

Does the Use of Topical Lignocaine Spray during Microlaryngeal Surgery Under General Anaesthesia have Significant Clinical Benefit? - A Prospective Double-Blind Randomized Placebo-Controlled Trial

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Abstract

Objective: To determine if topical lignocaine used during microlaryngeal surgery under general anaesthesia confers significant clinical benefit by reducing the pressor response and laryngospasm that often occur during recovery.

Study Design: Prospective double-blind randomised placebo-controlled trial in a UK Otolaryngology department. 85 patients undergoing elective microlaryngeal surgery receiving either 4 ml 4% lignocaine spray to the vocal cords and piriform fossae or 4 ml 0.9% saline spray to the same areas at induction of anaesthesia.

Methods: Primary outcome measures were pulse and blood pressure recorded immediately before spray application and at 5 minute intervals during recovery for 20 minutes and the degree of laryngospasm or cough (absent, mild, moderate, severe) recorded at the same intervals. Secondary outcome measures included patient grading of post-operative throat discomfort on a visual analogue scale (1 to 100 mm) and analgesia requirements in the first 6 hours post-operatively.

Results: 44 patients (mean age 58 years, 22 male, 22 female) were randomised to receive lignocaine and 41 patients (mean age 57 years, 24 male, 17 female) saline spray. No statistically significant difference was found between groups in mean pulse or mean systolic and diastolic blood pressure immediately before application of spray or during the recovery period. There was no difference in the degree of post-operative coughing or laryngospasm or analgesia requirements between the groups. Topical lignocaine was associated with more throat discomfort than saline ($p=0.03$; Diff 0.9; 95% C.I. 0.1 to 1.8).

Conclusion: The use of topical lignocaine spray conferred no clinical benefit in this study.

Keywords: Microlaryngeal surgery; Topical lignocaine

Abbreviation: Level of Evidence: Level Ib

Introduction

The pressor response and coughing which follow extubation are well documented during the immediate recovery period after many types of surgery. The pressor response is a sympathomimetic stress response. It comprises tachycardia and hypertension which can in turn lead to dysrhythmias, myocardial ischaemia and even myocardial infarction. It is therefore routine practice for some anaesthetists to apply topical anaesthetic to the larynx at induction to prevent or reduce these problems. Bidwai et al. demonstrated a reduced pressor response upon extubation in patients given topical lignocaine approximately five minutes before extubation in lower abdominal and gynaecological surgery [1]. Staffel et al. found the risk of laryngospasm and stridor post adenotonsillectomy to be reduced by topical lignocaine applied just prior to intubation [2]. There is however no evidence available at present to support the use of topical lignocaine in this way for microlaryngeal surgery.

Lignocaine is an amide local anaesthetic agent which causes reversible block to conduction along nerve fibres by blocking sodium channels. It is effectively absorbed from mucous membranes and can give plasma concentrations comparable to those obtained by injection. Some studies have shown that peak plasma levels are reached at up to thirty minutes after topical administration [3]. Such topical use in the airway blocks mucosal cough receptors as well as blocking c pain fibre endings directly. It is available commercially as Laryng-O-jet[®] for

laryngotracheal anaesthesia. The aim of this study was to determine if topical lignocaine spray used during

microlaryngeal surgery under general anaesthesia confers significant clinical benefit. We hypothesized that there was no difference in the pressor response or degree of coughing or laryngospasm using topical lignocaine spray compared to topical saline during microlaryngeal surgery.

Methods

Local research ethics committee approval was obtained for a prospective double-blind randomised placebo controlled trial. Informed written consent was obtained from adults undergoing microlaryngeal surgery under general anaesthesia. Consecutive

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consenting patients were randomised by computer on an intention to treat basis to receive either 4 ml topical 4% lignocaine hydrochloride spray (160 mg) or 4 ml 0.9% saline spray to the vocal cords and piriform fossae at induction of anaesthesia. Spray contained in coded and otherwise unmarked identical bottles was applied to both vocal cords and piriform fossae at induction of anaesthesia. The code was held in the hospital pharmacy and was only broken upon completion of the study and after data analysis. Thus participants and investigators, outcome assessors and data analysts were blinded to each participant's spray allocation. Exclusion criteria included a history of lignocaine sensitivity, pregnancy, complete heart block, porphyria and inability to give informed consent. The primary outcome measures included pulse rate, systolic and diastolic blood pressure and the degree of coughing or laryngospasm. Coughing or laryngospasm was recorded as absent (no coughing), mild (single episode), moderate (2 episodes) or severe (3 or more episodes) in each 5 minute period during recovery. An episode of coughing was defined as a single cough or a series of coughs and was deemed to have ended after ten seconds of no coughing. Each of these parameters was recorded immediately before application of spray, at the start of recovery and at intervals of 5, 10, 15 and 20 minutes during recovery. That time immediately after removal of the laryngoscope or immediately after extubation was defined as the start of recovery (t=0). Secondary outcome measures included pain as indicated by the patient post-operatively on a 100 mm visual analogue scale, where 0 represented no pain and 100 represented extreme pain, and patient requirements for analgesia in the first six hours following microlaryngeal surgery.

It was calculated that a minimum of seventeen patients would be required in each arm of the trial to show a difference if one existed at the 0.05 significance level with a power of 80%. Statistical analysis was performed using Chi-Square test, unpaired t-test and Mann-Whitney

U test (SPSS Version 11.0). Confidence intervals were calculated for the p values obtained (CIA Software).

Results

The flow of participants through the trial is summarised in the trial profile (Figure 1). Of the 4 patients excluded, one had their procedure cancelled on medical grounds, one took his own discharge from the ward prior to commencement of the theatre list and in two cases intubation was deemed not to be possible by the anaesthetic team pre-operatively. For two patients randomised to placebo but not subsequently reaching the end point, in one case the spray was lost and in another the data collected was lost. One patient randomised to receive lignocaine spray failed to reach the end point as the procedure was cancelled when it was found that the medical notes were not available.

The youngest patient recruited was 31 years and the oldest 87 years. There was no significant difference between the groups with respect to mean age. (p=0.665, Diff 1.22; 95% CI -4.4 to 6.8) (Table 1). Nor was there any significant difference in the sex distribution between the two arms of the trial (p=0.43 Diff 0.1; 95% CI -0.1 to 0.3). Participants undergoing microlaryngeal surgery had a range of diagnoses including dysplasia, carcinoma in situ or carcinoma (n=32), chronic laryngitis (n=19), nodule, polyp or cyst (n=11), papillomatosis (n=4), Reinke's oedema (n=3), subglottic stenosis (n=3), tracheal stenosis (n=2) and vocal cord palsy (n=1). The findings at microlaryngoscopy were normal in 7 participants.

The term 'microlaryngeal surgery' in this study incorporated a range of specific procedures which included microlaryngoscopy alone (n=7), microlaryngoscopy with biopsy (n=47), microlaryngoscopy combined with laser therapy (n=16), microlaryngoscopy and biopsy combined with rigid oesophagoscopy (n=14) and microlaryngoscopy with vocal cord injection (n=1).

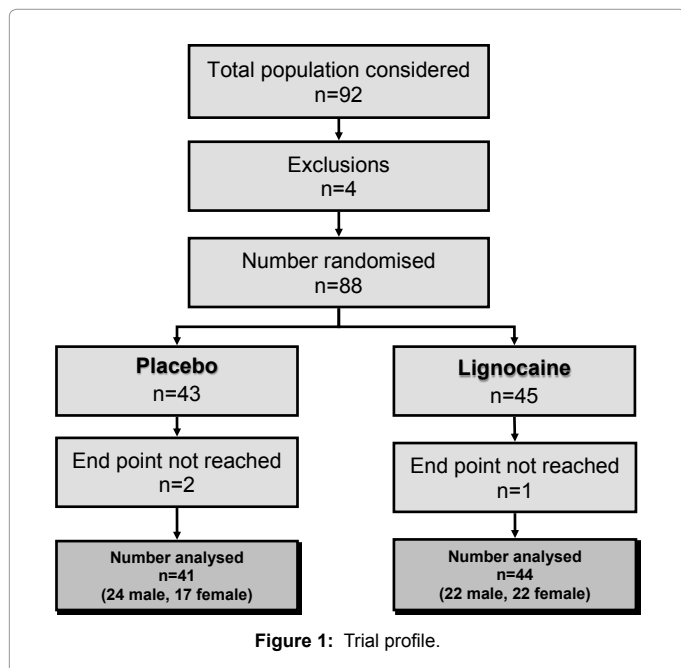
The mean duration of microlaryngeal surgery overall was 24 minutes with a range of 6 to 60 minutes. The mean duration of surgery was 23 minutes in the placebo group (range 8-55 minutes) and 25 minutes in the lignocaine group (range 5-60 minutes) (p=0.465 Diff 2.0; 95% CI -3.2 to 6.9).

The mean pulse rate for the placebo group and the lignocaine group recorded immediately before application of spray and at time intervals 0, 5, 10, 15 and 20 minutes during recovery are shown in Figure 2. An initial pressor response was evident in both groups but this was not sustained in either group. There was no statistically significant difference between the groups at any of the recorded time intervals.

With respect to the mean systolic and diastolic blood pressure recorded at the same time intervals a similar initial pressor response was observed. On this occasion the elevation of both systolic and diastolic blood pressure was sustained during the recovery period in the lignocaine group but returned towards baseline in the placebo group during the same timeframe (Figure 3). None of the differences in the recorded blood pressure levels between the groups at any of the time intervals reached statistical significance with the exception of the difference between the systolic pressure in the two groups recorded at 20 minutes during recovery (p=0.001, Diff 14.9; 95% CI 6.6 to 23.3).

As time progressed during the recovery period more coughing was observed in both groups. There was, however, no statistically significant difference between the groups in the severity of the coughing at any of the recorded time intervals (Figure 4).

The mean pain scores recorded on a 100 mm visual analogue scale



Spray	Mean Age	SD	Range
Placebo	57	11.3	33 - 84
Lignocaine	58	13.9	31 - 87

Table 1: Mean age and age range of participants randomised to placebo and lignocaine spray.

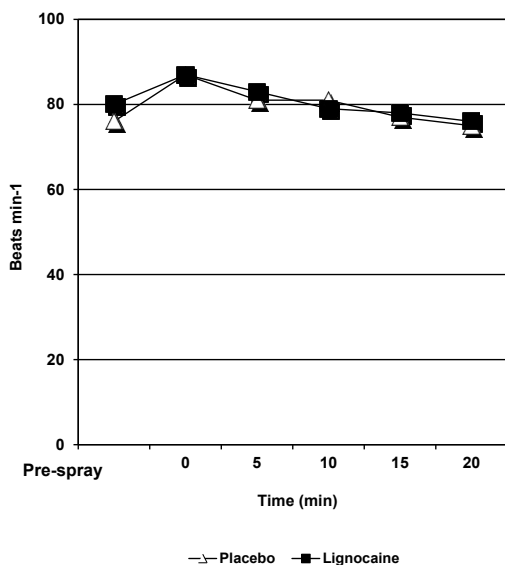


Figure 2: Mean pulse rate in the two study groups immediately before application of spray and at time intervals of 0, 5, 10, 15 and 20 minutes during recovery.

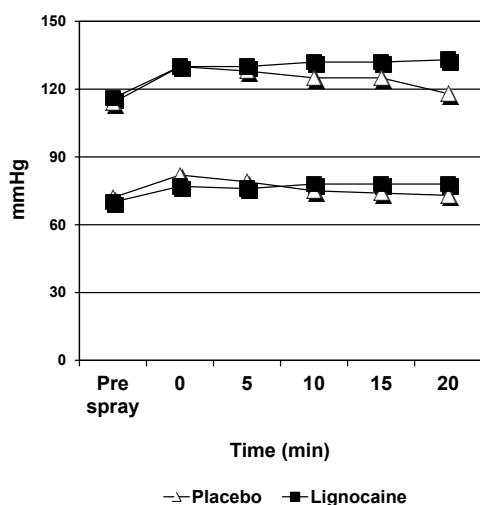


Figure 3: Mean systolic and diastolic blood pressure in mmHg immediately prior to application of spray and at time intervals 0, 5, 10, 15 and 20 minutes during recovery.

six hours post-operatively are shown for each group in Figure 5. The mean pain score for participants randomised to receive lignocaine spray was higher than that for participants receiving placebo. This difference reached statistical significance ($p=0.03$, Diff=0.9; 95% CI 0.1 to 1.8).

Although the degree of post-operative throat discomfort was greater in the lignocaine group there was no significant difference between the groups in analgesia requirements during the first six hours post-operatively (data available for 64 patients) ($p=0.3$, Diff =0.2; 95% CI -0.2 to 0.2). The majority of patients in fact required no post-operative analgesia ($n=50$, 78%) (Table 2).

Discussion

This study showed no benefit of topical lignocaine spray over

placebo in suppressing the pressor response or coughing in the recovery period after microlaryngeal surgery. Nor was any benefit conferred over placebo in reducing post-operative throat discomfort or analgesia requirements. One can hypothesize why lignocaine spray exhibited no advantage over placebo. It could be that the lignocaine was absorbed poorly and that the resulting plasma concentration of lignocaine was too small. The absorption characteristics of the mucosa, epithelial thickness, number of membrane pores, and tissue pH probably all serve to delay absorption. Clearly these factors vary according to the diagnosis.

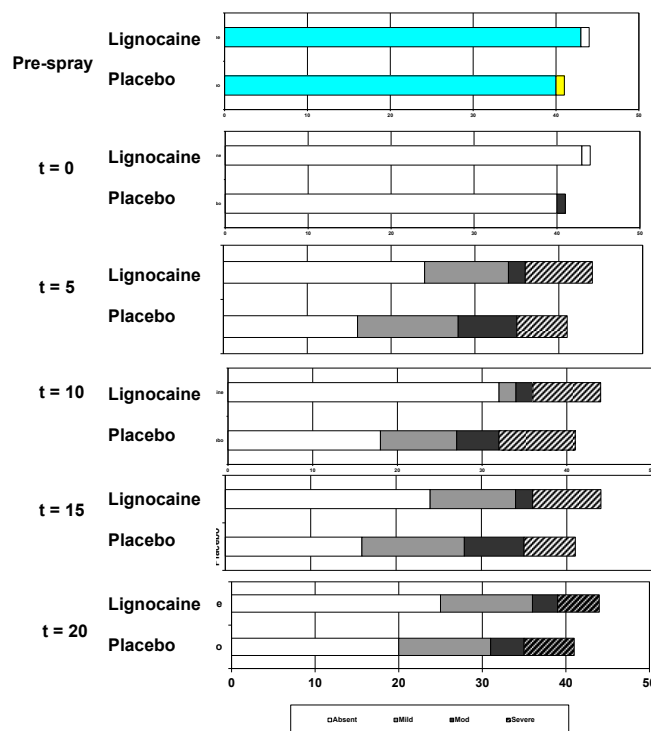


Figure 4: Degree of coughing in seconds immediately before spray and at t=0, 5, 10, 15 and 20 minutes during recovery.

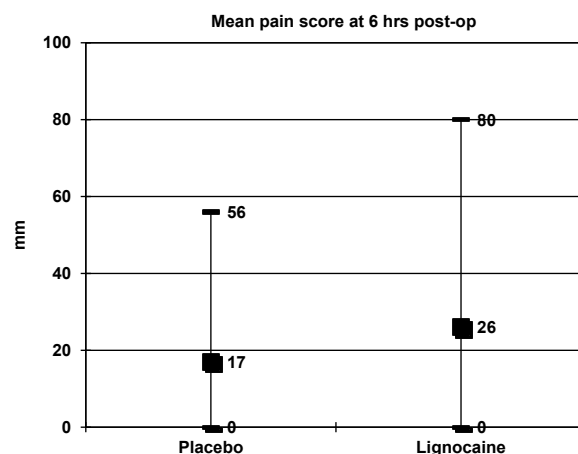


Figure 5: Mean pain score as assessed by participants on a 100 mm visual analogue scale at 6 hours post-operatively.

Spray received	No post-op analgesia requirements	Post-op analgesia required	Total
Lignocaine	28	8	36
Placebo	22	6	28
Total	50	14	64

Table 2: Post-operative analgesia requirements (data available for 64 patients).

Topical lignocaine was associated with a greater degree of post-operative throat discomfort than placebo in the study. Sore throat is in fact a known potential side-effect of topical lignocaine [4]. Frosh et al. also found that the routine use of topical lignocaine spray in the nose prior to fiberoptic nasendoscopy makes the experience more painful for the patient [4]. It is the low pH of lignocaine solutions that has been found to be responsible for post-operative sore throat [5]. In an animal study interestingly a degree of oedema and cell damage developed in the mucosa of the cat's larynx after it was sprayed with a 10% aerosol preparation of lignocaine [6].

There were no major adverse events during the trial. One 60 year old female participant receiving placebo spray, and who underwent laser excision of a subglottic intubation granuloma, developed mild laryngospasm at 15 and 20 minutes during recovery. This was self-limiting. Based on our results it is unlikely that the laryngospasm in this case occurred because topical lignocaine was not received. A single case of supraventricular tachycardia (SVT) was recorded intraoperatively in a 75 year old male participant. This was short-lived and also self-limiting. From the results of the study we cannot conclude that this episode of SVT was definitely induced by topical lignocaine application.

A potential weakness in the trial was in our assessment of coughing by using an unvalidated and subjective scoring system. Nonetheless it was piloted for ease of use prior to the trial using two independent assessors. No significant interobserver variation was found. We acknowledge that a more objective and reliable measure of coughing could have been employed such as a microphone recording of cough frequency and intensity using an ambulatory recorder or an automatic cough counters.

Topical adrenaline is frequently applied on neurosurgical pledgets to the surgical site during microlaryngeal surgery to achieve a bloodless operative field or secure haemostasis at the completion of surgery. In this study topical adrenaline was applied in 40 cases overall (47%). Of participants in whom topical adrenaline was used in this way 20 received lignocaine spray (45%) and 20 received placebo (49%). There was no statistically significant difference between the groups in the use of topical adrenaline ($p=0.6$, Diff=0; 95% CI-0.2 to 0.2). We accept however that this is a potential source of bias as topical adrenaline itself is also readily absorbed from the mucosal surfaces of the airway. It could have haemodynamic effects including tachycardia, hypertension and increased myocardial irritability.

It is worth noting that during the trial period a range of procedures were performed in the two study groups under the umbrella of

microlaryngeal surgery. Furthermore a single anaesthetic technique was not employed during the study with some participants having a tubeless field whilst others were intubated. We acknowledge that these are both potential sources of bias in the study. Assessment of the lignocaine effect in the face of different anaesthetic techniques would clearly require a much larger study.

Conclusions

Topical lignocaine did not reduce the pressor response to microlaryngoscopy or extubation in this study. There was no significant reduction in post-operative coughing or laryngospasm conferred by topical lignocaine either. Topical lignocaine did however appear to be associated with a greater degree of post-operative throat discomfort than placebo. The post-operative analgesia requirements were comparable between groups. Topical lignocaine spray applied at induction for microlaryngeal surgery under general anaesthesia confers no significant clinical benefit.

Acknowledgement

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