EFFECTS OF I.V. LIGNOCaine ON AIRWAY REFLEXES ELICITED BY IRRITATION OF THE TRACHEAL MUCOSA IN HUMANS ANAESTHETIZED WITH ENFLURANE

T. NISHINO, K. HIRAGA AND K. SUGIMORI

SUMMARY

We have investigated the effects of bolus administration of lignocaine 1.5 mg kg\(^{-1}\) i.v. on respiratory responses to airway irritation induced by instillation of distilled water into the trachea in 10 patients anaesthetized with enflurane (1.5\% end-tidal). Before administration of lignocaine, airway irritation elicited not only the cough reflex, but also other respiratory reflexes such as expiration, apnoea and spasmodic panting. Immediately after administration of i.v. lignocaine, when plasma concentrations of lignocaine exceeded 4.7 \(\mu\)g ml\(^{-1}\), tracheal irritation elicited only brief apnoea. Other reflex responses were suppressed completely; they recovered gradually with progressive decrease in plasma concentration of lignocaine. The apnoeic reflex was not eliminated at plasma lignocaine concentrations greater than 7.0 \(\mu\)g ml\(^{-1}\), whereas the expiration reflex, cough reflex and spasmodic panting were eliminated effectively by plasma concentrations of lignocaine greater than 3.5, 2.8 and 2.2 \(\mu\)g ml\(^{-1}\), respectively.

KEY WORDS

It is accepted generally that anaesthesia suppresses airway reflexes. We have shown previously that tracheal stimulation causes several reflex responses in humans anaesthetized with enflurane, and that the character of these responses is dependent on depth of anaesthesia [1]. I.v. administration of local anaesthetics such as lignocaine has been shown also to suppress both mechanically- and chemically-induced airway reflexes [2–6]. However, little qualitative or quantitative information is available on suppression of airway reflexes produced by i.v. local anaesthetics. The purpose of the present study was to characterize respiratory response to tracheal irritation following administration of i.v. lignocaine and to assess if suppression of reflex responses is related to plasma concentrations of lignocaine.

PATIENTS AND METHODS

The studies were performed on 10 female patients (ages 40–46 yr, mean (SD) height and weight 157.0 (2.8) cm and 54.6 (3.5) kg, respectively) undergoing elective radical mastectomy. None had clinical evidence of respiratory, cardiovascular or neuromuscular disorders. The study was approved by the Ethics Committee of our institution, and each patient gave informed consent.

All patients received atropine 0.5 mg and hydroxyzine 50 mg i.m. 1 h before induction of anaesthesia with thiamylal 4–5 mg kg\(^{-1}\) followed by suxamethonium 1 mg kg\(^{-1}\). The trachea was intubated using a cuffed tracheal tube with a fine, movable balloon catheter, through the anterior internal wall (Uni-vent tube, 8 mm i.d.) [7]. Anaesthesia was maintained with 66% nitrous oxide and 2–3\% enflurane in oxygen. Immediately after completion of surgery (which lasted for 3–4 h with a total blood loss of 100–200 ml), anaesthesia was maintained with enflurane in oxygen, and spontaneous ventilation was allowed to resume.

After the return of spontaneous ventilation, the tracheal tube was connected to an anaesthetic circuit to facilitate measurement of respiratory
I.V. LIGNOCAINE AND AIRWAY REFLEXES

variables. Details of the apparatus used have been described elsewhere [1]; to summarize, airflow \( (\dot{V}) \) was measured using a Fleisch pneumotachograph (No. 2) and tidal volume \( (V_T) \) was obtained by electrical integration of the inspired flow. Tracheal pressure \( (P_{tr}) \) was measured with a pressure transducer (DDL-0.05, Toyo, Baldwin). End-tidal carbon dioxide partial pressure \( (P_{\text{ET}}CO_2) \) and end-tidal enfurane concentration were monitored continuously with a Normocap infra-red carbon dioxide analyser (Datex) and a Normac anaesthetic monitor (Datex), respectively. All ventilatory signals were recorded on a Nihon Kohden eight-channel recorder (RJG-4128). Minute ventilation \( (\dot{V}_T) \) was obtained by multiplying \( V_T \) and ventilatory frequency \( (f) \).

The study was started at least 20 min after discontinuation of nitrous oxide while all ventilatory variables were stable and a constant end-tidal enfurane concentration \((1.5\%)\) was maintained in each patient. Nitrous oxide was discontinued to avoid potential hypoxia during prolonged interruption of normal breathing after tracheal irritation. In order to elicit airway reflexes, distilled water 0.5 ml was injected through a movable catheter with a tip located 1–2 cm above the carina. Injections of distilled water were repeated three times at intervals of 3 min. Injections were repeated also 2, 5, 8, 11 and 15 min after bolus administration of lignocaine 1.5 mg kg\(^{-1}\) i.v. and the responses compared with those to injection of water before administration of i.v. lignocaine (controls). In each patient, arterial blood samples were obtained via an indwelling arterial cannula immediately before each stimulation of the tracheal mucosa for measurement of plasma concentrations of lignocaine by enzyme-immunoassay [8].

Major reflex responses observed in this study were the expiration reflex, cough reflex, apnoea and spasmodic panting. The type and intensity of responses were not uniform in all patients. The expiration reflex was defined as an isolated forceful expiration without prior inspiration, and the cough reflex as a sudden, forceful expiration.

![Figure 1](https://academic.oup.com/bja/article-abstract/64/6/682/264127)

**Fig. 1.** Prestimulation respiratory variables (mean, SD) before and after i.v. lignocaine. \( V_T \) = Tidal volume; \( f \) = ventilatory frequency; \( \dot{V}_T \) = minute ventilation; \( P_{\text{ET}}CO_2 = \) end-tidal \( P_{CO_2} \). **\( P < 0.01 \)** compared with control (C).
after inspiration. Apnoea was defined as an absence of inspiration for > 5 s and spasmodic panting as a period of > 10 s when ventilatory frequency was > 60 b.p.m.

Statistical analysis was performed using ANOVA (two-way) followed by Tukey's test, and Student's $t$ test where appropriate.

RESULTS

Tracheal irritation before administration of lignocaine elicited a variety of respiratory reflex responses, causing irregular patterns of breathing, which subsided within 2 min. Responses to repeated stimulation before lignocaine were almost identical in type, magnitude and duration of response.

Mean (SD) respiratory variables before the challenge with water are shown in figure 1. Significant decreases in $V_t$ and $V_i$, and a significant increase in $PE'_{CO_2}$ were observed 2 min after administration of lignocaine. Thereafter, both $V_t$ and $PE'_{CO_2}$ returned to the control values.

Figure 2 shows responses to tracheal irritation before and after lignocaine administration in a single patient. In this patient, responses before lignocaine (A) consisted of the expiration reflex, apnoea, spasmodic panting and cough reflex. The irregular pattern of ventilation following irritation of the tracheal mucosa lasted for 60 s, after which ventilation became regular. Two minutes after lignocaine (B), tracheal mucosal stimulation elicited a brief apnoea, while other types of reflex responses were suppressed completely. The suppressed reflex responses recovered partially 8 min after lignocaine (C) and at 15 min (D); the responses were almost identical to those observed before suppression.

Figure 3 shows the incidence of various types of respiratory reflex responses and the plasma concentrations of lignocaine after administration of lignocaine in all patients. The expiration reflex, cough reflex and spasmodic panting were inhibited completely 2 min after administration of lignocaine when plasma concentrations of lignocaine exceeded 4.7 $\mu$g ml$^{-1}$. Thereafter, these

![Graph showing respiratory reflex responses](https://academic.oup.com/bja/article-abstract/64/6/682/264127)

**Fig. 2.** Respiratory reflex responses before and after i.v. lignocaine. A = Control, B = 2 min, C = 8 min and D = 15 min after i.v. lignocaine. At arrows, distilled water was injected into the trachea. $P_{tr}$ = Pressure in tracheal airway; $\dot{V}$ = airflow, inspiration upward; $V_t$ = tidal volume; $PE'_{CO_2}$ = end-tidal $PCO_2$; $E'_{ent}$ = end-tidal enfurane concentration.
responses recovered gradually with decrease in plasma concentrations of lignocaine. The expiration reflex started to appear 5 min after lignocaine, whereas the cough reflex and spasmodic panting were never observed until 8 min, when plasma concentrations of lignocaine were less than 3 μg ml⁻¹. Figure 4 shows more detailed analysis of the relationships between plasma concentrations of lignocaine and occurrence of respiratory reflexes. Apnoea was not eliminated at plasma concentrations of lignocaine in excess of 7 μg ml⁻¹, whereas the expiration reflex, cough reflex and spasmodic panting were suppressed at plasma lignocaine concentrations in excess of 3.5, 2.3 and 2.2 μg ml⁻¹, respectively.

Response duration, defined as the period from the onset of response to the point where the disturbed $V'T$ and $f$ returned to 90–110% of the prestimulation values, was significantly shorter at 2, 5 and 8 min after administration of lignocaine compared with control values (fig. 5).

DISCUSSION

Several investigators have shown that i.v. lignocaine suppresses respiratory reflex responses [2–6]. However, none of these studies described changes in reflex responses after i.v. lignocaine other than suppression of the cough reflex. In the present study, we have shown that, 2 min after administration of lignocaine 1.5 mg kg⁻¹ i.v., tracheal irritation caused the apnoeic reflex only, while other reflex responses were suppressed completely. Five minutes after administration of lignocaine, the expiration reflex reappeared while coughing and spasmodic panting remained depressed. The cough reflex and spasmodic panting recovered partially within 8 min after lignocaine and returned to control values at 11–15 min.

Spasmodic panting was never observed when plasma concentrations of lignocaine exceeded 2.2 μg ml⁻¹, whereas the cough reflex was eliminated effectively by plasma concentrations of lignocaine in excess of 2.3 μg ml⁻¹. Similarly, the expiration reflex was never observed when the plasma concentration of lignocaine exceeded 3.5 μg ml⁻¹. The apnoeic response to tracheal stimulation was not eliminated effectively at twice this concentration.

Suppression of the cough reflex occurring at plasma concentrations of lignocaine in excess of 3 μg ml⁻¹ is compatible with the findings of other
Although the mechanisms by which i.v. lignocaine suppresses airway reflexes are unknown, rapid equilibration of local anaesthetics between blood and brain suggests that a depressant effect on the central nervous system may have contributed to this action [10]. A similar effect was shown by Himes, Munson and Embro [11], who demonstrated that arterial plasma concentrations of lignocaine 1-4 µg ml⁻¹ produced dose-related decreases in enflurane requirement in dogs. Therefore, it is likely that the mechanism of action of i.v. lignocaine is an increase in the depth of anaesthesia. The suppression of airway reflexes produced by i.v. lignocaine is similar to that produced by an increase in dose of enflurane [1]. Furthermore, a relatively small but significant decrease in ventilation observed immediately after i.v. lignocaine is consistent with i.v. lignocaine causing a transient increase in the depth of anaesthesia.

In conclusion, our findings suggest that i.v. lignocaine has a dose-dependent effect on the expiration reflex, cough reflex and spasmodic panting in patients anaesthetized with enflurane. Under these conditions, it is reasonable to assume that lignocaine 1.5 mg kg⁻¹ i.v. can suppress the cough reflex and other related reflexes during tracheal intubation, extubation, bronchoscopy and laryngoscopy when the duration of these procedures is relatively brief.

REFERENCES


I.V. LIGNOCAINE AND AIRWAY REFLEXES


