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The clinical efficacy of TA-064, a new cardiotonic agent, was investigated in 9 patients (pats) with refractory and/or bradycardiac heart failure. For each subject, clinical conditions were compared before and after 1 to 2 weeks of therapy (10 mg t.i.d.).

After the treatment, all 9 pats showed no significant changes in functional and Killip's classification, cardiothoracic ratio (CTR), and echocardiographic findings despite improved subject impressions in 4 cases. Heart rate (HR), systolic blood pressure and pressure-rate product (PRP) also increased significantly.

In 6 pats with refractory heart failure, TA-064 caused little change in Killip's classification, CTR, or left ventricular function judged by echocardiography, although subjective symptoms improved in 3 pats. Also, HR and PRP increased after TA-064.

After TA-064 treatment of 5 pats with heart failure accompanying bradycardia, their subjective impression improved, CTR, LVDD (57.2 to 52.0 mm, $p < 0.05$) and LVDs (45.0 to 39.4 mm, $p < 0.05$) decreased, and fractional shortening increased (22.2 to 25.8%). HR (48.0 to 57.0/min, $p < 0.1$) and PRP also increased.

Pharmacokinetic analysis indicated good drug absorption and fast excretion even with heart failure.

Apparently TA-064 is a salutary agent in heart failure accompanying bradycardia, but the drug appears to be ineffective for refractory heart failure and alternative agents, such as vasodilators, should be considered.

-244- HEMODYNAMIC AND METABOLIC EFFECTS OF DIBUTYRYL CYCLIC AMP IN PATIENTS WITH CONGESTIVE HEART FAILURE

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To evaluate the benefit of Dibutyryl cyclic AMP (DBcAMP), a new inotropic-vasodilating agent, in the treatment of congestive heart failure, its hemodynamic and metabolic effects were investigated in 14 patients with chronic heart failure (NYHA II-IV). DBcAMP was infused intravenously in three different doses, 0.025, 0.075, and 0.200 mg/kg/min, respectively, for 60-30 min with every 6-12 hours interval. Hemodynamics was monitored with a triple lumen Swan-Ganz catheter and venous blood was sampled to analyse for glucose and lipid metabolism. Heart rate was increased by 6-17 beats/min and mean arterial pressure was decreased by 14-19 mmHg ($p < 0.05$, 0.001). Cardiac index and stroke volume index were significantly increased by 0.80-1.88 L/min/m² and 7.3-16.0 ml/m² ($p < 0.001$, 0.001). Mean pulmonary arterial pressure and pulmonary capillary wedge pressure were decreased at 0.200 mg/kg/min of DBcAMP ($p < 0.05$). Both systemic and pulmonary vasoculuar resistance were significantly decreased ($p < 0.001$, 0.001). These hemodynamic effects of DBcAMP were dose-dependent and lasted for 30-90 min after discontinuation. Blood glucose and immunoreactive insulin (IRI) were significantly increased by 85-70 mg/dl and 12.4-15.4 μ U/ml ($p < 0.001$, 0.001). Non esterified fatty acid was significantly decreased ($p < 0.01$). Plasma renin activity, aldosterone concentration, plasma epinephrine and norepinephrine were not significantly changed during DBcAMP infusion. There were no side effects during the study. Thus, DBcAMP improved hemodynamics of heart failure in a dose-dependent manner, with favorable

metabolic effects, therefore, DBcAMP would become to be a useful drug in the management of patients with congestive heart failure.

Chairmen

245-255 Y. Kitaura, *Takatsuki*
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-245- SIGNIFICANCE OF ANOMALOUS MUSCULAR BAND IN HUMAN ATRIUM ON SUPRAVENTRICULAR ARRHYTHMIAS

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The atriums of total 140 necropsy cases, 18 with atrial fibrillation (AF), 22 with premature atrial contraction (PAC) and 100 without supra-ventricular arrhythmia on ECG in life, were patho-morphologically examined. In 14 of 140 examined hearts, an anomalous muscular band traversing the right atrium from crista terminalis to superior margin of the A-V node, was recognized separating from pectinate muscles. These muscular bands were 8 to 30 mm in length, 0.5 to 1.2 mm in diameter, and histologically surrounded by fibrous connective tissue with a single small artery in the central part. These constituent cells were larger (20 to 40 μ m in diameter) and clearer and contained fewer myofibrils than ordinary working atrial myocytes, resembling in some respects the Purkinje fibers of the ventricular conduction system. Of the cases with the anomalous band, 10 cases (71%) were with AF or PAC, and the anomalous band was seen in 4 cases of AF group (22%), and 6 cases of PAC group (27%) instead of 4 cases of control group (4%).

Conclusion: These newly found anomalous muscular band in human atriums may play an etiologic role in the occurrence of supraventricular arrhythmias.

-246- QUANTITATIVE STUDY ON GROWTH AND AGING CHANGES IN HUMAN ATRIOVENTRICULAR NODE -BY USING BOTH CYTOFLUOROMETRY AND COLOUR IMAGE ANALYZER-

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Nuclear DNA determinations of the atrioventricular (AV) nodal cells were performed by using cytofluorometry in order to investigate the cell kinetics of them and in addition to this, histological changes of AV node during growth and aging were investigated by using colour image analyzer.