the three groups, but the respiratory quotient during ergometer exercise of DM group was lower than those of N and HL groups significantly. Exercise therapy for about 1 month induced falls of serum concentrations of T-cho, triglyceride, and atherogenic index ((T-cho-HDL-cho)/HDL-cho), but no changes of serum concentrations of HDL-cho, phospholipid, and free fatty acid. In DM group, by exercise therapy for about 1 month, Hb-A_{1c} was decreased and the respiratory quotient during ergometer exercise for 30 minutes was increased significantly. These results were interpreted that exercise therapy has beneficial effects for patients with DM or HL, and that the improvement of glucose utilization during exercise of DM patients may be evaluated by measurement of the respiratory quotient during exercise.

-110- METABOLIC AND CIRCULATORY REGULATION DURING GRADED EXERCISE IN CHRONIC HEART FAILURE

Yamabe Hiroshi, Matsunaga Kimio

Hyogo Medical Center for Adults

The metabolic processes and the circulatory regulation during exercise were studied in chronic heart failure (CHF). Thirteen patients of functional class II and III and 18 normal subjects underwent graded treadmill exercise test, measuring oxygen consumption ($\dot{V}O_2$), blood lactate and, in 6 cases, mixed venous oxygen content. The blood lactate curve showed tri-phasic pattern to $\dot{V}O_2$ increment in both groups, that is, phase I is the first period with small change of blood lactate, phase II the second period with continuous increase of lactate, and phase III the last period with rapid increase of lactate. During phase I, mixed venous oxygen content rapidly fell, then it was gradually decreasing during phase II and III. The values of $\dot{V}O_2$ at the onset of phase II and phase III, and $\dot{V}O_2$ max were significantly smaller in CHF than in control. However, the relative $\dot{V}O_2$ ratio to the observed $\dot{V}O_2$ max at the onset of phase II and phase III were same level in both groups, that is $41.6 \pm 10.0\%$ and $78.6 \pm 9.9\%$ in CHF, and $41.3 \pm 9.2\%$ and $78.0 \pm 8.8\%$ in control, respectively. It is considered that phase I consists of high aerobic circumstance owing to rapid increase of oxygen extraction, resulting in complete catabolization of produced lactate. During phase II, the produced lactate may exceed its catabolizing threshold. During phase III, the rapid lactate increment indicates a severe shortage of aerobic energy production to the total energy demand, and this may prove the advanced regulatory failure of blood flow to the working muscle. It is concluded that the metabolic processes and circulatory regulation during maximal graded exercise shows the tri-phasic change in both CHF and normal subjects. This phenomenon may be useful to investigate the physiologic basis of life activity in patients with CHF.

-111- VENTILATORY CHANGES IN PATIENTS WITH CHRONIC HEART FAILURE

Toshikazu Mizuno, H. Matsumoto, M. Azuma,
S. Shinohara, M. Nomura, H. Chiba, J. Ohno.

Division of Cardiology,
Mimihara General Hospital

One minute incremental supine exercise test was performed in 30 cases, to evaluate the ventilatory changes. Cardiac output (C.O.) was calculated in every minutes with Fick Principle. Simultaneously, to evaluate anaerobic threshold (A.T.) and respiratory compensation threshold (R.C.T.), ventilatory parameters were measured.

In normal cases, the increase of CO (ΔCO) was proportional to the increase of arteriovenous O_2 difference (ΔavO_2D), and the $\Delta CO/\Delta avO_2D$ ratio showed the value of 1.05 ± 0.3 . By using this ratio, 25 patients of CHF were divided into two Groups: 12 patients showed normal valve GI and, 13 patients, under the valve of 0.7 GI. AT Point and RCT Point, detected by ventilatory changes, were noted in 9 cases (70%) in GII and 6 (50%) in GI. But the delay time of RCT from AT was different between 2 Groups. The mean delay time of GI showed 5 minutes and GII 1 minute. These findings demonstrate the impaired CO Response during exercise might be noted non invasively with the ventilatory parameter changes.

-112- DECREASE OF FINGER TEMPERATURE (FIT) DURING EXERCISE AS A FUNCTION OF THE INDIVIDUAL MAXIMAL POINT

Hirota Nishijuma, Naoya Matsumura,
Akikazu Nomura, Shunichi Kojima,
Ichiro Sakuma, Isao Sato,
Hisakazu Yasuda

Cardiovascular Medicine, Hokkaido University
School of Medicine, Sapporo, Japan

The purpose of the study was to evaluate the applicability of finger temperature monitoring as an indicator of peripheral vasoconstrictor response during maximal (MAX) exercise (Ex) testing. Ex testing with FIT monitoring by a thermistor on the mid-finger was done in 6 athletes (A), 16 normal (N), 8 mild cardiac (MIC) and 15 moderate cardiac (MOC) subjects using multi-stage protocol with a 3-min rest period between 3-min Ex stages. Intermittent Ex protocol was necessary to ensure reproducibility and to yield progressive FIT changes during Ex. Anaerobic threshold (AT) was determined by respiratory measurements. FIT change in parallel with finger blood flow changes (by plethymography). At the mild Ex stage FIT decreased initially, only to rise at the latter half of Ex. As Ex stage increased, FIT continued to decrease throughout the 3-min Ex period. Near or at the individual maximal stage FIT decreased linearly (LD). Sympathetic blockade abolished FIT decrease and an acute rise in norepinephrine was observed concomitantly with an acute decrease in FIT. Among 48 subjects, mean max $\dot{V}O_2$ (kg/min) was 63, 47, 31 and 15, and mean HR; 188, 195, 165 and 142, respectively in group A, N, MIC and MOC. LD was observed in more than 90% of cases at the work load, 1.6-fold of AT and within 90% of MAX. CONCLUSION: Progressive decrease of finger temperature during exercise testing was the result of sympathetic vasoconstriction and is an excellent non-invasive indicator of approaching maximal point in exercise.

-113- TREADMILL EXERCISE TESTING IN PATIENTS WITH DILATED CARDIOMYOPATHY

Atushi Fukui, Tetsu Yamakado,
Yasuhide Nishimura, Satoru Higashiyama,
Yoshihisa Higashi, Takeshi Nakano,
Hideo Takezawa

The First Department of Internal Medicine,
Faculty of Medicine, Mie University, Tsu

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.

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

Shin Eno, Yoshiro Kato, Kouji Kido,
Ikuo Kanazawa and Akira Maruhashi.

Department of Internal Medicine,
Chugoku Rousai Hospital.
Kure, Hiroshima.

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.

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

JUNKO HONYE, MASAHIITO MORIUCHI, NAOTO KASEDA, TOMOHIKO KAMATA, MASAZUMI TSUJI,

YASUO TAMURA, SATOSHI SAITO, YUKIO OZAWA,
MICHINOBU HATANO

The 2nd Department of Internal Medicine,
Nihon University School of Medicine

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.

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DIRECT EFFECT OF PROSTAGLANDINS ON MYOCARDIUM

Seiichi Okusawa*, Katsunobu Miyata*, Hiromi Okutomi*, Masanori Takenoya*, Takeo Yamada*,
Satoshi Shimizu**, Yoshihiro Morimoto**,
Shinichiro Kinoshita**, Yutaka Dohi**

*Department of Internal Medicine, Josai
Dental University, Saitama Japan.

**2nd Department of Internal Medicine,
Saitama Medical College, Saitama Japan

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).