Title: VENTILATORY SENSITIVITY TO CO2 AFTER I.V. LIDOCAINE

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Introduction. Systemic administration of lidocaine has been shown to induce a dose-dependent depression of ventilation and of the ventilatory response to CO2 in dogs during enflurane anesthesia (1). On the other hand, it has been shown that aerosol inhalation of bupivacaine producing airway anesthesia in awake humans increases the ventilatory response to inspired CO2, whereas intravenous bupivacaine failed to induce similar changes (2). The ventilatory response to lidocaine alone, however, has not been examined. In recent years intravenous lidocaine has been frequently used, both for treatment and prevention of cardiac arrhythmias, and in the anesthetic practice, to blunt cardiovascular responses to laryngoscopy, tracheal intubation and extubation (3). Especially in view of this last practice, we asked if systemic levels of local anesthetic may interfere with normal ventilatory regulation. The aim of this study was to measure the ventilatory sensitivity to CO2 in healthy volunteers, after intravenous administration of a lidocaine bolus.

Methods. The study protocol received internal institutional approval. Written informed consent was obtained from all volunteers. We studied five healthy male subjects (age = 26.6 ± 2.5 years, mean ± 1 SD), weighing 68.5 ± 10.2 kg, with an average height of 178 ± 5 cm, 3 to 5 hr after a light meal. All subjects had a normal physical examination and denied in their history any respiratory, cardiovascular, hepatic or seizure disorders. Throughout the study ECG was continuously displayed on an oscilloscope and blood pressure was measured frequently from a sphygmomanometer cuff. All measurements were collected in the supine position: after control measurements, preservative-free lidocaine HCl (20 mg/ml) was injected in an antecubital vein over a 1 min period. The total dose of lidocaine was calculated as 100 mg/60kg. Ventilatory response to endogenous CO2 was assessed by rebreathing for 6-7 min from a 9 L spirometer filled with O2. End-tidal CO2 (PetCO2) was continuously measured with a calibrated Capnograph and recorded with an oscillograph. Minute ventilation (VE, BTPS) and respiratory rate (RR) were calculated from the spirometer tracings. Linear regression equations were calculated from $\dot{V}E$ and PetCO2 for each CO2 challenge curve, yielding a slope ($s\dot{V}E = \Delta\dot{V}E/\Delta PetCO2$) and an intercept, taken at a value of PetCO2 = 55 torr ($\dot{V}E55$). In similar fashion, tidal volume (VT) and RR parameters were calculated (sVT; VT55; sRR; RR55). Two curves were collected during the control period, and CO2 response curves were then sequentially obtained at 5, 30 and 60 min after lidocaine administration. Resting end-tidal PCO2 (PetCO2) were collected immediately before each CO2-challenge test. Total serum levels of lidocaine were measured spectrophotometrically (EMIT immunoassay technique) from blood samples obtained from the contralateral arm, during control, and 5, 15, 30 and 60 min following lidocaine injection. Statistical analysis of the data was performed by multiple analysis of variance including repeated measurements. Statistical significance was accepted for $p < .05$.

Results and Discussion. Immediately after the injection all subjects experienced, to various degrees, one or more sensory alterations comprising tinnitus, tongue and perioral numbness, tingling on the fingers and (2 subjects) mental confusion. All subjective alterations subsided within 7 - 10 min. Two subjects reported that the ventilatory effort elicited by the CO2-rebreathing maneuvre was more laborious after lidocaine. Heart rate and blood pressure changes after the intravenous drug were small (less than 15% of control), variable and of short duration (less than 5 min). Table I summarizes several other measured variables.

Table I. Control and serial values after i.v. lidocaine (100 mg/60 kg) in five subjects. Mean ± 1 S.E.

	Control	Minutes after Lidocaine 5'	15'	30'	60'
Serum Levels (μg/ml)	N.D.	1.03 ±0.11	.77 ±0.05	.60 ±0.04	.50 ±0.03
Resting PetCO2 (torr)	37.4 ±1.0	36.3 ±2.1	35.1 ±2.0	36.4 ±1.4	36.6 ±1.2
$s\dot{V}E$ (L/min·torr)	1.55 ±0.22	1.51 ±0.25	—	1.90 ±0.25	1.82 ±0.28
$\dot{V}E55$ (L/min)	35.2 ±1.3	34.9 ±1.8	—	38.7 ±1.8	35.6 ±1.8
VT55 (L)	2.6 ±0.1	2.6 ±0.1	—	2.6 ±0.1	2.5 ±0.1
RR55 (breaths/min)	14.0 ±0.6	13.9 ±0.8	—	15.0 ±0.9	15.0 ±0.8

Lidocaine levels during control were undetectable (N.D.). After injection, mean serum levels rose at the 5 min sampling period, and then decreased exponentially at the various study times. No significant change from control could be demonstrated at any study time for all respiratory variables analyzed. The CO2-challenge was not repeated 15 min after injection, in order to leave an adequate rest period between tests. Overall, no relationship was found between serum lidocaine levels and respiratory variables in any of the subjects, over the range of individual serum concentration observed. In conclusion, CO2 sensitivity in healthy, awake volunteers is not altered by lidocaine at this commonly employed intravenous dose.

References

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