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Respiratory Responses to Surgical Stimulation during Enflurane Anesthesia

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Surgical stimulation almost invariably causes an increase in ventilation in spontaneously breathing anesthetized patients, regardless of the anesthetic employed. Numerous studies have shown that anesthetics cause the CO_2 response curve to be both shifted to the right and depressed in slope.[1–6] Eger *et al.* have demonstrated that with isoflurane and isoflurane–nitrous oxide anesthesia there is an increase in ventilation at the onset of surgical stimulation and a decrease in Pa_{CO_2}.[7] Reasoning from the facts that anesthetics cause a decrease in CO_2 response curve slope and the Pa_{CO_2}-ventilation pair moves upward and leftward because of surgical stimulation, one must conclude that the CO_2 response curve itself changes in some way. It either increases in slope or shifts leftward, or both. Our study was designed to determine the change of the CO_2 response curve using clinical concentrations of enflurane and nitrous oxide–oxygen.

METHODS

With the approval of the New England Medical Center Human Investigation Review Committee, we studied 12 informed healthy men, ASA-I, aged 18–40 years. All subjects were scheduled for elective orthopedic surgical procedures on either ankle or knee, in the supine position. Subjects who were obese, were taking any medication, or had any pain associated with their lesions were not admitted to the study.

Subjects were not given sleep medication the evening before operation. All subjects were premedicated with atropine, 0.4 mg, and diazepam, 10 mg, im, approximately one and a half hours before anesthesia was started. In all cases, anesthesia was established with an inhalational induction by use of enflurane and 50 per cent nitrous oxide in oxygen. After adequate anesthetic depth was obtained as determined clinically, succinylcholine, 100 mg, iv, was administered for intubation. A 9.0-mm-ID endotracheal tube was inserted with the tube cut as short as possible to minimize dead space. Upon the return of spontaneous respiration, the gas circuit was changed to a low-resistance circuit through which anesthetics and various concentrations of CO_2 could be delivered to the subjects. Inspired and end-tidal CO_2 was sampled at the connection of the endotracheal tube to the circuit; mixed expired CO_2 was sampled from a mixing chamber in the expiratory limb. Sampled gases were analyzed by use of a Godard Capnograph MK II® and then returned to the circuit. Expired gases were collected in and measured by a Med-science® wedge spirometer, Model 270. Continuous recordings of the outputs of the spirometer and capnograph were made on a Hewlett Packard two-channel recorder. A similar system was described previously.[6]

After obtaining a steady state, as determined clinically, at an adequate depth of anesthesia, the preoperative, unstimulated CO_2 response curve was determined at both 3 and 6 per cent inspired CO_2. Inspired CO_2 concentrations were administered for 12 min, the first 8 min to establish a steady state and the last 4 for measurements. The unstimulated points were determined during periods of absolutely no stimulation. Following the beginning of the surgical procedure, the same measurements were repeated to determine the operative, stimulated CO_2 response curve. Immediately following the determination of each CO_2 response curve, mixed inspired and mixed expired gas samples were taken for chromatographic analysis of enflurane. Alveolar enflurane was calculated using a modification of the Bohr relation.[8,9] All strip-chart records were adjusted for calibration factors and results corrected to BTPS.[10]

Since each subject served as his own control, statistical results are reported as the probability of

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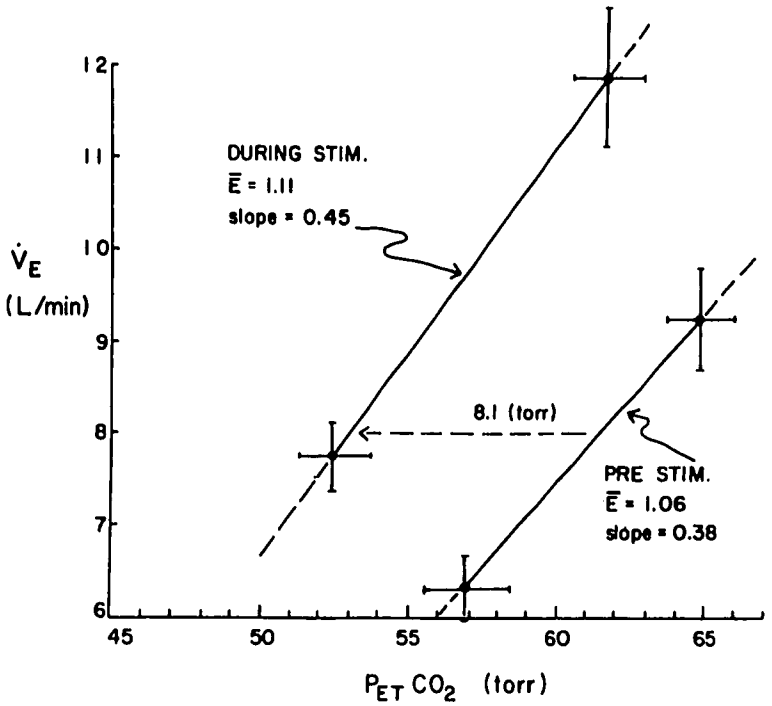

FIG. 1. Carbon dioxide response curves during anesthesia with enflurane and 50 per cent nitrous oxide without stimulation and during painful surgical stimulation. Differences in slope and enflurane concentrations were not significant at $P = 0.05$. The 8.1-torr difference in positions was significant, $P < 0.01$.

a type I error, using the Student t test for paired variables with population standard deviation unknown. $P \geq 0.05$ was considered not a significant change from the control value.[11]

RESULTS

Table 1 summarizes the end-tidal and minute ventilation data for the four points used to determine the two CO_2 response curves. There was no statistically significant difference between alveolar enflurane concentrations in the unstimulated and the surgically stimulated condition, confirming the clinical impression of the existence of a steady state (table 1). Likewise, there was no difference between the CO_2 response curve slopes of the stimulated and unstimulated curves (fig. 1 and table 2). However, at 8 l/min minute ventilation, $\dot{V}_E$, the CO_2 response curve determined during surgical stimulation was shifted 8.1 ± 1.45 torr to the left of the curve obtained during no stimulation (significant, $P < 0.01$) (fig. 1 and table 2).

At 3 per cent inspired CO_2, respiratory frequencies were similar for both curves, but tidal volumes, V_T, were significantly different ($P < 0.01$) (table 3). On the other hand, at 6 per cent inspired CO_2, the V_Ts were similar, while the respiratory rates were significantly different (table 3).

TABLE 1. Ventilation and CO_2 Values for the Four Points Used to Determine the Two CO_2 Response Curves

	$\dot{V}_E$ (l/min)	$P_{ET}CO_2$ (torr)
F_{ICO_2} 0.03		
Before stimulation	6.33 ± 0.33	56.9 ± 1.4
After stimulation	7.75 ± 0.45*	52.4 ± 1.2*
F_{ICO_2} 0.06		
Before stimulation	9.30 ± 0.49	64.8 ± 1.2
After stimulation	11.92 ± 0.86*	61.6 ± 1.1*

* Significant change, $P < 0.01$.

TABLE 2. Enflurane Concentrations, Slopes of CO_2 Response Curves, and Positions of CO_2 Response Curves at 8 l/min $\dot{V}_E$

	Slope (l/min/torr)	$P_{ET}CO_2$ 8 l/min $\dot{V}_E$ (torr)	Alveolar Enflurane (Per Cent)
Before stimulation	0.38 ± 0.05	61.4 ± 2.3	1.06 ± 0.08
After stimulation	0.45 ± 0.06	53.4 ± 2.0*	1.11 ± 0.07

* Significant change, $P < 0.01$.

TABLE 3. Tidal Volumes and Respiratory Frequencies (f) at Four Points Used to Determine Two CO_2 Response Curves

	V_T (ml)	f (/min)
F_{ICO_2} 0.03		
Before stimulation	337 ± 20	19.1 ± 0.8
After stimulation	398 ± 30*	19.8 ± 1.0
F_{ICO_2} 0.06		
Before stimulation	560 ± 50	17.9 ± 0.6
After stimulation	590 ± 50	20.3 ± 0.7*

* Significant change, $P < 0.01$.

Of the other modalities observed, the only values of interest were dead space and the dead space-to-tidal volume ratio. At 3 per cent inspired CO_2, the unstimulated dead space was significantly less than the stimulated value, 0.140 ± 0.006 l *vs.* 0.156 ± 0.008 l. At 6 per cent inspired CO_2, differences in dead space were not significant. At 3 per cent inspired CO_2, the differences in the dead space-to-tidal volume ratio was significant, 0.430 ± 0.016 unstimulated *vs.* 0.404 ± 0.022 stimulated, but it was not significantly different at 6 per cent inspired CO_2.

Discussion

Enflurane MAC is 1.68 per cent.[12] Based on our subjects' alveolar enflurane concentrations, they received a combined MAC multiple for enflurane and nitrous oxide of approximately 1.2. The mean slope of the unstimulated CO_2 response curves, 0.38 l/min/torr, is in agreement with similar data for other anesthetics previously reported.[1] In this setting we confirm the clinical impression that spontaneous ventilation increases with the onset of surgical stimulation. Our results agree with Eger's, that spontaneously breathing patients at constant anesthetic concentration both increase ventilation and lower Pa_{CO_2} due to surgical stimulation.[7] We show further that in the circumstance of clinical concentrations of enflurane and nitrous oxide with light diazepam premedication, this increase in ventilation and decrease in Pa_{CO_2} is entirely due to a leftward shift of the CO_2 response curve. The arbitrary value of 8 l/min $\dot{V}_E$ was chosen to be above the curved lower end of the CO_2 response curve, but not so high as to bias the results.

The finding of a near-normal P_{CO_2} (*i.e.*, Pa_{CO_2} in the 36–44 torr range) in spontaneously breathing anesthetized patients intraoperatively should not delude the anesthetist into believing that patients are protected against rising levels of CO_2. Response to increasing CO_2 levels relates to the slope of the CO_2 response curve. In our study, the slope of the CO_2 response curve during surgical stimulation at clinical anesthetic levels was significantly depressed, 0.450 ± 0.064 l/min/torr, compared with approximately 1.5 l/min/torr in the normal resting awake individual.

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