Title : INTRANASAL ADMINISTRATION OF NITROGLYCERIN

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Introduction. Sublingual nitroglycerin (NTG) is effective in decreasing myocardial work-load and increasing coronary blood flow thereby relieving the pain of angina. During anesthesia for cardio-pulmonary by-pass the presence of an endotracheal tube, oral airway, esophageal stethoscope, and temperature probe make sublingual administration difficult. In addition, pre-medication with atropine may slow the dissolution and absorption of sublingual tablets. Therefore we now commonly employ an intra-nasally administered NTG solution. The present study was designed to determine the (1) time-course, (2) vascular distribution, and (3) dose-related uptake of intra-nasal NTG solution.

Methods. The protocol was approved by our Institutional Review Committee as regards informed consent. All patients studied were scheduled for coronary artery by-pass surgery. Prior to induction of anesthesia an arterial catheter, Swan-Ganz catheter, and at least one peripheral venous catheter were placed. Anesthesia was then induced and maintained with either (1) morphine, diazepam, nitrous oxide and oxygen, or (2) fentanyl and oxygen. EKG (leads II and V5), and arterial and pulmonary artery pressures were recorded continually. If S-T segment changes were observed or if pulmonary artery end-diastolic pressure increased by 5 torr, NTG solution (0.8 mgm/ml normal saline) was instilled intra-nasally. Two experiments were performed: the first group of 5 patients all received 1 ml of NTG solution and blood samples were withdrawn simultaneously from the arterial catheter, the central venous port of the Swan-Ganz catheter, and a peripheral vein after 1/2, 1, 2, 4, 8, 16 and 32 minutes; the second group of 13 patients received, on a random basis, 1/2, 1, or 1 1/2 ml of NTG solution and central venous samples only were withdrawn at 1/2, 1, 2, 4, and 8 minutes.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 while dose-response data were subjected to regression analysis.

Results. Initially the highest levels of NTG were observed in central venous blood (Table 1). Levels peaked at 1 minute and remained above therapeutic levels for 8 minutes. Arterial levels peaked at 1-2 minutes while peripheral venous levels peaked at 2 minutes. The highest concentrations were seen in central venous blood, followed by arterial and peripheral venous blood, respectively. There was a linear relationship between the volume of NTG solution administered and the levels of the drug in central venous blood at 1/2, 1, 4 and 8 minutes following administration (Table 2). The wide variation in central venous levels 2 minutes after administration (Table 1) may account for the lack of a linear relation at this point. In all patients the desired clinical effect was seen within 2 minutes: lowering of pulmonary artery pressure and/or improvement in S-T segment changes.

Discussion. In our institution therapeutic levels of NTG are considered to be 3 ngm/ml in central venous blood, 1.7 ngm/ml in arterial blood and 0.4 ngm/ml in peripheral venous blood. This study suggests that these levels are readily and rapidly attained within 2 minutes following intra-nasal administration. Intravenous NTG has the advantage of continuous infusion which can be maintained over a prolonged period. However preparation of the sterile solution is difficult and time-consuming. Therefore we suggest that intra-nasal administration of a non-sterile solution of NTG which can be freshly prepared by an anesthesiologist is a rapid and convenient alternative.

TABLE 1. PLASMA NITROGLYCERIN LEVELS*

TIME OF SAMPLING (MIN)	CENTRAL VENOUS	ARTERIAL	PERIPHERAL VENOUS
1/2	6.7 ±2.5	2.9 ±1.0	1.3 ±0.4
1	11.4 ±5.1	5.1 ±1.2	1.5 ±0.6
2	8.2 ±3.6	5.1 ±1.4	2.6 ±0.6
4	6.4 ±3.1	4.8 ±2.0	2.4 ±0.4
8	3.7 ±2.1	2.3 ±1.0	1.3 ±0.2
16	1.3 ±0.3	0.9 ±0.3	1.2 ±0.4
32	1.1 ±0.2	0.8 ±0.2	0.9 ±0.2

*Mean values ± standard error

TABLE 2. REGRESSION COEFFICIENTS*

TIME OF SAMPLING (MIN)	SLOPE (m)	INTERCEPT (b)	CORRELATION COEFFICIENT	P
1/2	16.6	-1.2	0.66	<0.05
1	23.5	4.7	0.59	<0.05
2	15.1	9.0	0.32	N.S.
4	11.5	6.0	0.61	<0.05
8	6.2	-0.7	0.63	<0.05

*Using the equation y=mx+b when x=dose of NTG (ml) and y=plasma level of NTG (ngm/ml).

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