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TITLE : VASCULAR UPTAKE OF NITROGLYCERIN

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Introduction. Following intranasal administration of nitroglycerin (NTG), central venous levels of the drug are consistently higher than arterial levels[1]. Although NTG is known to be rapidly cleared by the liver[2], the possibility of pulmonary clearance of the drug has not been investigated. Accordingly, the following study was performed.

Methods. Five dogs (mean weight 22 kg) were anesthetized with pentobarbital 50 mg/kg. After tracheal intubation, respiration was controlled with O_2 in N_2O to maintain PaO_2 between 80 and 120 torr and $PaCO_2$ between 35 and 45 torr. A Swan-Ganz catheter was inserted via the right jugular vein and both femoral arteries and veins were cannulated. Following midline sternotomy catheters were inserted into both atria and the pulmonary artery. Arterial, pulmonary artery, and central venous pressures were recorded continuously on a Gould recorder. Following a period of stabilization NTG was infused for 15 min through the right femoral vein at a rate of 16 µgm/kg/min using a Harvard pump. On discontinuation of the infusion (time 0), simultaneous blood samples were drawn from the right and left atria, the pulmonary artery and the left femoral artery. Sampling was repeated at 1,2,4,8,16 and 32 minutes. Plasma NTG levels were determined using gas-liquid chromatography with electron capture detection following extraction with n-pentane. Paired data were compared using Student's paired t-test; regression analysis was used to express the log plasma level as a function of time and to determine the rate of clearance.

Results. Right atrial levels of NTG were highest followed, in decreasing order, by pulmonary arterial, left atrial and femoral arterial levels (Table 1). There was a significant difference between right atrial levels and pulmonary arterial levels at all points except 16 and 32 min. A similar difference was observed between pulmonary arterial and left atrial levels. There was no significant differences between left atrial and arterial levels at any time.

Equations describing the clearance of NTG at each sample site appear in Table 2. The half-line of the drug did not differ between sampling sites and was similar to the 4.4 mins reported previously[3] following sublingual administration of NTG[3].

Discussion. Our results demonstrate a significant clearance of NTG from blood between the right atrium and pulmonary artery, as well as between pulmonary artery and left atrium. There is no difference between levels of NTG in the left atrium and femoral artery. The fact that half lives of the drug are similar at all sample sites suggest that there is early uptake of the drug by the right heart and pulmonary vasculature. One of the major effects of NTG is reduction in preload, and our data suggest that the site of action is in part the right heart and pulmonary vessels.

TABLE 1: NTG LEVELS (ngm/ml, mean ± SD)

TIME	RIGHT ATRIUM	PULMONARY ARTERY	LEFT ATRIUM	FEMORAL ARTERY
0	125±44	91±38*	56±19†	51±9
1	80±19	56±25*	38±12†	32±10
2	47±16	39±17*	26±11†	23±17
4	18± 9	14± 7*	10± 5†	5± 2
8	4± 2	3± 2*	2.3±1.7†	1.4±.4
16	.7±.9	.3±.4	.5± .6	.2±.1
32	.2±.3	.2±.3	.06±.08	.03±.05

*p 0.05 vs right atrium
†p 0.05 vs pulmonary artery

TABLE 2: PLASMA DISAPPEARANCE OF NTG

SITE OF SAMPLING	REGRESSION* EQUATION	r	p	HALF† LIFE
Right atrium	log P=1.68 -0.09t	-.88	<0.001	3.34
Pulmonary artery	log P=1.54 -0.09t	-.87	<0.001	3.46
Left atrium	log P=1.39 -0.09t	-.89	<0.001	3.54
Femoral artery	log P=1.29 -0.09t	-.89	<0.001	3.38

*P = plasma NTG level (ngm/ml), t = time (min) † min

References.

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