

Title : CHANGES IN VENTILATORY PATTERN INDUCED BY A CONTINUOUS INFUSION OF ETOMIDATE

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Introduction. Etomidate is believed to produce minor respiratory effects. However the reported data are controversial because of methodological differences such as the association of premedication agents to the drug (1-2).

The purpose of the study is to measure with a noninvasive technique the respiratory effects of a continuous infusion of etomidate in unpremedicated patients.

Method. 9 ASA I-II patients, mean weight 64 ± 11 kg ($\bar{x} \pm SD$) and mean age 37 ± 15 years, undergoing minor elective surgery, consented to participate in our institutionally approved study.

Tidal volume (V_T), respiratory rate (f), minute ventilation (\dot{V}_E), mean inspiratory flow (V_T/T_I), relative contribution of the rib cage to V_T (RC/V_T), and changes in end-tidal volume (ΔV_T) were continuously measured with a noninvasive method using bellows pneumographs, as recently described and validated (3); oxygen saturation was continuously monitored with an ear oxymeter (HP 472011).

The unpremedicated patients were investigated on the operating table in the supine position 30 minutes before the onset of surgery. All patients were equipped with an EKG monitoring, a noninvasive blood pressure device (Dinamap^R), an ear oxymeter, and with two air-filled bellows pneumographs attached circumferentially around the rib cage and the abdomen. A 20 g venous catheter was inserted and allowed hydration (500 cc normal saline infusion over 30 min.) and i.v. administration of the drugs.

Once the calibration of the noninvasive respiratory device was performed by matching the signals of the bellows pneumographs and the volumes measured with a pneumotachograph (Godard 17212), 0.5 mg of atropine was injected i.v. in order to avoid possible airway irritation by increased salivation. After a 5 minute rest period, base-line respiratory variables were monitored during 5 minutes (control). Etomidate was then administered i.v. as a bolus over 60 seconds (0.3 mg/kg) followed by a constant infusion of 0.06 mg/kg/min during 10 minutes under continuous respiratory monitoring. Any upper airway obstruction was immediately relieved by supporting the chin. The study ended at the termination of the etomidate infusion and anesthesia was carried on as usual.

The data, expressed as mean \pm SD, were cumulated during the three following periods: control (5 min), injection (2 min), steady-state infusion (8 min). Comparison between the different periods were analyzed with a Wilcoxon rank-sum test or paired t test according to the distribution of the values, $p < 0.05$ being considered significant.

Results. 8 out of the 9 patients experienced some discomfort at the injection site during the administration of the bolus of etomidate. Central apneas

defined as an absence of breathing for more than 10 sec occurred in 7 subjects 3.8 ± 2.4 min after the beginning of the injection; their mean duration was 22 ± 13 sec. The largest decrease in O_2 saturation was recorded during the apneas and was not significant ($90 \pm 5\%$) when compared with the control values ($95 \pm 3\%$). Upper airway obstruction occurred in 5 subjects. Unvoluntary muscle movements were observed in 5 patients but disturbed the respiratory measurements in only one subject during 2 min.

As indicated in table 1, during infusion, there was a significant decrease in V_T ($p < 0.01$) associated with an increase in f ($p < 0.01$) when compared with control and injection; the resulting \dot{V}_E did not statistically change. The increase in RC/V_T observed between control and infusion was also significant ($p < 0.01$). ΔV_T and V_T/T_I remained stable throughout the study. All the changes became significant at the first minute of the infusion period and remained constant thereafter.

Discussion. This study demonstrates that a constant infusion of etomidate produces a significant decrease in V_T , an increase in f , without altering \dot{V}_E . This reduction in V_T is mainly due to a diminished abdominal contribution to V_T , since RC/V_T increased significantly during the infusion. The absence of observed respiratory effects during the injection period is probably related to the discomfort produced by the drug injected in bolus. The unchanged V_T/T_I suggests that the decrease in V_T induced by etomidate is not mediated by a depression in central respiratory drive.

Table 1 : Mean value ($\bar{x} \pm SD$) of tidal volume (V_T), respiratory rate (f), minute ventilation (\dot{V}_E). Contribution of rib cage to V_T (RC/V_T), mean inspiratory flow (V_T/T_I) and changes in end tidal volume (ΔV_T) before, during a bolus injection and a constant perfusion of etomidate (N=9)

	V_T (ml)	f (breath/min)	\dot{V}_E (l/min)	RC/V_T (%)	V_T/T_I (ml/sec)	ΔV_T (ml)
Control (5 min)	408 ± 142	14.9 ± 4.3	5.8 ± 1.8	26.4 ± 18	325 ± 144	-
Injection (2 min)	428 ± 191	14.4 ± 5.8	5.8 ± 2.7	34 ± 18	366 ± 105	-7 ± 132
Infusion (8 min)	320 $\pm 46^{**}$	18.9 $\pm 4.0^{**}$	5.5 ± 1.6	41 $\pm 18^{**}$	338 ± 136	+52 ± 272

** $p < 0.01$ when compared with control/injection
** $p < 0.01$ when compared with control only

References.

- 1 Morgan H et al. Br J Anaesth 49, 233, 1977.
- 2 Daehlin L et al. Curr Ther Res 27, 706, 1980.
- 3 Morel D et al. J Appl Physiol 55, 598, 1983.

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