TITLE: INOTROPIC EFFECTS OF NITROGLYCERIN, NITROPRUSSIDE AND TRIMETHAPHAN ON ISOLATED RABBIT MYOCARDIUM

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Currently nitroglycerin (NTG), nitroprusside (NP) and trimethaphan (TM) are among the most commonly used vasodilating agents in acute medicine as well as in deliberate hypotensive anesthesia. By exerting direct and indirect relaxant effect on vessels, these agents are frequently employed to manipulate preload and afterload to control blood pressure and improve cardiac performance. However,their effects on myocardial contractility have not been clearly evaluated and characterized. This study was designed to compare the direct effects of these three vasodilators on inotropism of isolated rabbit myocardium.

Nine New Zealand white rabbits, weighing 2-3 kg, were anesthetized with 45 mg/kg i.v. pentobarbital. The heart was immediately removed. The first septal perforator of the left coronary artery was cannulated with a small polyethylene tube (PE-50) and perfused with warmed (37°C) oxygenated modified Kreb-Ringer bicarbonate buffer (KRB) solution at 1 ml/gm/min. The septum was then dissected out and suspended from a Grass FT03 tension transducer. The other two corners were fixed with tension by opposing clamps through which a 5-volt/5 msec electrical stimulation was given from a Grass stimulator at 1.6Hz. The peak developed tension (PDT) and the maximal acceleration (dT/dt) were recorded. After reaching fully stabilized contractions for at least 30 min, perfusions with NP, TM, NTG diluted in KRB were then started alternately at doses of 0.5, 1, 10, 25, 50, 100, 200, 400 and 2500 mcg/ml respectively, each for 10 min. The plain oxygenated KRB solution was perfused in between as the control. The PDT and dT/dt were calculated as % of control values. The results were analyzed with non-paired t-test.

Figs. 1 and 2 show progressive significant decrease of PDT and dT/dt with NTG infusion as the concentration increases, while NP and TM do not significantly change the inotropism throughout the wide range of concentration.

NTG, clinically considered a better drug for myocardium, causes a significant dose-related depressant effect while NP, a potentially cyanide toxic agent, and TM, a ganglionic blocker, exert relatively negligible effect on myocardial contractility in isolated rabbit myocardium even at very high concentrations.

References
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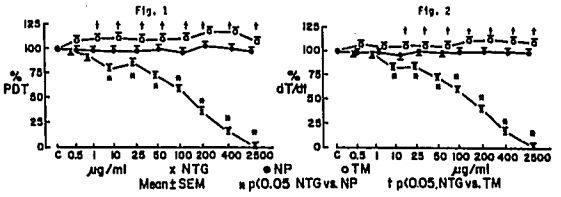
2. Circulation 54:624-628, 1978



Title: PHLEBOTOMY REVERSES THE HEMODYNAMIC CONSEQUENCES OF AORTIC CROSS-CLAMPING

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Introduction: Cross-clamping the thoracic aorta (AXC) causes 1) proximal aortic hypertension (MAP_p), 2) increased preload, 3) decreased distal aortic pressure (MAP_d) and 4) increased cerebrospinal fluid pressure (CSFP). Decreased MAP_d and increased CSFP place patients at risk for paraplegia. We hypothesized that phlebotomy would control increased MAP_p and preload following AXC without compromising spinal cord blood flow (SCBF).

Methods: Eleven dogs, 17.4±2.3 kg (mean±SEM) were studied. Anesthesia was induced with pentobarbital 25 mg/kg and deepened until the EEG was isoelectric. Cannulae were placed in the femoral and brachial arteries, femoral vein, left atrium, and superior saggital sinus for pressure measurements and blood sampling. The cisterna magna was cannulated to measure CSFP. Total cerebral blood flow (tCBF) and SCBF (cervical, thoracic and lumbar) in ml/g/min were measured, using radioactive microsphere methodology, at: 1) baseline, 2) AXC on, 3) phlebotomy to return MAP_p to baseline values and 4) AXC off. Data was considered significant at $p \leq 0.05$ (ANOVA).

Results: With AXC on, MAP_p, central venous pressure (CVP) and CSFP increased while MAP_d decreased significantly (Table). The spinal cord perfusion pressure (SCPP = MAP_d - CSFP) and thoracic and lumbar SCBF decreased. With phlebotomy, MAP_p, CVP and CSFP decreased to baseline values. There was no change in SCPP or in thoracic and lumbar SCBF. Total CBF was unchanged throughout. The CSFP and CVP moved in parallel fashion.

Discussion: Phlebotomy reverses the hemodynamic and CSFP consequences of AXC. The cerebral circulation autoregulates during AXC. Following AXC, the CSFP increases secondary to increases in CVP.

Variable	Baseline	AXC on	Phlebotomy
MAP_p mmHg	104±6	156±6*	106±5†
MAP_d mmHg	98±6	14±1*	7±1*
CVP mmHg	3.7±0.4	5.2±0.7*	1.6±0.6†
CSFP mmHg	3.3±0.7	5.2±0.8*	1.2±1.1†
SCPP mmHg	95±6	9±1*	6±1*
tCBF	0.39±.03	0.41±.03	0.39±.03
$SCBF_{cervical}$	0.15±.01	0.13±.01	0.13±.01
$SCBF_{thoracic}$	0.12±.01	0.02±.01*	0.03±.01*
$SCBF_{lumbar}$	0.16±.02	0.01±.01*	0.02±.01*

Mean ± SEM; n = 11 Flows: ml/g/min
*$p \leq 0.05$ *vs* Baseline †$p \leq 0.05$ *vs* AXC on
Least squares means test with Bonferroni's correction