

## **Plasma endothelin and big endothelin levels in cardiovascular subjects and effects of bosentan**

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**Purpose** Various cardiovascular diseases especially metabolic syndrome is partly prevented by exercise training. Endothelin is a strong vasoconstrictor with vasoproliferative activity. The purpose is to study whether changes in endothelin production is involved in this beneficial effects of training, and whether endothelin antagonist becomes anti-metabolic syndrome treatment. For this purpose, we also measured plasma endothelin and big endothelin levels in patients with cardiovascular diseases.

**Methods and Results (1)** Plasma endothelin levels increased with aging. Plasma levels of both endothelin and big endothelin were increased in hemodialysis patients, and intensity of increase was higher in endothelin than in big endothelin. Plasma endothelin and big endothelin levels were increased in patients with acute and chronic heart failure. We also measured plasma endothelin in aged healthy subjects before and after 3 months of exercise training (jogging), and plasma endothelin level decreased significantly after exercise training. We also applied high-dose bosentan (500 mg od/person po: 4-fold higher than in treatment of patients with pulmonary hypertension) to these subjects. Before training, carotid arterial compliance increased significantly with administration of high-dose bosentan, whereas after training the increase by high-dose bosentan was abolished.

**Conclusion and Discussion** Plasma endothelin and big endothelin levels were increased in various cardiovascular diseases especially metabolic syndrome, and the beneficial effects of exercise training on these patients were partly attributed to decrease in endothelin production. When these patients can not do exercise training, endothelin antagonist application could partly be an alternative therapy for increasing arterial compliance (distensibility) thereby improving cardiovascular diseases.