Nitroprusside-Epinephrine Administration in Acute Myocardial Ischemia

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Administration of nitroprusside (NP) and epinephrine (EP) was investigated in 2 groups of dogs during periods of acute myocardial ischemia. Blood flow to a normal area, to a marginal area of ischemia, and to an area of maximal ischemia was measured using the radioactive microsphere technique before periartrial balloon occlusion of the left anterior descending coronary artery, during NP infusion alone, and in combination with EP. In 10 awake, unanesthetized animals (group 1), NP infusion alone significantly increased blood flow to the subendocardium of the maximally ischemic zone. NP-EP infusion increased transmural and regional flow significantly to the marginal and normal zones. In a second group of 8 anesthetized animals, NP-EP infusion significantly increased coronary sinus flow without a corresponding increase in myocardial oxygen consumption, cardiac index, or left ventricular stroke work. As in group 1, significant increases in transmural flow were noted to the marginal and normal zones with NP-EP infusion. These findings suggest that the combination of a vasodilating agent and an inotropic agent will improve coronary flow during periods of acute myocardial ischemia, and favorably alter the ratio of oxygen supply to oxygen demand.

The purpose of this study was to investigate the effects of such a combination on hemodynamics, coronary blood flow, and myocardial oxygen consumption during acute myocardial ischemia in both the awake unanesthetized dog and in the anesthetized animal.

Materials and Methods

Group 1 (Unanesthetized)

Ten adult mongrel dogs weighing 15–20 kg were subjected to a sterile left lateral thoracotomy under standard barbiturate (Surital®) anesthesia. A periarterial balloon occluder was placed around the left anterior descending coronary artery (LAD) just proximal to its first diagonal branch. A silicone rubber catheter was secured in the left atrium, and the ends of the arterial catheter and the balloon occluder were tunneled subcutaneously to a point posteriorly between the scapulae, and anchored to the skin. The thoracotomy incision was closed and the animals were allowed to recover for 7 days.

On the day of the study, each animal was pretreated with Demerol® (5–10 mg) one-half hour prior to operation. Under local anesthesia, bilateral femoral artery catheters were placed by cutdown for microsphere reference sampling [6] and for measurement of systemic blood pressure. Electrocardiogram (EKG), systemic blood pressure (BP), and left atrial pressure (LAP) were monitored with a multichannel recorder. The periarterial balloon occluder was then inflated to a volume known to cause complete coronary occlusion (IPO) as determined from the initial preparatory thoracotomy. Hemodynamic parameters were recorded, and after 30 minutes the first microspheres (85strontium) (3M Manufacturing Company, St. Paul, Minnesota) were injected via the left atrium, and a reference...
blood sample was withdrawn. The microspheres employed were 8–10 micron in diameter. Nitroprusside (6 $\mu$g/kg per min) was infused via a peripheral vein and after hemodynamic stabilization, the second microspheres ($^{14}$cerium) were injected. Previous work in our laboratory and a review of the literature demonstrated that this dose of nitroprusside would cause significant vasodilatory effects if administered peripherally. Epinephrine (EP) (1.4 $\mu$g/kg per min) was then infused simultaneously with NP and after 30 minutes, the final microspheres ($^{51}$chromium) were injected. This average dose of epinephrine was found to be the minimal dose which, in combination with nitroprusside, caused sustained vasopressor effects. The animal was then killed and the heart excised.

**Group 2 (Anesthetized)**

Eight adult mongrel dogs were intubated and subjected to a left lateral thoracotomy under standard barbiturate anesthesia (Fig. 1). A Statham electromagnetic flow probe was placed around the ascending aorta for measurement of cardiac output. A specially designed platinized, hydrogen-sensitive electrode [7] was threaded via the jugular vein into the coronary sinus for measurement of coronary sinus blood flow. For each measurement, the animal was allowed to inhale a mixture of hydrogen and oxygen, and a hydrogen decay curve proportional to blood flow was recorded. By semi-logarithmic extrapolation, the half time ($t_{1/2}$) decay of hydrogen could be determined, and flow calculated. This catheter could also be used for obtaining samples of coronary sinus blood for measurement of oxygen content. A left atrial catheter was inserted for microsphere injection and pressure recording, and a periarterial balloon occluder was placed in the same position as in group 1 animals. Bilateral femoral artery catheters were placed, one for microsphere reference sampling and one for measurement of systemic blood pressure.

Coronary sinus flow (CSF), cardiac output, EKG, and left atrial and coronary sinus oxygen contents were recorded prior to coronary occlusion, after 30 minutes of occlusion (IPO), during NP infusion (6 $\mu$g/kg per min) alone, during infusion of EP (1.4 $\mu$g/kg per min) and NP (6 $\mu$g/kg per min), and during EP infusion alone, after termination of NP for at least 15 minutes. Microsphere injections were accomplished immediately after occlusion (IPO), during NP infusion (NP), and with NP and EP combined (NP + EP).

At the conclusion of the study, the animal was killed, the heart excised, and its weight recorded. Tissue specimens were divided into normal, marginal and central ischemic zones as reported by Cox and Pass [8]. All tissue specimens were weighed and counted with the reference samples in a Nuclear Chicago well scintillation counter. Counts were converted to flow in cc/g per min by the method of Rudolph via a specially written computer program [6].

Cardiac index (CI), left ventricular stroke work index (LVSWI), and the rate-pressure-product (RPP) were calculated according to standard formulas. The myocardial oxygen consumption (MVO$_2$) was calculated using coronary sinus flow and the arteriovenous oxygen difference between the left atrium and the coronary sinus. Data were analyzed using the Student’s t-test for paired variables, and differences were considered significant when $p < 0.05$.

**Results**

**Group 1**

Heart rate did not change significantly with any intervention (Table 1). Left atrial pressure, systolic, diastolic, and mean arterial pressure fell significantly during NP infusion. Rate-pressure-product (RPP) declined significantly with NP infusion alone. With NP and EP combined, RPP remained decreased, but this value was not significantly lower than IPO level. Addition of EP to NP increased mean arterial pressure, but it was still significantly less than IPO. Left atrial pressure increased to IPO levels during EP + NP infusion.