TITLE: INHIBITION OF PLATELET ACTIVATING FACTOR RELEASE BY MAGNESIUM SULFATE IN GUINEA PIG ALVEOLAR MACROPHAGES

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Platelet activating factor (PAF) is a bioactive mediator released from numerous cell types that has potent inflammatory properties[1]. Because PAF induces bronchoconstriction in guinea pigs and triggers pulmonary and systemic hemodynamic changes in man, it is believed to be involved in human asthma and in airway hyperreactivity[2]. Recently[3], the possible usefulness of magnesium sulfate as a bronchodilator in bronchial asthma was studied. This investigation was designed to study the effect of magnesium sulfate on PAF levels in guinea pig alveolar macrophages.

Paired alveolar macrophage cultures from control and pretreated guinea pigs (250-300 grm) were used. Pretreatment consisted of an intravenous injection of magnesium sulfate (0.5mM) 45 minutes before bronchial lavage with normal saline + 0.1% EDTA. Cells were washed in RPMI 1640 twice, plated ($3\text{-}4x10^6$) and attached for 60 minutes in a CO_2 incubator. Cells from both groups were then stimulated with zymosan particles (0.5mg/ml) and calcium ionophore (1µg/ml).

We found that zymosan and ionophore were good stimuli for PAF production in our cells. Magnesium sulfate was shown to be a good inhibitor of net PAF production when both stimuli were given (Table 1). Statistical analyses were done by paired Student t-test and analysis of variance.

This preliminary study suggests that Mg^{++} inhibits PAF production from alveolar macrophages by which mechanism most probably is inhibition of slow inward CA^{++} current and possibly inhibition of CA^{++} induced Ca^{++} release. The future of magnesium sulfate as a bronchodilator seems promising although more studies are warranted.

References:
1. Cellular Immunology 57:281-292, 1981.
2. Euro J of Pharmacol 65:185-192, 1980.
3. JAMA Vol. 257, No. 8, 1987.

Table 1. Net PAF production % total radioactivity. (Means ± Standard Error of Mean)

	CONTROL	MAGNESIUM SULFATE
IoA	49% (cells) ± 2.68 44% (media) ± 2.45	29% (cells) ± .57 30% (media) ± 2.34
Zy	15% (cells) ± .69 38% (media) ± 1.55	2% (cells) ± 1.25 16% (media) ± 1.2

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Title: THE INFLUENCE OF HALOTHANE AND FENTANYL ON THE TIME COURSE OF PULMONARY BLOOD FLOW REDISTRIBUTION DURING ONE LUNG VENTILATION

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Halothane has been reported to inhibit hypoxic vasoconstriction in the lung,[1] thus potentially altering ventilation/perfusing matching. However, clinical studies have failed to demonstrate an increase in intrapulmonary shunt (Q_S/Q_T) when halothane is administered after conversion to one lung ventilation (OLV).[2] This study was designed to compare the influence of halothane and fentanyl on the redistribution of blood flow and Q_S/Q_T during conversion to right OLV in open chest dogs.

Following approval of the protocol by the Animal Studies Committee of this institution, 8 dogs were used for the study. Animals were anesthetized with thiopental (25 mg/kg bolus followed by an infusion of 5 mg/kg/hr) and pentobarbital (5 mg/kg). Dogs were instrumented for measurement of systemic arterial, pulmonary arterial, left atrial and central venous pressures as well as blood flow through the left branch of the PA (LPAF) and the ascending aorta (CO). A left endobronchial tube was placed via tracheostomy for differential lung ventilation. Animals were placed in the right lateral decubitus position for the experiment. In four control dogs, initial hemodynamic measurements were obtained and simultaneous arterial and mixed venous blood samples drawn for gas analysis and oxygen saturation determination during two lung ventilation (TLV). Right OLV was then initiated and all measurements obtained 2, 5, and 10 minutes after conversion. The left lung was then re-expanded and measurements obtained 10 minutes later. This procedure was performed three times at 30 minute intervals in the control animals to demonstrate stability of the preparation. In the other four animals, measurements were obtained during TLV, OLV alone, OLV and 20 minutes of 1.5% halothane, and OLV after fentanyl (10 ug/kg). Data were analyzed by analysis of variance for repeated measures with $p<0.05$ considered significant (*).

Control animals demonstrated the same response to OLV each time it was initiated. In the other dogs (figure), halothane had no effect on the time course of blood flow redistribution at any of the time points but did increase Q_S/Q_T suggestive of a predominant effect on ventilation/perfusion matching in the ventilated lung. Conversely, fentanyl appeared to lessen the effect of OLV on Q_S/Q_T.

This preliminary study indicates that while 1.5% halothane may increase intrapulmonary shunt, it has minimal effect on the redistribution of blood away from the non-ventilated lung during conversion to OLV.

1. Anesthesiology 72:125-133, 1990.
2. Anesth Analg 65:9460954, 1985

	TLV Baseline	OLV 2 min	OLV 5 min	OLV 10 min	TLV
Pentothal					
Q_S/Q_T(%)	11±3	19±4*	19±3*	19±3*	11±4
LPAF/CO(%)	28±3	15±2*	13±2*	9±2*	30±3
PaO_2	488±12	345±15*	356±16*	386±15*	465±17
Halothane					
Q_S/Q_T(%)	14±4	24±6*	21±5*	18±5*	13±4
LPAF/CO(%)	35±2	10±2*	8±2*	8±1*	31±2
PaO_2	449±11	210±15*	300±18*	347±20*	450±12
Fentanyl					
Q_S/Q_T(%)	10±4	15±5*	14±5	14±6	9±5
LPAF/CO(%)	32±2	19±2*	14±1*	12±1*	32±1
PaO_2	507±15	402±9*	430±12*	429±10*	520±18