

Title : ISOFLURANE DOES NOT INHIBIT HYPOXIC PULMONARY VASOCONSTRICTION

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**Introduction.** A previous report showed that isoflurane inhibits hypoxic pulmonary vasoconstriction (HPV) to a greater extent than any of the commonly used volatile anesthetics.<sup>1</sup> The authors suggested that this observation would make isoflurane relatively contraindicated in patients with either pre-existing lung disease or who were undergoing lung surgery since inhibition of HPV would predispose the patient to greater hypoxemia than might otherwise be the case. Because our clinical experience using isoflurane in such patients does not confirm the above observations and because of the rising clinical use and value of isoflurane, we have re-examined this question; i.e., Does Isoflurane Inhibit HPV?

**Methods.** Six mongrel dogs were anesthetized with pentobarbital 25mg/kg, intubated and ventilated with one side of a dual piston ventilator. Via a left thoracotomy, electromagnetic flow probes were placed around the main pulmonary artery and the pulmonary artery perfusing the left lower lobe (LLL). Blood flow to the LLL is expressed as a fraction of the cardiac output ( $\dot{Q}_{LLL}/\dot{Q}_T$ ). The bronchus to the LLL was separately intubated from within the chest and ventilated independently but synchronously with the rest of the lung (RL) with 100% oxygen (LLL-O<sub>2</sub>). End expired CO<sub>2</sub> was held equal in both lung segments by appropriate manipulation of tidal volume and/or dead space. Femoral artery, left atrial (LAP), and pulmonary artery pressures (PAP) were directly measured. HPV was induced by ventilating the LLL with 95% N<sub>2</sub> and 5% CO<sub>2</sub> (LLL-N<sub>2</sub>) and noting the change in  $\dot{Q}_{LLL}/\dot{Q}_T$ . After obtaining a control response to LLL hypoxia the LLL was returned to 100% O<sub>2</sub>. Isoflurane, 1.3% end tidal concentration (1 MAC) was then administered to both sides and the LLL hypoxic response retested. In five animals following elimination of the isoflurane, the above sequence was repeated using 2 MAC (2.6% end tidal) isoflurane. The LLL HPV response was computed as the percent decrease  $\dot{Q}_{LLL}/\dot{Q}_T$  during nitrogen breathing from the value during O<sub>2</sub> breathing.

**Results.** Table 1 shows the hemodynamic values associated with control, 1 MAC and 2 MAC isoflurane. Increasing anesthetic depth resulted in a progressive and statistically significant fall in MAP and  $\dot{Q}_T$ . However, (Table 2) there was no statistically significant difference between the LLL HPV responses during LLL-N<sub>2</sub> without isoflurane from those LLL-N<sub>2</sub> responses while the dogs were breathing 1 MAC or 2 MAC isoflurane. The percent decrease  $\dot{Q}_{LLL}/\dot{Q}_T$  during LLL-N<sub>2</sub>, LLL-N<sub>2</sub>-1MAC,

and LLL-N<sub>2</sub>-2MAC was 66.5, 72.5, and 70.9 respectively. In other words, HPV was as intact during light and deep isoflurane as it was without isoflurane. The integrity of the HPV response was further confirmed by the fact that PaO<sub>2</sub> during LLL-N<sub>2</sub> was as high during isoflurane breathing as it was without isoflurane.

**Conclusion.** HPV was not inhibited during light or deep isoflurane anesthesia in dogs. These results imply that isoflurane might be indicated for anesthesia in the presence of lung disease or during one lung anesthesia for lung resection since arterial oxygenation might be better preserved than would be the case with an anesthetic that inhibits HPV. Of course, these animals were free of lung disease and each had a brisk and intact control HPV response. It may be that the presence of longstanding lung disease would modify the hypoxic response seen in healthy animals or humans. We are unable to explain why the results of this study are at variance with the previous study, but believe this question should ultimately be studied in humans.

#### References.

1. Mathers J, Benumof JL, Wahrenbrock EA: General anesthetics and regional hypoxic pulmonary vasoconstriction. *Anesthesiology* 46:111-114, 1977

TABLE 1

Hemo-dynamic variable	Control		Isoflurane			
	LLLO <sub>2</sub>	LLLN <sub>2</sub>	LLLO <sub>2</sub> -1MAC	LLLN <sub>2</sub> -1MAC	LLLO <sub>2</sub> -2MAC	LLLN <sub>2</sub> -2MAC
MAP (torr)	111+ 6.9	116+ 5.3	* 69+ 6.5	* 69+ 6.9	* 48+ 7.1	* 42+ 8.
PAP (torr)	17+ 1.8	17+ 1.5	15+ 1.2	16+ 1.3	15+ 1.4	16+ 1.4
LAP (torr)	8+ 1.2	7+ 1.1	8+ 1.2	8+ 1.2	9+ 1.4	10+ 1.5
$\dot{Q}_T$ (ml)	3215+ 429	3160+ 318	1986+ * 261	2013+ * 251	1575+ * 145	1445+ * 133

All values expressed as mean  $\pm$  S.E.

\*P < .05 versus control.

TABLE 2

	LLL Condition		
	LLL-N <sub>2</sub>	LLL-N <sub>2</sub> -1MAC	LLL-N <sub>2</sub> -2MAC
Percent Decrease $\dot{Q}_{LLL}/\dot{Q}_T$	66.5+ 4.4	72.5+ 4.3	70.9+ 3.4
PaO <sub>2</sub> (torr)	365+ 27	366+ 17	361+ 23

All values expressed as mean  $\pm$  S.E.