TITLE : DUAL EFFECTS OF LIDOCAINE INFUSION ON THE VENTILATORY RESPONSE TO CO2

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INTRODUCTION. Intravenous lidocaine infusion is reported to induce an increase in the slope of the ventilatory response to CO2 (1). However, the resting ventilatory parameters and the intercept value of the CO2 response curve have not been examined. The present study was thus designed to obtain more complete data on the effects of an intravenous infusion of lidocaine on the control of ventilation.

METHODS. Eight male ASA 1 volunteers who had given informed consent were studied after approval by our Institutional Committee. Their mean (±SD) age, height and weight were 32±4 years, 177±5 cm and 74±10 kg respectively. All subjects had fasted and took no caffeine -or alcohol- containing beverages overnight. After a control set of measurements a bolus of 1.5 mg/kg of lidocaine was injected intravenously over a 5 min period and followed by a continuous infusion of 60 µg/kg/min of lidocaine. At 30 min a new set of measurements was performed and the infusion was discontinued. Two other sets of measurements were performed 20 and 40 min after discontinuation of lidocaine infusion. Each set of measurements consisted of : (i) plasma lidocaine analysis by the EMIT immunoassay from venous samples, (ii) minute ventilation ($\dot{V}E$) and end tidal CO2 (PETCO2) measurements while the subjects were breathing room air for 5 min, and (iii) ventilatory response to CO2 measured by rebreathing from a 7 l spirometer filled with a mixture of CO2 (6 per cent) in oxygen. Linear regression equations were calculated from $\dot{V}E$ and PETCO2 for each CO2 challenge curve. Both the slope of $\dot{V}E$/PETCO2 and the extrapolated PETCO2 intercept value (zero-ventilation) were examined. For each subject, comparison between each control and the post-lidocaine infusion response to CO2 was made using the analysis of variance. Difference between values at each time interval and control values were tested using the t-test for paired data.

RESULTS. All the subjects reported a feeling of sedation during lidocaine infusion. Table I shows that lidocaine infusion did not change resting $\dot{V}E$ and PETCO2 values. The slope of $\dot{V}E$/PETCO2 and the PETCO2 intercept increased from their control values both at 30 min after the onset of lidocaine infusion (figure 1) (significant increases ($p < 0.05$) in all the 8 subjects and in 7 subjects respectively) and at 20 min after its discontinuation (significant increases ($p < 0.05$) in 6 and 4 subjects respectively). The correlations between the serum lidocaine level and the changes in the slope of $\dot{V}E$/PETCO2 (figure 2) and in the PETCO2 intercept value (figure 3) were both significant ($r = 0.58$, $p < 0.01$ and $r = 0.46$, $p < 0.05$ respectively).

DISCUSSION. Our data are consistent with those of Gross et al (1) who also found an increase in the slope of the CO2 response curve during lidocaine infusion. In our study resting $\dot{V}E$ and PETCO2 values did not change suggesting that lidocaine infusion did not increase the metabolic rate. On the other hand, the increase in the slope of $\dot{V}E$/PETCO2 was combined to a shift to the right of the zero-ventilation intercept. This phenomen may be due to the combination of a sedative and an excitatory action of lidocaine on the central nervous system. An alternate explanation for the increase in the slope of $\dot{V}E$/PETCO2 may be the effect of hypercapnia, which is known to increase per se the central nervous system toxicity of lidocaine (2). In conclusion, lidocaine infusion induces a dual effect on the control of ventilation suggesting a combination of excitation and depression of the central nervous system.

REFERENCES.

1.GROSS JB, CALDWELL CB, SHAW LM et al : The effect of lidocaine on the ventilatory response to carbon dioxide. Anesthesiology 59 : 521-525, 1983.

2.DE JONG RH, WAGMAN IH, PRICE DA : Effect of carbon dioxide on the cortical seizure to lidocaine. Exp. Neurol. 17 : 221-229, 1976.

Table I . : * $p < 0.05$ vs control ; mean values ± SD

	Control	Lidocaine Infusion 30 min	Lidocaine Post Infusion 20 min	Lidocaine Post Infusion 40 min
Serum lidocaine (µg/ml)	0	3.14 ± 0.82	1.70 ± 0.58	1.17 ± 0.54
Resting $\dot{V}E$ (l/min)	10.9 ± 4.3	8.9 ± 3.6	10.6 ± 3.2	10.6 ± 3.9
Resting PETCO2 (mmHg)	36.3 ± 5.6	39.1 ± 3.3	37.1 ± 5.5	35.0 ± 3.7
Slope of $\dot{V}E$/PETCO2 (l/min/mmHg)	2.62 ± 1.22	4.20 ± 1.62*	3.26 ± 1.32*	2.73 ± 1.03
PETCO2 intercept (mmHg)	38.7 ± 8.5	47.5 ± 4.2*	43.6 ± 5.7*	40.6 ± 5.0

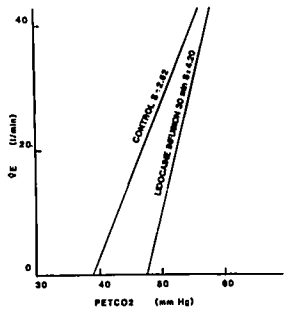

Figure 1 : During lidocaine infusion the increase in the slope of VE/PETCO2 (S) was counterbalanced by a shift to the right of the PETCO2 intercept.

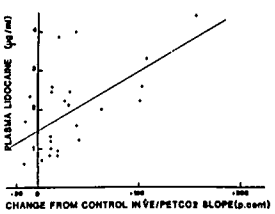

Figure 2

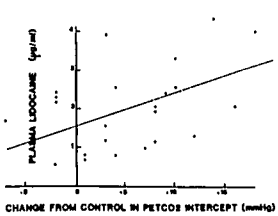

Figure 3

Correlations between serum lidocaine level and changes from control in the slope of $\dot{V}E$/PETCO2 (figure 2) and in the PETCO2 intercept value (figure 3).