suppression and Satisfaction During Bronchoscopy

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Introduction: The optimum lignocaine concentration that can achieve an acceptable level of satisfaction for both bronchoscopist and patient has not been established. The aim of this study was to compare the equivalence of the 2 lignocaine strengths in suppressing cough, and its effect on satisfaction of bronchoscopist and patient during bronchoscopy.

Methods: This was a prospective, double-blind, randomized-controlled study involving patients undergoing bronchoscopy at a single tertiary center. Patients were randomly assigned to receive either lignocaine 1% or 2% for local anesthesia. Bronchoscopy was performed by experienced bronchoscopists from the same center according to a standard protocol. A digital recorder was used to record the number of coughs. Upon completion of a bronchoscopy, both the bronchoscopist and patient charted their overall satisfaction and perception of cough on a 10-cm visual analog scale.

Results: All 61 patients’ recruited (39 males) completed the study. There were 32 in lignocaine 1% group and 29 in lignocaine 2% group. There was no difference in the mean number of coughs \( (P = 0.749) \) between the 2 groups. Bronchoscopists’ overall satisfaction and perception of cough were equal as well. Similar responses were elicited from the patients when asked to chart their perceptions for both lignocaine concentrations. The only difference \( (P < 0.001) \) seen was in the median dose of lignocaine given, lignocaine 1% group received half of what was eventually administered to lignocaine 2% group.

Conclusions: In terms of cough and perceived satisfaction for both bronchoscopist and patient, 1% is similar to 2%. Those parameters, however, were achieved with much less dose of 1%

compared with 2%. Based on our results we would advocate 1% lignocaine for bronchoscopy.

Key Words: anesthesia, flexible bronchoscopy, lignocaine, visual analog scale

During flexible bronchoscopy (FB) lignocaine is the most common local anesthesia used.\(^1\)\(^,\)\(^2\) It is the drug of choice because of its relatively quick onset of action, short duration of action, and decreased toxicity compared with other agents.

The control of cough is very important for the quality of bronchoscopy.\(^3\) Studies have shown that cough is one of the most distressing symptoms experienced by patients.\(^4\)\(^,\)\(^5\) Application of topical local anesthetic to the upper airway, larynx, and tracheobronchial tree can reduce excessive cough.\(^6\) Patient’s tolerability toward bronchoscopy depends largely on the effectiveness of local anesthesia.\(^7\) Therefore, the use of lignocaine as a topical anesthesia during FB is an important factor in determining patient’s tolerance and satisfaction of the procedure.

Recommendation for the use of lignocaine solution has been suggested by various bronchoscopy guidelines.\(^1\)\(^,\)\(^6\) The British Thoracic Society (BTS) guidelines on diagnostic FB recommends maximum dosage of 8.2 mg/kg body weight (approximately 29 mL of a 2% solution and 58 mL of a 1% solution for a 70 kg patient).\(^1\)

Both the BTS and the Thoracic Society of Australia and New Zealand guidelines have recommended the use of endobronchial lignocaine in 1% to 4% concentration for FB.\(^1\)\(^,\)\(^6\) Several other studies have advocated the dose to be between 3 and 4 mg/kg of body weight,\(^7\)\(^,\)\(^8\) to 6 to 7 mg/kg of body weight.\(^9\) These guidelines had concentrated predominantly on safety aspects of the technique,\(^1\)\(^,\)\(^6\) but the optimum lignocaine concentration that can achieve an acceptable level of satisfaction for the patient and the bronchoscopist has not been established. One study\(^10\) used various concentrations (1%, 1.5%, and 2%) and volumes of lignocaine to anesthetize the airways during bronchoscopy to determine the lowest dosage for effective anesthesia of the airway; however, it was found that all
dosages compared in the study were equally effective in producing airway anesthesia. The effectiveness of anesthesia was measured by the number of patients with sustained coughing lasting longer than 5 seconds during bronchoscopy.

We designed this study to investigate the efficacy of 1% and 2% endobronchial lignocaine during bronchoscopy. Ours was an equivalence study conducted to evaluate 2 different strengths of lignocaine during FB relating to its efficacy and satisfaction from both the patient’s and bronchoscopist’s viewpoint. Subjective assessments by bronchoscopist and patient were carried out using visual analog scale (VAS) for cough perception and overall satisfaction. Both scores were then compared with objective measurements of cough and total quantity of the drug required for the procedure.

**METHODS**

This was a 2-arm prospective, double-blind, randomized-controlled, and equivalence study. Sixty-one patients undergoing FB were recruited between February 2006 and August 2006. The patients, the bronchoscopists, and the investigator were blinded to the concentration of lignocaine solution used for the procedure. Convenient sampling was used for the sampling method. All FBs were performed on an elective basis using Olympus CV-200 bronchoscope (Shirakowa Olympus Co, Ltd, Tokyo, Japan). The patient selection criteria included those who were older than 18 years and able to give signed informed consent. We excluded those who were illiterate and could not give informed consent or answer the questionnaire. Patients with known allergy to lignocaine were also excluded. Emergent bronchoscopy procedures were not included in this study.

On the basis of the formula for equivalence study and the number of samples used previously, we required a sample size of 28 patients in each arm to obtain a power of 90% with a level. Sixty-one patients were randomly assigned to receive either endobronchial lignocaine 1% or 2% using computer-generated randomization program. The variables for randomization were patient’s age group, sex, race, baseline cough severity (patient subjective perception of his/her cough before bronchoscopy), and the different bronchoscopists involved. Thirty-two patients were in the lignocaine 1% group and 29 patients were in the lignocaine 2% group. Blood pressure and body weight were recorded before the procedure. The oxygen saturation and pulse rate were documented and monitored continuously during the procedure. Lignocaine spray (Xylocaine) 10% (Egis Pharmaceutical Ltd, Budapest, Hungary) was sprayed 5 times (4.8 mg of lignocaine each spray ie, about 25 mg in total) to the oropharynx. Approximately 5 mL of lignocaine gel 2% (Pharmacia & Upjohn, UK), equivalent to 100 mg of lignocaine, was administered in one of the nasal cavity into which the bronchoscope would be introduced. All patients received supplemental oxygen at 2 to 5 L/min via a nasal cannula.

**Cough Assessment**

The number of cough episodes was recorded using the digital recorder. The patient’s recording was solely analyzed by the primary investigator to avoid bias. A single cough was defined as an expiratory sound of varying lengths that started abruptly and frequently and that occurred several times in a single breath. A digital voice recorder (Sanyo ICR-B34T, Tokyo, Japan) recorded the number of cough via a microphone attached to the patient’s hospital gown.

Two minutes before bronchoscopy, a stat bolus dose of 1 to 2 mg intravenous midazolam was given. Patients were also supplemented with additional 1 to 2 mg if required during the procedure. The lignocaine solution was delivered through the bronchoscope using the “spray as you go” technique, 2-mL aliquots each time. Seven bouts of 2-mL lignocaine were administered: the first 4 to the vocal cord, then to the carina, and the last 2 for each upper lobar bronchus. This initial volume of lignocaine solution was standardized to patients in both arms of the study.

Extralignocaine aliquot was given as a “rescue” treatment if deemed necessary. Both standardized and rescue treatment volumes made up the total volume of lignocaine solution used. All bronchoscopic procedures performed were documented during the study.

The bronchoscopist was given the VAS to assess patient’s tolerance immediately after the procedure. Once fully alert and conscious, the patients recorded their tolerability using VAS to assess satisfaction and comfort depicted on a 10-cm horizontal straight line. The end anchors of the scale were labeled as extreme boundaries of the sensation being evaluated. The scores for satisfaction (0 = Very satisfactory; 10 = Totally unsatisfactory) and cough perception (0 = Very tolerable; 10 = Most unpleasant or awful) on VAS were marked independently by patients and bronchoscopists.

**Statistical Analysis**

Analysis of data was performed using Statistical Package for Social Sciences, version 11.5 (SPSS Inc, Chicago, IL), and a P value of less than 0.05 was considered statistically significant. Two-tailed Pearson χ² test or Fisher exact test was used to analyze categorical variables and numerical data were expressed as mean ± SD. Non-normally distributed data were subjected to nonparametric tests and median was used as a central measure with interquartile range. Student paired t test was used to compare the means within each group whereas Mann-Whitney U test was used for comparison between groups (non-normal distribution). The study was approved by the Medical Research and Ethics Committee of the Medical Faculty, Universiti Kebangsaan Malaysia (Ethics Committee Approval Code: FF-214-2005).

**RESULTS**

Sixty-one patients were recruited and all successfully completed the study without any complications. The mean age was 59.0 ± 14.3 years for the lignocaine 1%
group, and 59.2 ± 10.7 years for the other. Demographic parameters were similar in the 2 groups (Table 1). Each bronchoscopist performed a similar number of cases from both groups and the number of procedures performed was equal among the bronchoscopists. The indications for FB were also similar between the groups.

The number of cough was the same in both groups (Table 2) but the total amount of lignocaine 1% given (in mg or mg/kg) was significantly lower than lignocaine 2% (P < 0.001). Both groups received similar dose of sedation.

The VAS score of overall satisfaction and coughing sensation for both bronchoscopists and patients were shown in a box plot form in Figures 1A and B, respectively, and expressed as median (interquartile range) as the data were not normally distributed. The VAS scores for overall satisfaction by bronchoscopists were 2.2 (2.0) and 1.1 (2.6) for lignocaine 1% and 2%, respectively, whereas cough perception scores were 2.35 (2.8) and 2.4 (3.5), respectively. VAS scores for patients’ satisfaction were 0.75 (1.5) and 1.1 (2.6) and for cough perception were 2.0 (4.6) and 3.9 (6.4) for lignocaine 1% and 2%, respectively. No statistically significant difference was noted in all the VAS scores between the 2 groups, for both bronchoscopists and patients.

Five patients in lignocaine 2% group required dosing in excess of 8.2 mg/kg body weight but remained free of side effects. The median amount of 8.7 mg/kg body weight was administered. These patients had median body weight of 41 (39 to 48) kg, which was lower than the mean body weight for the overall cohort in the study (53.0 ± 11.4 kg).

### DISCUSSION

It has been found that different concentrations of lignocaine (1%, 1.5%, and 2%) were equally effective in producing anesthesia of the airway.10 However, the effectiveness was measured only by the number of patients with sustained coughing lasting longer than 5 seconds during the procedure. In our study, the equivalence of lignocaine 1% and 2% was measured subjectively by the VAS score and objectively by the total number of cough.

Both patients and bronchoscopists reported higher scores for cough perception. Previous studies4,5 had found that coughing was one of the most distressing symptoms patients experienced. Some studies14,16 had compared patient satisfaction by analyzing VAS score for cough for patients and bronchoscopists. One study, for example,14 looked at cough suppression using combined sedation with midazolam and hydrocodone, whereas the other16 was a study involving nebulized lidocaine. Our results were consistent with these studies in that the VAS score for cough perception was the main subjective measurement that reflected patient satisfaction level.

The median total dose of lignocaine received by patients in 1% group was nearly half of that in 2% group 161 (51) mg versus 340 (60) mg and this was statistically significant (P < 0.001). We found that lignocaine 1% could achieve similar equivalence and patients’ satisfaction with a much lower dose compared with lignocaine 2%. Although 1% caused similar number of cough but overdosing was not an issue. These findings are important for our future practice as there have been reported cases of death of healthy volunteers from presumed lignocaine toxicity after FB.17–19 A possible explanation for this has been suggested to be related to ignorance of the side effects of lignocaine toxicity within the medical community.20 A report from anesthetists attending training course in airway local anesthesia alluded to this fact further. In the study, the anesthetists used doses of up to 14.77 mg/kg of lignocaine by a spray-as-you-go method; some delegates were reported to have experienced involuntary movements, symptoms which may precede convulsions which is a sign of lignocaine toxicity.21 There has never been any such incidence reported locally but we

### TABLE 1. Patients’ Baseline Characteristics, Bronchoscopy Duration, and Cough Severity

<table>
<thead>
<tr>
<th>No. patients, N</th>
<th>Lignocaine 1%</th>
<th>Lignocaine 2%</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (mean ± SD)</td>
<td>59.0 ± 14.3</td>
<td>59.2 ± 10.7</td>
<td>0.946</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>22 (68.7%)</td>
<td>17 (58.6%)</td>
<td>0.411</td>
</tr>
<tr>
<td>Female</td>
<td>10 (31.3%)</td>
<td>12 (41.4%)</td>
<td></td>
</tr>
<tr>
<td>Body weight, kg (mean ± SD)</td>
<td>52.7 ± 12.1</td>
<td>53.5 ± 11.0</td>
<td>0.802</td>
</tr>
<tr>
<td>Duration of bronchoscopy (min)</td>
<td>22.8 ± 8.2</td>
<td>23.1 ± 12.0</td>
<td>0.939</td>
</tr>
</tbody>
</table>

*C Patients subjective baseline cough perception before bronchoscopy.

### TABLE 2. Total Number of Coughs Recorded and Amount of Medications Given

<table>
<thead>
<tr>
<th>Lignocaine 1%, Mean ± SD, Median (IQR), Range: Minimum-Maximum</th>
<th>Lignocaine 2%, Mean ± SD, Median (IQR), Range: Minimum-Maximum</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. cough</td>
<td>287 ± 172</td>
<td>304 ± 213</td>
</tr>
<tr>
<td>Total lignocaine dose (mg)</td>
<td>161 (51) 120-395</td>
<td>340 (60) 280-500</td>
</tr>
<tr>
<td>Total lignocaine dose (mg/kg)</td>
<td>3.5 (1.1) 2.2-7.2</td>
<td>6.5 (1.9) 4.1-9.2</td>
</tr>
<tr>
<td>Total volume of lignocaine (mL)</td>
<td>16.1 (5.1) 12.0-39.5</td>
<td>17.0 (3.0) 14.0-25.0</td>
</tr>
<tr>
<td>Total midazolam dose (mg)</td>
<td>2.0 (1.1) 1.0-4.0</td>
<td>2.0 (0.8) 1.0-3.5</td>
</tr>
</tbody>
</table>

*P value is significant at P < 0.05; IQR indicates interquartile range.
believe that this is due to under reporting. It is therefore essential to monitor the amount of lignocaine given during bronchoscopy. By using lignocaine 1%, there will be less risk of potential toxicity based on lower required dosing. Theoretically, the duration of bronchoscopy should not influence the frequency of coughing as “top-ups” with lignocaine should avoid such adverse effects. It has been suggested that local anesthesia is achieved within 2 to 3 minutes of endotracheal lignocaine application, and that topical preparation given 5 minutes before intubation blunts the reflex responses (eg, cough reflex) effectively. Furthermore, tissue-bound lignocaine produces effective local anesthesia for 35 to 45 minutes after its topical application. Essentially, the amount that is safe to use differs according to site of administration because absorption of the drug varies. In fact, even at the same site, such as the airway, different techniques of administration may have differing absorption profiles. Other studies had found that there was no correlation between the dose of lignocaine administered and the serum concentration. They also found that there was no correlation between the doses administered and the patient comfort scores during bronchoscopy. Interestingly, a study had concluded that the direct local anesthesia effect of lignocaine rather than systemic absorption from the airway was more important in controlling cough reflex during intubation.

Sedation has been shown to improve patients’ comfort. It reduces pain and provides amnesia to the procedure. This study used similar dosage of midazolam (mg/kg body weight) for the 2 groups of patients and there was no overdose. There was also no statistically significant difference in the dose given to 2 groups. The amnesia is desirable from the patients’ point of view but may cause tolerability toward the procedure. Tolerability assessment taken 2 hours postbronchoscopy may therefore be an overestimation. Midazolam may also affect ability to recall. Some studies, however, suggested that the wake up time for sedation was only 35 to 60 minutes after which patients were alert enough to assess their discomfort. In our study, VAS score was obtained 1 to 2 hours after procedure for out-patients and more than 2 hours for in-patients. We therefore believe that the patients in our study were able to reliably estimate their discomfort during bronchoscopy after the procedure.

There were several factors in our study that could affect the number of cough recorded and the various VAS scores taken. These were the number of bronchoscopists, duration of bronchoscopy, the indications, amount of sedation, lignocaine dose, and concomitant procedures. When analyzed, all these factors, however, did not show any significant difference between the 2 groups. The number of bronchoscopists, however, could be limited to 1 or 2 to reduce potential bias. Although they were all similarly experienced, inevitably they will have their own unique style and ways of maneuvering the bronchoscope and performing its procedures, and different mode of comforting the patients. Extension of the period of the study will enable a single or a pair of bronchoscopists to perform all the cases and this will result in less bias.

We conclude that the use of lignocaine 1% during FB achieved similar efficacy and resulted in comparable patients’ and bronchoscopists’ satisfaction levels compared with lignocaine 2%. It is safe and the usage will reduce the incidence of lignocaine overdose, hence reducing any adverse events that could be due to lignocaine administration during bronchoscopy. We recommend the use of lignocaine 1% for local anesthesia of the larynx and bronchial tree during bronchoscopy.

REFERENCES


