THE EFFECTS OF ENDOTOXIN AND TNFa ON PULMONARY VASCULAR RESISTANCE.

D. Johnson M.D., T. Hurst M.V.Sc.,
I. Mayers M.D.
Departments of Anaesthesia and Medicine, University of Saskatchewan, Saskatoon, Canada, S7N 0X0

The pulmonary manifestations of septic shock may be mediated by both endotoxin (E) and tumor necrosis factor (TNFa). We examined the effects of E and TNFa on pulmonary vascular resistance (PVR) and hypoxic pulmonary vasoconstriction (HPV) in 24 isolated left lower canine lung lobes. Twelve lobes were perfused with whole blood (WB) and twelve lobes were perfused with granulocyte/platelet depleted blood (B-GP). All lobes received paired periods of ventilation with control (35% O_2) and hypoxic (3% O_2) gas mixtures. Then either 1 mg/kg E or 50 ug/kg TNFa (courtesy Genentech) was administered and paired ventilation periods were repeated. Group differences were compared by ANOVA and multiple t-tests with correction for multiple comparisons. Values for PVR (cm H_2O/ml/min x 10^{-2}) are illustrated below.

	35%O_2	3%O_2	35%O_2+E	3%O_2+E
WB	5.1 ±0.7	7.6[a] ±0.9	5.2 ±0.6	5.1 ±0.6
B-GP	5.8 ±1.3	9.0[a] ±2.0	8.2[b] ±2.1	10.9[a] ±2.3

	35%O_2	3%O_2	35%O_2+TNF	3%O_2+TNF
WB	7.6 ±2.0	13.0[a] ±4.9	7.9 ±4.9	11.8[a] ±3.7
B-GP	8.5 ±1.3	14.7[a] ±4.7	4.9[b] ±1.6	4.8 ±1.6

Where a denotes difference between paired periods 35% O_2 and 3% O_2 ($p<0.05$) and b denotes differences between equivalent 35% O_2 periods ($p<0.05$) before and after E or TNFa. During ventilation with 35% O_2, PVR increased after endotoxin administration in the granulocyte/platelet depleted group but not in the whole blood perfused group. However, PVR decreased during 35% O_2 following TNFa administration in the granulocyte/platelet depleted group. This suggests that endotoxin causes granulocytes or platelets to produce a vasodilator while TNFa causes granulocytes or platelets to produce a vasoconstrictor. The effects of endotoxin and TNFa on HPV also occur in opposite directions. The pulmonary vascular effects of sepsis are not entirely mediated by TNFa.

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TITLE: EFFECTS OF ISOFLURANE ON SPLANCHNIC OXYGENATION DURING NORMOVOLEMIC HEMODILUTION

AUTHORS: GF Nöldge,MD, HJ Priebe,MD, M Schmidt, KH Kopp,MD, K Geiger, MD
AFFILIATION: Anes. Dept., Univ. Hospital, 7800 Freiburg, FRG

Introduction. With increasing acceptance of perioperative hemodilution (HD), knowledge of interactions between HD and anesthetic agents becomes important. This study evaluates the effects of isoflurane (ISO) on splanchnic oxygenation during severe normovolemic HD.

Methods. In 9 pigs following laparotomy for instrumentation (catheterization of hepatic and portal [P] veins, placement of EMF probes around hepatic artery [HA], portal vein [PV] and superior mesenteric artery [SMA], and of PO_2 surface electrodes onto liver [HEP] and small intestine [SI]), hematocrit (Hct) was lowered to 14% (HD) by replacing blood with equal amounts of 6% hydroxyethyl-starch. Subsequently, ISO (1.4% end-tidal) was added.

Results (Table). When compared to HD alone, ISO (superimposed on HD) caused pronounced decreases in all flows. HABF fell below control values. DO2, VO2 and surface PO2 decreased. O2 extractions (elevated during HD) did not increase further. Summary liver surface PO2 histogram showed a marked leftward shift with 35% of values in the hypoxic range (0-5 mmHg).

Discussion. ISO abolishes compensatory mechanisms (increasing flows and O2 extractions) necessary to maintain splanchnic oxygenation during severe normovolemic HD. ISO should, therefore, be used with extreme caution during severe HD.

VARIABLE	CONTROL	HD	HD + ISO
MAP(mmHg)	92±3	81±3*	39±3*&
CVP(mmHg)	2.8±0.4	2.8±0.4	2.9±0.5
CO(l/min)	3.5±0.2	4.4±0.2*	3.0±0.2*&
THBF(ml/min)	634±24	864±36*	672±56&
HABF(ml/min)	83±6	149±14*	64±9*&
PBF(ml/min)	561±33	732±45*	616±56&
SMABF(ml/min)	410±31	492±47*	447±42
DO2TH(ml/min)	59±5	39±3*	22±3*&
DO2HA(ml/min)	10±1	9±1	3±1*&
DO2PV(ml/min)	52±5	30±2*	19±3*&
DO2SMA(ml/min)	47±3	29±3*	22±3*&
VO2H(ml/min)	17±2	18±3	12±3*&
VO2SI(ml/min)	10±1	9±1	8±1*
PO2HEP(mmHg)	56±3	37±4*	15±4*&
PO2SI(mmHg)	54±3	45±2*	39±3*

Means±SEM. *, &=$p<0.05$ compared to control values (*) and to HD (&). BF=blood flow. TH =total hepatic. DO2=O2 delivery. VO2=O2 uptake. (See text for further abbreviations.)