Combined nebulization and spray-as-you-go topical local anaesthesia of the airway

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Background. Twenty-five anaesthetists underwent awake fibreoptic intubation using a combination of nebulization and topical local anaesthesia. Plasma lidocaine concentrations were measured and the quality of the local anaesthesia was assessed.

Methods. After i.v. glycopyrrolate 3 μg kg⁻¹ and intranasal xylometolazone 0.1%, lidocaine 4% 200 mg was administered by nebulizer. Supplementary lidocaine to a maximum total of 9 mg kg⁻¹ was applied directly and via a fibreoptic endoscope. Nasotracheal intubation was performed once the vocal cords became unreactive. Heart rate, non-invasive blood pressure and oxygen saturation were recorded at 5-min intervals. Blood sampling commenced with a baseline sample and continued at 10 min intervals until 60 min after final administration of local anaesthetic. Subjects graded levels of anxiety, pain and coughing using written and visual analogue scales.

Results. Conditions for fibreoptic endoscopy and intubation were good. Seventeen received the maximum lidocaine dose of 9 mg kg⁻¹. The average dose used was 8.8 mg kg⁻¹. All plasma lidocaine concentrations assayed were below 5 mg litre⁻¹. Four volunteers reported feeling lightheaded after the procedure, despite normal blood pressure. Of these, two had the highest plasma lidocaine concentrations recorded: 3.5 and 4.5 mg litre⁻¹. Twenty-two of the 25 subjects found endoscopy and intubation acceptable, three found it enjoyable and no subject rated it as distressing.

Conclusions. This method of airway anaesthesia was acceptable to this small group of unsedated subjects. It produced good conditions for fibreoptic intubation. A maximum calculated lidocaine dose of 9 mg kg⁻¹ did not produce toxic plasma concentrations of lidocaine.

Keywords: airway, tracheal intubation; anaesthetics local, lidocaine; anaesthetic techniques, fibreoptic; anaesthetic techniques, laryngoscopy; toxicity, local anaesthetics

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Awake fibreoptic intubation is often regarded as a cornerstone in the management of the predicted difficult airway.1–3 The Department of Anaesthesia at the Norfolk and Norwich University Hospital provides a training course in local anaesthesia of the airway and awake fibreoptic intubation. Anaesthetists act as subjects whilst they learn and practise on each other.4,5 A technique for topical anaesthesia of the airway was evolved for this purpose; it uses a combination of nebulization and spray-as-you-go topical anaesthesia.

A local anaesthetic technique acceptable to unsedated volunteers undergoing awake fibreoptic intubation may have applications where avoidance of sedation is desirable, when haemodynamic stability is important,5,7 or, as used here, when providing instruction in awake fibreoptic intubation. Though well tolerated, the acceptability of the procedure might be improved by the application of more lidocaine. However, when using this method of airway anaesthesia we have observed symptoms that could possibly be attributed to lidocaine toxicity.5 Therefore, we undertook this study to assess the acceptability of the technique and measure peak plasma lidocaine concentrations achieved.

Methods

After Local Research and Ethics Committee approval, course applicants were sent an information sheet detailing the background, method and risks of the study. Those willing to participate returned a completed consent form. The applicants were accepted for the training course irrespective of their consent to take part in the study. Risks of fibreoptic intubation under local anaesthetic were explained and written consent was obtained for an awake fibreoptic intubation as described previously.5 Subjects were excluded because of pregnancy, hypertension, heart disease, liver disease,
epilepsy, diabetes, asthma, a history of epistaxis, nasal problems, allergy to drugs used during the procedure (xylometolazone, lidocaine, phenylephrine, glycopyrrolate) or a current infectious disease.

The subjects fasted for 4 h before endoscopy. The administration of local anaesthetic and performance of endoscopy took place in an anaesthetic room or operating theatre with a full range of resuscitation equipment immediately available. After initiation of non-invasive monitoring, a 20 gauge i.v. cannula was inserted and an infusion of Hartmann’s solution was established. Intravenous glycopyrrolate 3 μg kg⁻¹ was administered and two puffs of xylometolazone 0.1% were delivered to each nostril. Over the following 20 min, with the subject sitting upright, lidocaine 4%, 200 mg, was nebulized with an Intersurgical Cirrus nebulizer using oxygen 8 litre min⁻¹ as a driving gas. After nebulization, 2 ml of 5% lidocaine (100 mg) containing 0.5% phenylephrine (Aurum) and 4 aliquots (40 mg) of 10% lidocaine were sprayed into the nose and oropharynx respectively. Endoscopy was then performed in the supine position; supplementary doses of lidocaine 4% up to a maximum total dose of 9 mg kg⁻¹ were administered to the airway via the fibrescope. Most of the drug delivered by nebulization is wasted. For purposes of lidocaine dose calculation, it was assumed that 75% of the nebulized drug was lost, therefore only 50 mg of the nebulized lidocaine was included in the dosage calculation.

A 1.1 mm end hole epidural catheter was threaded through the working channel of the endoscope. Proximally this was attached to a three-way tap and an oxygen supply of 1 litre min⁻¹ (Fig. 1A). Lidocaine injected via the three-way tap (Fig. 1B) emerged distally as a fine spray. When the vocal cords ceased to react to further lidocaine administration, the endoscope was advanced into the trachea and a nasotracheal tube was inserted.

The weight of each subject was recorded together with the time and total dose of lidocaine and glycopyrrolate administered. The application of local anaesthetic was performed by course delegates under direct supervision. ECG and oxygen saturation were monitored continuously throughout the procedure. Heart rate, non-invasive blood pressure and pulse-oximetry readings were recorded at 5 min intervals. The highest recorded values of mean arterial blood pressure (MAP) and heart rate (HR) for each subject were compared with their baseline values and the percentage increase for each subject was calculated.

A baseline blood sample was taken using the i.v. cannula before any lidocaine was administered (T0). The second sample was taken 20 min later, after nebulization (T20). Subsequently, additional topical lidocaine was administered directly and via the endoscope to the lower airway. Further blood samples were taken at 10 min intervals until 60 min had elapsed after the last dose of lidocaine. Two 5 ml samples of blood were drawn via a three-way-tap from the cannula; the first 5 ml, containing dead space fluid, was discarded. Blood samples were then separated in a centrifuge and stored at 4°C. Assays were performed using high-performance liquid chromatography with UV detection accurate to 0.01 mg litre⁻¹.

After the procedure, all delegates completed an anonymous questionnaire. They graded levels of anxiety, pain and coughing using written and visual analogue scales. Subjects were asked to record any local anaesthetic side-effects they may have experienced.

**Results**

Twenty-six delegates were studied over a 2-year period. Blood sampling was abandoned in one subject because of poor flow through the i.v. cannula; this subject was removed from the study. In the remaining 25 subjects, fibreoptic endoscopy and nasotracheal intubation were completed.

Continuous oximetry and ECG monitoring revealed no abnormalities. The average increase in MAP was 16.2%, with a range of 1.0–33.3% (Fig. 2). HR values were more variable, with an average increase of 30.2% and a range of 0–158.3% (Fig. 3).

The time from start (T0) to final application of local anaesthetic ranged from 40 to 60 min (T60). Blood sampling continued for a further 60 min. The total duration of sampling ranged from 100 to 120 min (T100–T120).
Seventeen volunteers received the maximum calculated lidocaine dose of 9 mg kg\(^{-1}\). The median dose of lidocaine used was 8.9 mg kg\(^{-1}\), with a range of 7.3–9.2 mg kg\(^{-1}\). All levels assayed were below 5 mg litre\(^{-1}\), a level commonly regarded as toxic.\(^{11–14}\) These are represented graphically in Figure 4.

Four volunteers (subjects 9, 13, 18 and 23) reported feeling lightheaded with no evidence of hypotension. Subjects 9 and 18 recorded the highest peak plasma lidocaine concentrations, 4.5 and 3.5 mg litre\(^{-1}\) respectively. Subjects 13 and 23 recorded peak concentration levels below 3 mg litre\(^{-1}\). Subjects noted other symptoms: these included dysphoria, euphoria, dizziness, nausea and shivering.

All 25 subjects reported endoscopy and intubation to be acceptable; three found it enjoyable. The visual analogue scores for pain, anxiety and coughing/gagging averaged 6.3, 6.3 and 6.5 respectively (where 0 was described as absolutely awful and 10 as enjoyable).

Discussion
Nebulized lidocaine has been shown to modify the haemodynamic response to fibreoptic intubation under sedation\(^{7,11}\) and to direct laryngoscopy under general anaesthesia.\(^{6}\) We use nebulized lidocaine before topical anaesthesia in order to
render subsequent direct application of local anaesthetic more tolerable. This combination of techniques provides effective local anaesthesia for endoscopy and intubation. All 25 unsedated volunteers rated the experience as acceptable. This is supported by their visual analogue scores for pain, anxiety and coughing. However, side-effects such as lightheadedness, dysphoria, nausea and shivering were reported, symptoms suggestive of lidocaine toxicity.

Rapid absorption, or the administration of excessive doses of local anaesthetic (lidocaine), is well known to cause toxicity. The toxic plasma concentration of lidocaine is commonly accepted as 5 mg litre\(^{-1}\)\(^{11-14}\) though concentrations of up to 18 mg litre\(^{-1}\) have been recorded without apparent toxicity.\(^{15}\) Side-effects of lidocaine administration\(^{16-19}\) are reported to develop when plasma concentrations reach 4 mg litre\(^{-1}\). Early features include tinnitus, lightheadedness and circum-oral numbness. Visual disturbances may occur with a plasma concentration of 6 mg litre\(^{-1}\), involuntary muscle spasms at 8 mg litre\(^{-1}\), convulsions at 10 mg litre\(^{-1}\) and cardiac depression at 20 mg litre\(^{-1}\). The adoption of 5 mg litre\(^{-1}\) as a toxic plasma lidocaine concentration appears to be somewhat arbitrary; however, the acceptance of 5 mg litre\(^{-1}\) as an upper limit affords a margin of safety with regard to serious side-effects, such as convulsions and cardiac arrest.

The highest plasma lidocaine concentration we observed was 4.5 mg litre\(^{-1}\). Only two subjects experienced peak plasma lidocaine levels greater than 3 mg litre\(^{-1}\). Both subjects complained of lightheadedness and of feeling unwell immediately after the procedure. Symptoms coincided with the peak plasma lidocaine concentration observed 20–60 min after the last administration of lidocaine. These symptoms might alert the clinician to limit further administration or indicate the need for continued close monitoring after the procedure.

In eight of the 25 subjects studied, the highest lidocaine concentration was observed in the final sample, 60 min after the cessation of lidocaine administration (subjects 1, 6, 8, 10, 13, 16, 19 and 22). It is possible that plasma lidocaine levels continued to rise in these subjects. However in all eight cases the highest measured concentration level was less than 3 mg litre\(^{-1}\) and the rate of increase was decreasing. The highest plasma lidocaine concentrations were noted in those subjects in whom concentrations increased most rapidly.

Lidocaine pharmacokinetics are complex;\(^{18}\) absorption varies with site and mode of delivery\(^{20}\) and the use of anticholinergic drugs.\(^{21}\) Direct application of an average lidocaine dose of 9.3 mg kg\(^{-1}\) has been used for diagnostic bronchoscopy without clinical manifestations of toxicity,\(^{13}\) although a peak plasma lidocaine concentration of 9.5 mg litre\(^{-1}\) was observed in one subject.

Parkes and colleagues\(^{12}\) reported peak plasma lidocaine concentrations of less than 0.5 mg litre\(^{-1}\) after nebulization of 6 mg kg\(^{-1}\). Mostafa and colleagues\(^{11}\) recorded a peak plasma lidocaine concentration of 1.51 mg litre\(^{-1}\) with the same dose and delivery method. Where many factors influence the absorption of lidocaine, subtle changes in the overall technique, such as the use of anticholinergic drugs or possibly even the position of the subject, may alter the site or speed of absorption. Each method of airway anaesthesia must be assessed independently with regard to local anaesthetic toxicity, particularly where high doses of local anaesthetic are used.

The median dose of lidocaine we used was 8.9 mg kg\(^{-1}\), with a range 7.3–9.2 mg kg\(^{-1}\). It has been estimated that only 8–12% of lidocaine given by a nebulizer will reach the airway as a result of wastage.\(^{8}\) If the nebulized lidocaine is ignored, a median dose of 8.27 mg kg\(^{-1}\) (range of 6.7 to 8.5 mg kg\(^{-1}\)) of lidocaine was administered to the airway. This correlates closely with recent guidelines issued by the

![Fig 4 Plasma lidocaine concentration in each subject.](image-url)
British Thoracic Society;\textsuperscript{14} they recommend the total dose of lidocaine applied during bronchoscopy should be limited to 8.2 mg kg\(^{-1}\).

The death of a healthy volunteer from presumed lidocaine toxicity has occurred after fibreoptic bronchoscopy for research purposes.\textsuperscript{22,23} This may indicate ignorance of the significance of lidocaine toxicity within the medical community. More recently, a report of anaesthetists attending a training course in airway local anaesthesia raises concerns.\textsuperscript{24} Doses of up to 14.77 mg kg\(^{-1}\) of lidocaine were administered by a spray-as-you-go method; some delegates were reported to have experienced involuntary movements—symptoms which indicate cortical irritability and may precede convulsions.\textsuperscript{18,19} No involuntary movements were observed with the lower doses of lidocaine used during our study.

In conclusion, a combined method of nebulization and direct application of lidocaine to the airway was acceptable to this small group of unsedated subjects. It produced good conditions for fibreoptic intubation. In this series of 25 subjects a maximum calculated dose of 9 mg kg\(^{-1}\) produced one peak plasma lidocaine concentration of 4.5 mg litre\(^{-1}\) but none greater than 5 mg litre\(^{-1}\). When using combined nebulization and topical anaesthesia for training purposes, calculated lidocaine administration should not exceed 9 mg kg\(^{-1}\).

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