To investigate clinical significance of treadmill exercise testings in dilated cardiomyopathy (DCM), 22 patients with DCM were subjected to symptom-limited treadmill exercise testing and cardiac catheterization. For evaluation of exercise tolerance and blood pressure response, the data of DCM were compared with 175 normal control subjects. Results were as follows: (1) DCM had poor exercise tolerance and poor increase in systolic blood pressure during exercise. (2) Exercise tolerance in DCM showed positive correlations with left ventricular ejection fraction ($r = 0.53$) and stroke volume index ($r = 0.65$). (3) Ventricular arrhythmias (VPC) occurred on exercise in 13 out of 22 patients. Most of them (90%) were so called "malignant arrhythmia" (multifocal or paired VPC and ventricular tachycardia).

In conclusion, treadmill exercise testings in DCM were characterized by a decrease in exercise tolerance, blood pressure response and malignant arrhythmias during exercise.

-114-

EFFECTS OF NIFEDIPINE ON PLASMA RENIN ACTIVITY, PLASMA ALDOSTERONE & CORTISOL CONCENTRATIONS IN PATIENTS WITH ESSENTIAL HYPERTENSION

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Behaviors of plasma renin activity (PRA), plasma aldosterone concentration (PAC) and plasma cortisol concentration (PCC) to an acute sublingual administration of nifedipine were studied in 59 patients with essential hypertension. Also, in 24 patients, percent changes of portal blood flow and cardiac output were determined by pulsed Doppler and UCG-Teichholz methods, respectively.

Various indices such as mean blood pressure (mBP), heart rate (HR), portal blood flow (Q) and cardiac output (CO) were recorded just prior to, and 30, 60 min after nifedipine administration. Blood samples were taken for determinations of PRA, PAC and PCC just before and 60 min following the treatment.

mBP decreased significantly [mBP(0 min)=125, mBP(30 min)=99, mBP(60 min)=102 mmHg], whereas HR increased [HR(0)=66, HR(30)=77, HR(60)=76/min]. PRA was increased [PRA(0)=1.44, PRA(60)=2.70 ng/ml/hr], but both of PAC and PCC were decreased [PAC(0)=85.2, PAC(60)=64.3 pg/ml, PCC(0)=12.2, PCC(60)=10.2 µg/dl]. Q and CO elevated [% Δ Q(30)=+88.9, % Δ Q(60)=+100.6%, % Δ CO(30)=+38.1, % Δ CO(60)=+33.6%]. % Δ Q was significantly greater than % Δ CO.

Nifedipine caused significant elevation in PRA, but decrease in PAC. As aldosterone is metabolized mainly in the liver, hepatic blood flow most effects on its clearance. Therefore, the increase in portal blood flow resulting from nifedipine administration was possibly ascribed to decrease in PAC and PCC.

We now conclude that nifedipine reasonably effects on the blood pressure control in hypertensive patients.

-115-

EFFECT OF PROSTACYCLIN ANALOG (TEI-8166A) IN ACUTE MYOCARDIAL ISCHEMIA

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TEI-8166A (TEI) is a stable prostacyclin analog. We investigated the effects of TEI on coronary circulation and hemodynamics in experimental acute myocardial ischemia.

Electromagnetic flow probe and plastic constrictor were affixed to the left anterior descending artery (LAD) just beyond the first diagonal branch in twelve mongrel dogs. The approximately 70% reduction of coronary blood flow (CBF) was established by partial occlusion. In 6 dogs, TEI 80 ng/kg/min was administered for 15 min, while saline was given in another 6 dogs as control. Aortic pressure, mean coronary arterial pressure, aortic flow (AoF), left ventricular end-diastolic pressure (LVEDP), CBF and coronary vascular resistance (CVR) were measured before, 5, 10 and 15 min after occlusion. Blood samples were obtained from aorta and coronary sinus to calculate lactate extraction ratio (LER).

In results, occlusion caused decreases in CBF and CVR in both group. During 15 min occlusion, no change was seen in vehicle group, while an increase in CBF concomitant with a decrease in CVR was obtained in TEI group. In addition, an increase in AoF and a decrease in double product were observed in TEI group concomitant with no significant change in LVEDP. TEI also inhibited the decrease in LER.

Thus, these results indicate that TEI has favorable effects on hemodynamics and might protect ischemic myocardium.

-116-

DIRECT EFFECT OF PROSTAGLANDINS ON MYOCARDIUM

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The purpose of this experiment is to investigate the direct effect of prostaglandins on myocardium and the mechanism of its action. The effect of STA2 (TXA2 analogue) and OP41483 (PGI2 analogue) on myocardial cells of mouse was studied in aspect of morphological changes and enzyme release into the medium.

1. When incubated with STA2 in Tyrode solution containing 1 mM Ca, the cells initially showed irregular beating, developed morphological changes caused by hypercontraction, and at last the beating stopped. Cell damage was indicated by CPK and LDH release into the medium.

2. The morphological changes induced by STA2 similarly appeared in Ca-free Tyrode. TMB-8 (Ca release inhibitor from SR) prevented the morphological changes, but Verapamil and Diltiazem (Ca channel blocker) did not.

3. The effect of STA2 was enhanced in hypoxic medium (PO₂: 30 mmHg).

4.OP41483 prevented both morphological changes and enzyme release induced by STA2.

5.OP41483 also prevented the morphological changes induced by uncoupler DNP and Ca ionophore A2 3187.

These results indicate that STA2 and OP41483 have direct effect on development of hypercontraction-induced damage of myocardial cells. And it is suggested that STA2 may enhance the Ca release from SR.

-117-

EFFECTS OF GLUCOSE-INSULIN-POTASSIUM ON SYSTEMIC, CORONARY AND PERIPHERAL CIRCULATION IN PATIENTS WITH CORONARY HEART DISEASE

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Acute effects of glucose-insulin-potassium (GIK) on the systemic, coronary and peripheral circulation were studied in 12 patients with coronary heart disease. No patient had congestive heart failure or diabetes mellitus. Cardiac output was determined by the thermodilution method using Swan-Ganz catheter. Coronary blood flow was measured by the continuous thermodilution method using Webster catheter. Forearm blood flow was measured by the strain-gauge plethysmograph with a venous occlusion technique. Measurements were repeated at rest and 30 min after an intra-atrial infusion of GIK (glucose 300 g/l, actrapid monocomponent insulin 50 U/l, KCL 80 mEq/l, 2 ml/kg/hr). After administration of GIK, there were no significant changes in mean blood pressure, right atrial pressure, pulmonary capillary wedge pressure, heart rate, cardiac index, total peripheral resistance, rate-pressure product or forearm vascular resistance. GIK significantly increased coronary blood flow from 141 ± 10 to 169 ± 10 ml/min ($p < 0.01$) and significantly decreased coronary vascular resistance from 0.73 ± 0.07 to 0.51 ± 0.05 mmHg/ml/min ($p < 0.01$). After GIK, blood glucose (102 ± 4 vs 228 ± 13 mg/dl) and IRI (32 ± 11 vs 158 ± 32 μ U/ml) were significantly increased ($p < 0.001$, $p < 0.01$, respectively). GIK decreased total cholesterol (201 ± 9 vs 188 ± 7 mg/dl, $p < 0.01$), triglyceride (156 ± 19 vs 131 ± 17 mg/dl, $p < 0.01$), free fatty acid (1.7 ± 0.3 vs 0.5 ± 0.2 mEq/l, $p < 0.001$) and hemotocrit (35.0 ± 2.4 vs $33.8 \pm 2.0\%$, $p < 0.05$). Serum potassium remained unchanged during GIK infusion.

These results suggest that GIK may have a selective coronary vasodilator action in patients with coronary heart disease.

-118-

THE EFFECTS OF PARTIAL β -AGONIST, XAMOTEROL, ON HEMODYNAMICS AND REGIONAL LEFT VENTRICULAR WALL MOTION IN ACUTE MYOCARDIAL ISCHEMIA

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To evaluate the effects of β -partial agonist, xamoterol (Xa:ICI 118587) on hemodynamics and regional left ventricular wall motion in acute regional myocardial ischemia induced by occluding circumflex coronary artery, we measured left ventricular and aortic pressures by catheter-tip micromanometers, cardiac output by electromagnetic flowmeter and regional left ventricular wall thickening (%W) in ischemic (I), marginal (M) and non-ischemic (N) areas by ultrasonic dimension gauges in 9 anesthetized dogs. The effects of Xa (350μ g/kg, iv) was compared with those of isoproterenol (IP: 0.1μ g/kg/min, iv) and dobutamine (D: 3μ g/kg/min, iv). Results: Xa increased (+) dP/dt by 70%, which was approximately same as D and IP did. Xa increased cardiac output by 44% and decreased left ventricular end-diastolic pressure significantly, with less increase in heart rate (13%) compared with IP (44%). Xa decreased systemic vascular resistance by 35% as well as IP, but D did not (2%). So increment of cardiac output by Xa was greater than that of D. As for the regional wall motion, Xa augmented %W significantly in N (24.8 ± 8.4 to $34.6 \pm 9.2\%$, $p < 0.05$) and M (5.8 ± 4.2 to $10.7 \pm 5.3\%$, $p < 0.05$), but not in I (-4.0 ± 3.4 to $-2.7 \pm 4.9\%$ n.s.).

Xa suppressed both positive chronotropic and inotropic effects of IP significantly.

So we suggest that Xa may be beneficial in acute regional myocardial ischemia because of improvement of hemodynamics and suppression of excessive stimulation of catecholamine.

-119-

EFFECTS OF CALCIUM ANTAGONISTS ON SERUM β -METHYLDIGOXIN CONCENTRATION

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We investigated effects of various calcium antagonists on serum concentration of β -methyl digoxin in 12 patients with chronic congestive heart failure. A dosage of 0.1 mg~0.2 mg of β -methyl digoxin was continued to administer orally, and one of the calcium antagonists (40 mg of verapamil, 60 mg of diltiazem, 10 mg of nifedipine or 20 mg of nicardipine) was added three times a day for seven days. Co-administration of a calcium antagonist did not induce a significant change in the time to reach the maximum concentration (T max) of β -methyl digoxin. Maximum digoxin serum concentration (C max) increased by 25~55% in co-administration of verapamil or diltiazem or nicardipine, but no significant change in co-administration of nifedipine. The area under the digoxin concentration-time-curve (AUC) increased in co-administration of verapamil or diltiazem or nicardipine compared to only β -methyl digoxin administration, but no significant change in co-administration of nifedipine. Apparent distribution volume (Vd) of digoxin decreased in most cases, and digoxin total clearance decreased in all cases. Renal clearance of digoxin had a tendency to decrease.

The increase in serum β -methyl digoxin concentration in co-administration of a calcium antagonist would be due to decrease in digoxin total clearance, renal clearance and apparent distribution volume.