GLYCOPYRRONIUM PROLONGS TOPICAL ANAESTHESIA OF ORAL MUCOSA AND ENHANCES ABSORPTION OF LIGNOCaine

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SUMMARY

We have studied the effect of glycopyrronium on the anaesthetic action and absorption of topical lignocaine in 10 healthy, non-smoking volunteers. Lignocaine 100 mg was sprayed on the oral mucosa 15 min after random administration of glycopyrronium 4 μg kg⁻¹ or normal saline i.v. Glycopyrronium decreased the mean analgesia score from 2 to 0.1 (2 = baseline; 0 = anaesthesia) at 4 min compared with a change from 2 to 0.5 after normal saline (P < 0.05). All scores returned to baseline by 40 min and 20 min in the glycopyrronium and control groups, respectively. The mean (SD) peak plasma lignocaine concentration was 0.57 (0.29) ng ml⁻¹ after glycopyrronium and 0.31 (0.10) ng ml⁻¹ after saline (P < 0.05) and were attained in 17 min (range 10–40 min) and 29 min (range 8–40 min), respectively. Pretreatment with glycopyrronium enhanced absorption and prolonged the analgesic action of topically administered lignocaine. (Br. J. Anaesth. 1993; 70: 94–95)

KEY WORDS

Topical anaesthetics are often applied to mucous membranes of the airway before laryngoscopy or bronchoscopy [1–3]. The plasma concentrations of lignocaine vary after topical administration [1–4] and absorption is affected by the site and method of administration [3, 5]. It has been suggested that the anaesthetic efficacy and plasma concentrations of a topical local anaesthetic may be affected also by the conditions of the mucous membranes [1, 3, 5].

An anticholinergic agent may be administered before procedures in the mouth and upper airway to inhibit vagal responses and to dry mucous membranes. The present study was designed to evaluate the effect of i.v. glycopyrronium on duration of analgesia and plasma concentrations after topical administration of lignocaine.

METHODS AND RESULTS

After obtaining hospital Ethics Committee approval, we studied 10 healthy, non-smoking volunteers (five females and five males, ages 19–47 yr, weights 55–100 kg) in a randomized fashion. Each subject served as their own control. At least 24 h elapsed between each experiment.

Subjects were studied in the supine position with a 30° head-up tilt. An antecubital vein was cannulated for i.v. administration of drugs and for obtaining blood samples for measurement of plasma concentrations of lignocaine.

After baseline measurements, either glycopyrronium 4 μg kg⁻¹ or normal saline was injected in the same volume over 30 s. The time elapsed from drug administration to the point when the subject indicated dryness of the mouth was recorded.

Fifteen minutes after drug administration, the subjects inhaled and held their breath, then lignocaine 100 mg (Xylocain, Astra, Sweden) was sprayed over 10 s on the buccal surfaces and the upper part of the soft palate. Subjects were allowed to swallow, but not to spit. Sensation to pinprick in the soft palate was assessed and scored: 0 = no sensation (anaesthesia); 1 = feeling of touch only (analgesia); 2 = normal sensation (baseline). These tests were performed by the same investigator, who was unaware of the dryness score given by the subject.

During the study the ECG was monitored continuously. Heart rate (HR) and arterial pressures (AP) were recorded every 5 min until lignocaine spray. After the spraying, HR and AP were recorded, anaesthesia tested and blood obtained at 2, 4, 6, 8, 10, 15, 20, 30 and 40 min. Any symptoms of lignocaine toxicity were noted.

Blood samples for measurement of plasma concentrations of lignocaine were obtained in tubes containing dried lithium heparin. After centrifugation, samples were frozen. Lignocaine concentrations...
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It has been suggested that anticholinergic drugs, by drying the mouth, increase the degree of topical anaesthesia [5]. In this study, we found that analgesia scores were on average smaller and the duration of analgesia clearly longer after administration of glycopyrronium.

Absorption of lignocaine through the mucous membranes of the airway is rapid and depends not only on the characteristics of the drug, but also on the site of application, being more rapid from the lower than from the upper airway [5]. Efthimiou and colleagues showed that only 5% of variation in the absorption of lignocaine was attributable to sputum volume or cigarette consumption. The most important factor was the dose per unit body weight [3]. We did not find a positive correlation between the maximal concentration of lignocaine and the dose given, but our results indicate that anticholinergic drugs may enhance topically administered lignocaine absorption. This contradicts results of Morrell, Chappell and White [1]. Their study was not, however, focused on the effect of anticholinergics on lignocaine absorption.

The time to reach peak concentrations after topical lignocaine administration has been found to vary [1–4]. Efthimiou and colleagues sprayed lignocaine on the oral mucosa of unpremedicated volunteers. The dose was larger than ours, but the value of absorption was similar to our control data [3]. Absorption was significantly faster after glycopyrronium in our study. Without anticholinergic pretreatment, topical anaesthetic is diluted and washed by saliva, decreasing contact with the oral mucosa and increasing the amount swallowed. The swallowed lignocaine is probably absorbed slowly in the duodenum, perhaps explaining the slowly increasing and small plasma concentrations.

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**REFERENCES**