Title: NITROUS OXIDE EFFECT ON SHUNT DURING THIOPENTAL ANESTHESIA IN SHEEP

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Intravenous anesthesia may cause alterations in lung function such as reduction in functional residual capacity (FRC), with resultant airway closure, or in some other manner alter the distribution of ventilation with respect to blood flow (V_A/Q). But there is no evidence for a pharmacologic mechanism of shunt development due to intravenous anesthetic agents, e.g. suppression of hypoxic pulmonary vasoconstriction (HPV). Nitrous oxide, however, may produce shunt either by causing absorption atelectasis or by suppressing HPV. We therefore wished to test the null hypothesis, H_o, that nitrous oxide does not produce or enhance shunt development during intravenous anesthesia with thiopental. Furthermore, we wished to determine that differences in shunt were not due to differences in depth of anesthesia.

Methods. Five sheep age 1.5 to 2.0 years, 35 to 45 kg, were surgically prepared with a chronic tracheostomy and carotid artery exteriorization. Awake studies of distribution of ventilation with respect to perfusion (V_A/Q) were performed with multiple tracer inert gas elimination analysis, FRC with helium dilution, and blood gas tension from mixed venous and arterial samples, all during 30% oxygen in air breathing in lateral position. Ventilation was mechanically controlled with tidal volume 10 $ml \cdot kg^{-1}$ and minute ventilation sufficient to prevent spontaneous respiratory efforts in awake condition. Anesthesia was induced and maintained with intravenous thiopental infusion at varying rates of 15 to 150 $mg \cdot min^{-1}$ to a total cummulative dose of 2000 to 2730 mg. On alternate study days, nitrous oxide was used to replace nitrogen (70% inspired) during the induction, and continued for 90 minutes of anesthesia. One sheep was studied on two occasions (separate days) with each anesthetic regimen. Measurements of V_A/Q distribution and blood gas analysis were obtained at 15, 30 and 60 minutes. Estimates of oxygen consumption rate were obtained from arterial-venous oxygen content (PO_2, pH, P50, Hb) difference and cardiac output (tracer inert gas elimination, Fick method). Serum thiopental assay was performed with nitrogen-phosphorous detector gas chromatography.

Results. Awake control shunt values were 3.1 ± 4.2% prior to thiopental anesthesia with air breathing, and 1.3 ± 1.2% prior to thiopental plus nitrous oxide anesthesia ($p>0.05$). Thiopental anesthesia produced a consistent though small reduction in intrapulmonary shunt, with no significant change in arterial PO_2. Addition of N_2O produced small increases of 0.1% to 3.4% shunt, see Table 1 for mean ± SD values. Arterial and mixed venous PO_2 both showed modest increases, although comparison with nitrogen-thiopental values did not show a statistically significant difference. In addition, there was a greater reduction in oxygen consumption rate with nitrous oxide, and no significant change in cardiac output. Serum thiopental level varied from 26 to 112 $\mu g \cdot ml^{-1}$ with N_2O and from 38 to 125 $\mu g \cdot ml^{-1}$ without N_2O during anesthesia measurements of V_A/Q distribution. Mean ± SD serum thiopental levels were 49.0 ± 9.6 $\mu g \cdot ml^{-1}$ and 60.2 ± 23.1 $\mu g \cdot ml^{-1}$, respectively.

Table 1.

	Shunt Increase % Q_T	Arterial PO_2, torr F_IO_2=0.3	Venous PO_2, torr	Cardiac Output L·min-1	Oxygen Consumption Rate Reduction
N_2-Thiopental (n=6)	-0.5±0.4	132.2 ±21.3	52.8 ±7.3	4.8 ±0.9	26.2±20.7%
N_2O-Thiopental (n=6)	1.3±1.6	154.9 ±11.9	58.3 ±6.5	5.6 ±1.3	39.7±9.8%
ANOV	p<0.05	NS	NS	NS	NS

Mean ± SD values for the increase in intrapulmonary shunt as a % of cardiac output, arterial and mixed venous oxygen tension, cardiac output, and % reduction in oxygen consumption rate are presented from nitrogen-thiopental and N_2O-thiopental studies. Statistical comparison was provided with analysis of variance, ANOV, and significance level considered at $p<0.05$.

Discussion. The findings in this sheep population suggest that intravenous anesthesia alone did not cause shunt development, regardless of the presence or absence of pre-existing lung disease (i.e. awake shunt). No relationship between serum thiopental level and amount of shunt was apparent. We therefore conclude that the use of nitrous oxide did cause intrapulmonary shunt development which was unrelated to depth of anesthesia. The magnitude of this increase was so small, however, as to be of minimal physiologic significance. Since the addition of nitrous oxide to halothane anesthesia produced substantially greater shunt development in similar sheep studies in our laboratory, we propose that significant shunt development requires more than one single mechanism. For example, it may require profound chest wall relaxation plus absorption atelectasis. An alternative mechanism may be re-distribution of ventilation (with respect to lung volume) plus reduction in hypoxic pulmonary vasoconstriction.

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