($p < 0.01$), urinary electrolyte excretion (Na, Cl: $p < 0.01$, K: $p < 0.05$), and their clearance (Na: $p < 0.01$, K: $p < 0.05$) were increased. Renal vascular resistance was reduced ($p < 0.01$). No adverse reactions were observed.

The augmented renal blood flow and profound natriuresis after TA-8704 were comparable with those of parenteral dopamine. Our results confirmed beneficial cardiorenal effects of an orally active TA-8704 in patients with severe chronic congestive heart failure. However, further studies on the evaluation of chronic administration of the drug are needed.

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HEMODYNAMIC AND ANTIPLATELET EFFECTS OF PGI₂ ANALOG (OP-41483) IN PATIENTS WITH CONGESTIVE HEART FAILURE

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Prostaglandin I₂ (PGI₂) is known to have a strong vasodilating effect as well as an antiplatelet effect. In the previous paper, we have demonstrated salutary effects of PGI₂ in patients with severe congestive heart failure using it as a vasodilating agent. However, because PGI₂ is a very unstable substance, there are difficulties in its clinical use. In this study, we evaluated hemodynamic and antiplatelet effects of a newly synthesized, stable analog of PGI₂, OP-41483(OP). Its effects were compared with nitroprusside (NP) and PGI₂ in patients with severe congestive heart failure using a Swan-Ganz catheter and a standard platelet aggregation test by 3 μ M ADP.

In a group of nine patients with severe congestive heart failure, OP (20 ng/kg/min) was infused for one hour and its hemodynamic and antiplatelet effects were measured. After an hour for wash-out, NP (1.0 μ g/kg/min) was subsequently infused for one hour and the measurements were similarly done. In another group of nine patients with severe congestive heart failure, PGI₂ (22 ng/kg/min) was infused for one hour and hemodynamics and platelet aggregation were similarly measured. OP showed salutary hemodynamic effects similar to NP and PGI₂. Although NP did not show any inhibitory effect on platelet aggregation, OP inhibited ADP aggregation to a similar extent as PGI₂. No adverse effects were seen during infusion of either drug. These findings suggest that OP may become a new efficacious regimen with an antithrombotic effect in the management of congestive heart failure, especially, associated with ischemic heart disease.

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EFFECTS OF NEW INOTROPIC AGENT, OPC-8212, ON AORTIC INPUT IMPEDANCE AND VENOUS RETURN PROPERTY IN ACUTE OPEN CHEST DOGS

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While positive inotropic effects of OPC-8212 (OPC) have been extensively studied, whether its effects on the vascular system are advantageous or not in treating patients with congestive heart failure is not known. We, therefore, evaluated in 6 dogs effects of OPC on the arterial system properties with Windkessel parameters (total vascular resistance (TVR), arterial compliance (Ca) and characteristic impedance (Rc)) which were derived from high resolution (0.0122 Hz), wide band (0.0122-20 Hz) aortic input impedance. We evaluated in another 9 dogs its effects on the venous system properties with mean circulatory filling pressure, conductances of venous return and vascular compliances in systemic and pulmonary vascular bed. We administered 3mg/kg OPC in each experiment. Administration of OPC increased cardiac output by 53% [1303 $\pm$ 386 (mean $\pm$ sem) to 1709 $\pm$ 294 ml/min ($p < 0.05$)] and decreased mean aortic pressure by 10% [90.5 $\pm$ 4.8 to 81.7 $\pm$ 7.1 mmHg (statistically insignificant)]. In the arterial system, OPC decreased TVR by 30% [6.15 $\pm$ 1.76 to 3.23 $\pm$ 0.63 mmHg $\cdot$ sec/ml ($p < 0.05$)], whereas it increased Rc by 15% [0.18 $\pm$ 0.03 to 0.20 $\pm$ 0.03 mmHg $\cdot$ sec/ml ($p < 0.05$)] without changing Ca [0.42 $\pm$ 0.06 to 0.43 $\pm$ 0.05 ml/mmHg]. In the venous system, OPC affected none of the parameters listed above.

Since OPC decreased afterload without changing preload, we conclude that OPC as an inotropic agent has favorable vascular effects in treating patients with congestive heart failure to increase cardiac output.

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ACUTE AND CHRONIC EFFECTS OF XAMOTEROL (CORWIN) IN IDIOPATHIC DILATED CARDIOMYOPATHY

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Xamoterol (corwin, a β -partial agonist) was given to 10 patients with idiopathic dilated cardiomyopathy (DCM) in NYHA functional class II and III. The acute and chronic effect of xamoterol was assessed, based on the changes in plasma norepinephrine levels (NE), exercise tolerance measured by multistage bicycle ergometer tests, echocardiography, radionuclide ventriculography, and right heart catheterization. The acute effect was determined after a single intravenous injection on 0.2 mg/kg of xamoterol. Exercise heart rate decreased from 117 $\pm$ 9 beats/min ($p < 0.01$) but blood pressure and cardiac index were unaffected. When the drug was given orally at 200 mg/day for 3 months, exercise tolerance increased from 4.2 $\pm$ 2.3 min to 6.4 $\pm$ 2.6 min ($p < 0.01$), echocardiographic ejection fraction (EF) from 29 $\pm$ 12% to 39 $\pm$ 14% ($p < 0.01$), and radionuclide EF from 36 $\pm$ 11% to 45 $\pm$ 14% ($p < 0.01$), while pulmonary wedge pressure during exercise decreased from 32 $\pm$ 12 mmHg to 22 $\pm$ 9 mmHg ($p < 0.05$). Plasma NE levels which were high (> 0.6 ng/ml) in 3 patients before treatment showed a fall after treatment. In conclusion, xamoterol exerted both β -blocking and stimulating effects in a well-balanced fashion, and improved subjective symptoms, exercise tolerance, and parameters of the left ventricle in patients with DCM when used over a long period.

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STUDIES OF DENOPAMINE (TA-064) FOR TREATMENT OF REFRACTORY AND/OR BRADYCARDIAC HEART FAILURE

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