WEDNESDAY, MARCH 18, 1981
PM
CORONARY CIRCULATION AND MYOCARDIAL BLOOD FLOW
2:00-3:30

ADRENERGIC TONE IN THE CANINE CORONARY CIRCULATION. Edward D. Verrier, MD, Gus J. Vlahakes, MD, Robert W. Baer, PhD, J. David Bristow, MD, FACC, Julien I.E. Hoffman, MD, FACC, FRCP. Cardiovasc. Res. Inst., U. of Calif., San Francisco.

Adrenergic tone may influence myocardial blood flow despite metabolic autoregulation. We examined this question in anesthetized dogs with a maximally vasodilated coronary circulation. Pressures were measured in the AO, LV, LA, and coronary sinus; heart rate was held constant by SA node block and atrial pacing (mean rate 115 min^{-1}). Diastolic coronary pressure-flow (P-Q) relations were determined with a circumflex preparation: coronary artery pressure was measured distal to a flow probe and occluder. Chromonar (8 $mg \cdot kg^{-1}$ iv) produced maximal coronary vasodilatation, confirmed by absence of reactive hyperemia. Twelve brief, partial occlusions were done at various distal pressures; mean diastolic coronary pressures and flows were used to construct a diastolic P-Q relation, which, with maximal vasodilatation, was linear [mean $r=0.98 \pm 0.01$ (SEM)]. P-Q lines were described by their slope and pressure intercept at zero flow. In 6 dogs, diastolic P-Q lines were determined before (Control) and after alpha blockade (AB) with phentolamine (5 mg iv). AO, LV, LA, and coronary sinus pressures did not change.

mean ± SEM	Control	AB	Analysis of variance
slope ($ml \cdot mm\ Hg \cdot min^{-1}$)	4.45 ± 0.51	4.37 ± 0.67	N.S.
intercept (mm Hg)	20.3 ± 0.4	17.9 ± 0.4	$P < 0.007$

AB produces a small, parallel, left shift in the P-Q line, which, with a large value for slope, increases diastolic coronary flow substantially at any given pressure during maximal vasodilatation. This suggests that alpha constrictor tone can limit myocardial blood flow despite maximal coronary vasodilatation and anesthesia.

In 4 other dogs, propranolol (0.25 $mg \cdot kg^{-1}$ iv) did not change either the slope or intercept of the diastolic P-Q line, suggesting that there is no significant resting beta tone in the canine coronary circulation under anesthesia.

EFFECTS OF PROSTACYCLIN (PGI_2) ON CORONARY BLOOD FLOW IN OPEN-CHEST DOGS AFTER DIFFERENT ROUTES OF ADMINISTRATION
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Prostacyclin (PGI2) is a potent vasodilator in isolated perfused hearts of various species. The in-vivo effects of PGI2 infusions were investigated in anesthetized,open-chest dogs. Coronary flow (CBF) was measured with an electromagnetic flow probe around the left circumflex artery (LCX), and coronary vascular resistance (CR) was calculated while aortic pressure (AOP) and heart rate (HR)were recorded.

Intravenous infusion of PGI2 (0,05 to 1.0 µg/kg/min) reduced AOP and CR in a dose-dependent fashion but had only minor effects on CBF. A tachycardia occurred parallel to the pressure reduction. However, when administered intracoronary distal to the flow probe PGI2 increased CBF 3-4 fold (p at least <0.05) and reduced CR ($p<0.05$) without affecting AOP and HR in doses between 0.05 to 0.5 µg. Topical application of PGI2 on the right ventricle increased coronary sinus oxygen content with minor changes in pressure. Cyclo-oxygenase inhibition (indomethacin, 5 mg/kg/min i.v.) did not alter the hypotensive effects of PGI2 after i.v. administration and increased the coronary vasodilator potency of the compound.

The sensitivity of the coronary vasculature seemes to be enhanced to PGI2 when endogenous biosynthesis of prostaglandin-like substanses is inhibited. Only after direct administration of PGI2 into the coronary circulation its specific coronary vasodilating effects can be demonstrated thus excluding the metabolization in the lung after intravenous application. It is suggested that PGI2 might be involved into the regulation of the coronary ciculation and coronary blood flow changes.

BETA ADRENERGIC CONTROL OF LARGE CORONARY VESSELS IN CONSCIOUS DOGS
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While β adrenergic regulation of the coronary circulation has been studied extensively, an important aspect of this topic, i.e., β effects on large coronary vessels has not been examined in the intact animal. To study this, 8 dogs were instrumented with miniature, piezoelectric crystals on opposing surfaces of the left circumflex coronary artery, an electromagnetic flow probe on the same vessel and miniature pressure gauges in the aorta and left ventricle. One week after surgery isoproterenol, 0.1 µg/kg/min, in conscious dogs increased mean left circumflex internal coronary cross sectional area (CSA) by 17 ± 3%, decreased late diastolic coronary resistance (LDCR) by 42 ± 5%, while increasing heart rate by 66 ± 8% and left ventricular (LV) dP/dt by 58 ± 5%. Atenolol, 1 mg/kg, a β_1 adrenergic selective blocker, reduced CSA by 8 ± 1%, and increased LDCR by 12 ± 4% ($p<0.01$). After atenolol, isoproterenol with heart rate constant did not increase LV dP/dt and caused significantly less, $p<0.01$, increases in CSA (6 ± 1%) and decreases in LDCR (11 ± 2%). On a separate day, propranolol, 0·5 mg/kg, reduced CSA by 7 ± 1%, while LDCR rose by 13 ± 4%, $p<0.05$. Isoproterenol after propranolol induced no effect. Thus, β adrenergic stimulation causes substantial increases in large coronary vessel CSA. Surprisingly, the major fraction of this response was associated with β_1 mediated increases in LV dP/dt and heart rate, whereas β_2 dilation of these vessels played a much lesser role. Moreover, β blockade resulted in significant constriction of large coronary vessels, an effect which could be detrimental in the presence of coronary artery disease, where large coronary vessel CSA is of crucial importance.

INFLUENCE OF NIFEDIPINE ON MYOCARDIAL BLOOD FLOW DURING THREE GRADES OF CORONARY OCCLUSION
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The effect of nifedipine (Nif) on myocardial blood flow (MBF) at varying grades of partial coronary occlusion (PO) is unknown. Thus 22 open chest dogs underwent carotid to left anterior descending perfusion with flow and perfusion pressure monitoring. Grades of coronary occlusion were defined by minimum diastolic perfusion pressure (DPP). After DPP was reduced to 54 mmHg (6 dogs), 37 mmHg (10 dogs) or 24 mmHg (6 dogs) 10 ug Nif was given intracoronary. Regional MBF in ml/g/min was determined by tracer microspheres. The three partial occlusions showed differing increases in total flow (%CF) and regional flow.

	Ischemic Zone MBF				Normal Zone MBF				
DPP	Endo		Epi		Endo		Epi		%CF
mmHg	PO	Nif	PO	Nif	PO	Nif	PO	Nif	
54	1.06	1.14	1.15	1.96*	1.29	1.28	1.11	1.10	42.3
37+	.70	.60*	1.06	1.39*	1.28	1.28	1.16	1.15	18.6+
24+	.48	.48	1.01	.94	1.54	1.49	1.60	1.57	-8.3+

*compared to control, +compared to above $p<.01$

At 54 mmHg Nif caused an increase in Epi MBF but no change in Endo MBF. In contrast at 37 mmHg Nif caused Epi flow to increase but resulted in a decrease in Endo flow. At the lowest perfusion pressure (24 mmHg) Nif caused no change in zone MBF. Thus the severity of coronary stenosis determines the presence of coronary vascular reserve in the endo and epicardium and thus the effect of nifedipine on regional myocardial perfusion. In certain settings, vasodilators such as nifedipine cause a redistribution or steal of flow from endocardium to epicardium.