

Title : NITROGLYCERIN: PLASMA LEVELS AND EFFECTS IN PREGNANT EWES

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Introduction. Because of its potent and controllable hypotensive effects, nitroglycerin (NG) may be a useful agent in managing the preeclamptic patient undergoing anesthesia. Accordingly, we investigated the placental transport of NG as well as its effects on cardiovascular parameters and acid-base status in both normotensive and hypertensive pregnant ewes.

Methods. Six pregnant ewes, gestational age 120-130 d (term: 150 d) underwent induction of anesthesia with methoxyflurane, and maintenance with ketamine. Ventilation was controlled with added oxygen to maintain PaCO₂ near normal, and PaO₂ near 100 torr. The following vessels were cannulated: maternal femoral artery and vein, maternal jugular vein and fetal femoral artery. An electromagnetic flow probe was placed on the main branch of the uterine artery. Maternal and fetal mean arterial blood pressures (MAP), maternal EKG and heart rate (HR), and uterine blood flow (UBF) were continuously recorded. Two experiments were performed on each sheep; the order in which they were performed was determined randomly for each animal. The first experiment consisted of a 30 min control period followed by an infusion of NG sufficient to lower maternal MAP by 30%. At the end of both the control and experimental periods maternal and fetal cardiovascular parameters were noted, and blood samples were taken for measurement of maternal and fetal blood gases and NG levels. In the second experiment, similar measurements were made following (1) a 30 min control period, (2) an infusion of norepinephrine (NE) sufficient to raise maternal MAP by 25% for 15 min, and (3) following infusion of NG sufficient to lower maternal MAP while maintaining the previously established constant infusion of NE. At the termination of all experiments, cardiovascular parameters were allowed to return to control values. Plasma NG levels were measured using gas-liquid chromatography. The data were analyzed using student's t-test for paired data.

Results. In normotensive animals (table 1) NG lowered maternal MAP and UBF. Blood gases were unchanged except for a reduction in PaO₂. No significant changes were noted in the fetus. Ewes made hypertensive with NE had an increase in MAP, and a reduction in HR and UBF (Table 2). Maternal blood gases were not significantly altered. NE had no adverse effect on the fetus. Treatment of maternal hypertension with NG returned all maternal parameters to control levels with the exception of UBF.

Fetal blood gases exhibited a modest reduction in PaO₂, while HR and MAP were unaltered. NG was readily detected in maternal plasma and in all but two fetal samples (Table 3).

Discussion. The low fetal levels of NG may be due to rapid metabolism, poor placental transfer, or wide-spread binding. Although NG caused a disturbing reduction of UBF this resulted in minimal adverse fetal effects. Other agents with rapid onset and easy titratability such as nitroprusside and trimetaphan have undesirable effects (cyanide toxicity or tachyphylaxis). Therefore NG merits further evaluation.

TABLE 1. NORMOTENSIVE EWES (means±SE)

	CONTROL	NG
MATERNAL:		
MAP (torr)	102±2	70±3*
HR (bpm)	136±19	159±16
UBF (ml/min)	370±62	215±62*
pHa	7.29±0.02	7.27±0.02
PaCO ₂ (torr)	36±3	36±3
PaO ₂ (torr)	108±8	87±6*
BE (meq/l)	-7.6±1.9	-9.4±1.7
FETAL:		
MAP (torr)	52±3	51±4
HR (bpm)	164±7	174±39
pHa	7.26±0.02	7.26±0.02
PaCO ₂	50±3	50±2
PaO ₂	25±2	22±2
BE	-3.9±0.9	-5.2±1

*P < 0.05 versus control

TABLE 2. HYPERTENSIVE EWES (means±SE)

	CONTROL	NE	NE+NG
MATERNAL:			
MAP (torr)	98±4	122±4*	95±4
HR (bpm)	153±5	115±5*	160±11
UBF (ml/min)	373±58	214±57*	179±53*
pHa	7.28±0.02	7.29±0.03	7.28±0.02
PaCO ₂ (torr)	38±3	39±3	37±2
PaO ₂ (torr)	104±9	104±6	105±4
BE (meq/l)	-8.0±1.9	-6.7±1.9	-8.3±1.7
FETAL:			
MAP (torr)	52±3	54±4	47±3
HR (bpm)	168±8	178±7	171±20
pHa	7.26±0.02	7.26±0.01	7.25±0.01
PaCO ₂ (torr)	50±3	55±3	54±3
PaO ₂ (torr)	26±2	21±2	22±1*
BE (meq/l)	-5.2±0.9	-3.1±0.3	-4.2±0.9

*P < 0.05 versus control

TABLE 3. NITROGLYCERIN LEVELS (means±SE)

SAMPLE SITE	PLASMA NG (ng/ml)
Maternal vein	5.3±1.6
Maternal artery	40.7±17.5
Fetal artery	1.7±0.7
Fetal/maternal artery	0.15±0.07