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TITLE: INHALED NITRIC OXIDE DILATES HUMAN HYPOXIC PULMONARY VASOCONSTRICTION WITHOUT CAUSING SYSTEMIC VASODILATION.

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Introduction Nitric oxide (NO) has been identified as an endothelium-derived relaxing factor (EDRF)(1). Inhaled NO antagonizes hypoxic pulmonary vasoconstriction (HPV) in the awake lamb (2). We explored in humans whether inhaled NO could diffuse into pulmonary vascular smooth muscle producing lung vasodilation, avoiding contact with hemoglobin which rapidly inactivates NO (3), while simultaneously shielding the systemic circulation from vasodilation.

Methods Healthy adult volunteers (n=6) were catheterized with arterial and pulmonary artery catheters and studied supine. They inhaled gas mixtures of N_2, O_2, and (during NO inhalation) 40 ppm NO. Each mixture was inhaled for 10 min; blood sampling, recording of vascular pressures and cardiac output (CO) was performed at 6 min. We measured mean arterial (MAP) and central venous (CVP) pressures, pulmonary artery mean (PAP) and wedge (PCWP) pressures, as well as arterial oxygen (PaO_2) and carbon dioxide ($PaCO_2$) tensions. Pulmonary vascular (PVR) and systemic (SVR) resistances were calculated with standard formulas.

Results All subjects completed the protocol without subjective complaints. While inhaling 40 ppm NO during air breathing (21% O_2) no circulatory change was identified. During hypoxic breathing, PAP and PVR were elevated but rapidly decreased when 40 ppm NO was added to inspired gas, with no change in systemic circulatory parameters. One subject breathed 10, 20 and 40 ppm NO during hypoxia. In this subject, a marked reduction of PAP was evident after 2 min breathing 10 ppm NO.
Circulating endothelin levels did not increase during the study, methemoglobin levels increased <1%.

	AIR	12%O_2	12%O_2+NO
PaO_2 mmHg	99 ± 6	47 ± 2**	45 ± 2**
$PaCO_2$ mmHg	40 ± 2	35 ± 1*	34 ± 2*
PAP mmHg	14.4 ± 0.9	19.7 ± 1.2**	13.8 ± 0.6##
PCWP mmHg	8.8 ± 0.7	8.5 ± 0.5	8.6 ± 0.8
CO l/min	6.5 ± 0.4	8.5 ± 0.8*	8.1 ± 0.7*
PVR mmHg/l/min	0.9 ± 0.1	1.4 ± 0.2*	0.7 ± 0.1##
MAP mmHg	89 ± 3	89 ± 4	86 ± 3
CVP mmHg	5.9 ± 1.4	5.6 ± 1.0	5.2 ± 1.2
SVR mmHg/l/min	12.6 ± 0.5	9.9 ± 0.7**	10.0 ± 0.7**

Statistics: paired t-tests, (n=6, mean ± SEM);
*;** p <0.01;0.05, value differs from control (air)
#;## p<0.01;0.05, value during NO+hypoxia differs from hypoxia.

Conclusion We conclude that inhaling 40 ppm NO selectively antagonizes human HPV, reducing PAP and PVR with no effect on MAP or SVR.

References

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Title: METABOLIC AND ECG CHANGES ASSOCIATED WITH REPERFUSION DURING LIVER TRANSPLANTATION

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Reperfusion of the donor liver during liver transplantation (LT) frequently produces hypotension, dysrhythmias, and ECG changes. The metabolic and ECG changes that are associated with reperfusion of the donor liver are poorly understood and were investigated in this study.

Methods: The records of 30 adult patients who underwent LT were reviewed. All suffered from end-stage liver disease and underwent LT with the use of veno-venous bypass. Arterial blood gases, serum potassium determinations, and calibrated ECG tracings were routinely performed immediately prior to (PRE) and 60 seconds following (POST) liver reperfusion. Hemodynamics were also determined at these intervals using an automated anesthesia recordkeeping system (Sara Compurecord, PPG Industries, Lenexa, KS), and significant dysrhythmias were also noted. Data were analyzed using paired Student's T-tests, mulivariate analysis, and Fisher's Exact Test. Data are reported as means ± SD, and $P < 0.05$ was considered significant.

Results: There were 13 male and 17 female patients. The age was 47±15 years and the weight was 68±15 kg. Significant intraoperative changes are summarized in the Table. Nine patients developed significant dysrhythmias requiring treatment, including 2 cardiac arrests, and these episodes occurred more frequently in patients with serum $K^+ > 7.0$ mEq/L (P=0.032), and temperature < 32 °C. (P=0.014). Multivariate analysis showed that advanced age, higher body weight, lower pH and temperature were the most significant factors in the changes observed following reperfusion.

Discussion: Donor livers are preserved with University of Wisconsin solution which is hypothermic and hyperkalemic. The results demonstrated in the current study are most likely due to washout of this solution and toxic liver metabolites during the initial reperfusion period. Increasing age and body weight correlated strongly with the drop in temperature following reperfusion. This suggests that larger donor organs were the cause of the hypothermia. The results of this study suggest that hypothermia, increased age, and possibly larger donor organs are risk factors in the hepatic reperfusion syndrome.

Table. Intraoperative Results Means ± SD N=30

	PRE	POST	P
Potassium (mEq/l)	4.0±0.7	6.1±1.5	<0.001
pH	7.39±0.06	7.30±0.09	<0.001
Temp. (°C.)	33±1	31±2	<0.001
Mean Art Press (mm Hg)	93±15	74±25	<0.001
Heart Rate (bpm)	95±20	85±21	<0.002
Lead II:			
QRS width (msec)	91±25	118±65	<0.02
T wave height (mV)	0.2±0.1	0.4±0.4	<0.05
Lead V5:			
QRS width (msec)	82±24	101±63	N.S.
T wave height (mV)	0.1±0.1	0.2±0.2	<0.05

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