Title : ISOFLURANE AND THE CAROTID SINUS BARORECEPTOR REFLEX

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Introduction. Isoflurane (I) anesthesia may produce cardiovascular depression by lowering blood pressure, stroke volume, peripheral resistance, and autonomic efferent nerve activity. Isoflurane has been found to attenuate the changes in arterial pressure, heart rate, and efferent autonomic nerve activity produced by stimulation of the aortic depressor nerve[1]. The present study was performed to determine the effects of isoflurane on the carotid sinus reflex, examining specifically the effects on two levels of the reflex arc, the baroreceptors and the end-organ responses of the heart.

Methods. The effects of (I) on the carotid baroreceptor reflex were studied in four dogs in the conscious and anesthetized state. Resting ECG and blood pressure for the conscious dogs, measured through an exteriorized carotid loop, were monitored on a Grass recorder and recorded on a Vetter FM tape recorder. Reflex changes in heart rate were initiated by pressure changes produced by infusion of nitroprusside (100-300 ug/min) and phenylephrine (10-50 ug/min) through an intravenous line. The same dogs then underwent inhalational induction with (I) using an airtight plexiglass box through which 4% I in oxygen was administered. The anesthetized animal was intubated and exposed to 1.3% and 2.6% I in random order for 30 minutes, with blood pressure changes repeated after each exposure. In six additional dogs, maintained on a pentothal infusion of 5 mg/kg/hr, the left carotid sinus was isolated and placed on a separate perfusion system into which (I) was introduced using a vaporizor/oxygenator. Nerve activity from the left carotid sinus nerve was recorded during sine wave changes in sinus pressure, while the sinus was exposed to 0%, 1.3%. and 2.6% I in random order. R-R interval and nerve activity versus blood pressure for all trials were plotted and slopes of the reflex responses were statistically compared using a two-way ANOVA. The effects of (I) on the chronotropic response of the heart were determined by electrical efferent stimulation of the right vagus and ansa subclavia with supramaximal stimuli at varying frequencies in six pentothal anesthetized dogs exposed to 0%, 1.3%, and 2.6% I. Results were analyzed by plotting changes in heart rate versus stimulation frequency for each trial and comparing the mean slopes of the responses for each level of (I) using an ANOVA.

Results. Isoflurane produced a dose-dependent attenuation of the heart rate response to pressure changes (Table 1). The responses to increases in pressure were not significantly depressed at 1.3% I as were the responses to decreases in pressure.

The chronotropic changes produced by direct efferent stimulation of the heart showed a similar dose dependent depression due to (I) (Table 2).

Unlike the above responses, the slopes of carotid sinus nerve activity versus sinus pressure showed dose-dependent sensitization of the baroreceptors due to (I) (Table 3).

Table 1. Δ R-R Interval(msec)/Δ mmHg

| | Increased BP | Decreased BP |
|---|---|---|
| Conscious | 89.4±1.8 | 59.1±16.8 |
| 1.3% I | 65.0±31.7 | 8.8±1.9+ |
| 2.6% I | 13.7±3.7* | 3.3±0.9+ |

*p<.01 vs conscious,1.3%;+p<.01 vs conscious

Table 2. Δ Heart Rate(b/min)/Stim. Freq.(Hz)

| | Vagal Stim. | Sympathetic Stim. |
|---|---|---|
| 0.0% I | 6.16±0.17 | 10.56±0.29 |
| 1.3% I | 4.15±0.63* | 5.55±0.97* |
| 2.6% I | 2.76±0.72** | 2.78±0.28+ |

*p<.01 vs 0%;**p<.01 vs 1.3%;+p<.05 vs 1.3%

Table 3. Nerve activity (spikes/100mS)/mmHg

| | |
|---|---|
| 0.0% I | 0.22±0.05 |
| 1.3% I | 0.36±0.06* |
| 2.6% I | 0.42±0.06** |

*p<.01 vs 0%; **p<.05 vs 1.3%, p<.01 vs 0%

Conclusions. Isoflurane blunted both the baroreceptor reflex and the chronotropic response of the heart to direct stimulation. The greater depression of the pressor limb of the baroreflex suggests preferential depression of sympathetic versus parasympathetic efferent nerve activity. While the chronotropic responses of the heart to both sympathetic and parasympathetic stimulation were blunted by increasing concentrations of (I), the sympathetic response showed the greater depression due to the anesthetic. This may also result in the greater attenuation of the pressor versus depressor response. The sensitization of the baroreceptors by isoflurane might also have contributed to the blunted reflex responses by imposing baroreflex responses on already lowered sympathetic activity.

References. 1. Skovsted, P. et al., Can. Anaesth. Soc. J. 24:304-314, 1977.