Title: PROSTAGLANDIN E_1, NITROPRUSSIDE AND PULMONARY BLOOD FLOW DISTRIBUTION DURING ONE LUNG VENTILATION IN THE DOG

Authors: P.M. Heerdt, M.D., Ph.D.

Affiliation: Department of Anesthesiology, Washington University, School of Medicine, St. Louis, MO 63110

In patients with cardiogenic pulmonary hypertension, prostaglandin E_1 (PGE_1) appears to reduce pulmonary vascular resistance (PVR) without dramatically altering intrapulmonary shunt (Q_S/Q_T), while an equipotent pulmonary vasodilating dose of sodium nitroprusside (SNP) lowers PaO_2 and increases Q_S/Q_T.[1,2] How these two vasodilators differentially affect the distribution of blood flow between ventilated and atelectatic portions of the lung has not been determined. This study was designed to compare the influence of each drug on pulmonary blood flow distribution and Q_S/Q_T during one (OLV) and two lung ventilation (TVL) in open chest dogs.

After approval of the protocol by the Animal Studies Committee of this institution, 16 dogs were used for the study. Animals were anesthetized with thiopental (25 mg/kg, followed by infusion of 5 mg/kg/hr) and pentobarbital (5 mg/kg). A left endobronchial tube was placed through a tracheostomy. Systemic arterial (AP), pulmonary arterial (PAP), left atrial (LA) and central venous pressures (CVP) were monitored. Through a left thoracotomy, electromagnetic flow probes were placed around the left branch of the PA (LPAF)) and the ascending aorta (CO). Q_S/Q_T was calculated from simultaneously drawn mixed venous and arterial blood gases and oxygen saturations. In four dogs (time control) baseline hemodynamic measurements and Q_S/Q_T were determined and then right OLV initiated. These experiments demonstrated that in the right lateral decubitus position, blood flow to the nonventilated lung stabilizes after 20-minutes and remains constant for the next 70-minutes; in all subsequent experiments, drug infusions were administrated during this 70-minute "window" of stability. One group of dogs (n=6) received SNP (0.5, 1.0, 2.0 ug/kg/min) and another group (n=6) PGE_1 (50, 100, 200 ng/kg/min). Drugs were infused both during TLV and right OLV, and drug infusion rates were randomized. Dose response data were analyzed by analysis of variance for repeated measures with $p<0.05$ considered significant (*).

During two lung ventilation, SNP and PGE both lowered mAP and mPAP but neither changed Q_S/Q_T (SNP: baseline - 23 ± 5%, 2.0 ug/kg/min- 28 ± 3%; PGE: baseline - 23 ± 5%, 200 ng/kg/min - 24 ± 6%). Hemodynamic and shunt data during OLV are shown in table. At maximum infusion rate, both drugs lowered mAP and SVR. SNP lowered mPAP but not PVR. In contrast, PGE lowered PVR but did not change mPAP. SNP also reduced PaO_2 while increasing calculated Q_S/Q_T and the measured fraction of CO perfusing the non-ventilated lung. PGE had no effect. All drug responses were reversible.

This study suggests that while SNP and PGE both lower PAP or PVR, they have different effects on pulmonary blood flow distribution and oxygenation.

References

1. Anesth Analg: 69,665-7, 1989.
2. Ann Thorac Surg: 49,463-5, 1990.

SNP (ug/kg/min)

	BASELINE	2.0	OFF
mAP	111±9	88±9*	115±11
mPA	23±4	20±2*	24±2
SVR	3572±300	3102±440*	3501±400
PVR	456±40	482±47	446±57
LPAF/CO(%)	21±4	30±4*	21±2
PaO_2	256±14	204±15*	265±20
Q_S/Q_T(%)	24±2	32±2*	23±2

PGE (ng/kg/min)

	BASELINE	200	OFF
mAP	107±15	91±16*	112±16
mPA	24±3	23±3	25±3
SVR	3648±310	2784±520*	3752±386
PVR	508±41	390±68*	553±88
LPAF/CO(%)	15±5	16±2	17±4
PaO_2	280±28	272±32	282±29
Q_S/Q_T(%)	24±2	26±6	22±4

A600

TITLE: HALOTHANE INDUCED PERIPHERAL VASODILATATION MAY BE DEPENDENT ON ENDOTHELIUM-DERIVED RELAXING FACTOR

Authors: DJ Miletich, Ph.D., H Koenig, M.D., RF Albrecht, M.D.

Affiliation: University of Illinois - Chicago/ Michael Reese Hospital

INTRODUCTION: Furchgott and Zawadzki (1980) first reported that relaxation of isolated aortic smooth muscle strips induced by acetylcholine depends on the presence of endothelial cells lining the aorta. After removal of these cells, acetylcholine no longer causes relaxation. Within a few years of this discovery many other vasoactive substances were shown to be dependent on the endothelium for their vascular effects. Many drugs used in the practice of anesthesia produce direct vasodilatation. Halothane, for example, produces a fall in blood pressure which is due to myocardial depression and a decrease in peripheral vascular resistance. Past studies concluded that halothane causes direct vascular smooth muscle relaxation. However, all previous studies were conducted prior to the discovery of endothelial-derived relaxation. It was the purpose of this study, therefore, to reevaluate the relaxation effects of halothane on aortic strips with, and without endothelial cells in order to determine if endothelial cells are involved in the relaxation of smooth muscle by halothane

METHODS: Laboratory rats, (250 to 300g) were decapitated and the aorta rapidly cut into muscle strips. The muscle strips were then suspended in a tissue bath and bathed with Krebs-Ringer solution. Contractions of the muscle strips were measured with a force transducer. Removal of the endothelial layer was accomplished by gently rubbing the strip with a spatula. Both normal and endothelial denuded strips were then exposed to dosages of halothane. Prior to halothane exposure, however, each strip was placed into a contracted state with 2.3 M KCl. After maximal contraction was reached, the strips were then exposed to 1,2 and 3% halothane.

RESULTS/DISCUSSION: In agreement with past studies halothane causes relaxation of aortic smooth muscle strips. (A recent study[2] has reported that inhalational anesthetics actually cause aortic muscle contraction and not relaxation as widely believed. However, these authors used the adrenergic agonist phenylephrine to pre-contract muscle strips prior to anesthetic exposure whereas we used KCL. It is our experience that phenylephrine obscures the effects of halothane on smooth muscle.) At each dose halothane caused significantly greater relaxation in normal stips compared to endothelial denuded muscle strips suggesting that the endothelium mediates the halothane relaxation response. It is also apparent that a direct smooth muscle component is involved in the relaxing effect of halothane in higher doses since endothelial denuded strips show relaxation at 3%. However, at clinically relevant doses most of the relaxation to halothane appears to be dependent on the vascular endothelium.

	Halothane 1%	2%	3%
Normal Muscle Strip	24±4*	37±4	51±7
Endothelial absent	5±2+	13±3+	30±4+

*Mean % relaxation ±SE; +Significantly lower than normal, $p<0.05$, n=6

Ref. 1) Furchgott RF, Zawadzki JV: Nature 288:1980
2) Stone, DJ, Johns RA: Anesthesiology 71:1989