

REGULATORY MECHANISM OF THE HYPERPLASTIC VASCULAR
DISEASE FOLLOWING ENDOTHELIAL REMOVAL BY HIGH SALT DIET

Hiroshi AZUMA, Hidehisa HAMASAKI, Jun SATO, *Kimiyooshi HIRAKAWA, *Eiji ISOTANI,
**Takeshi ASO and **Satoshi OBAYASHI

*Department of Medicinal Chemistry, Institute for Medical and Dental Engineering, Departments of
*Neurosurgery, and **Gynecology and Obstetrics, Tokyo Medical and Dental University
2-3-10 Surugadai, Kanda, Chiyoda-ku, Tokyo 101, Japan.*

Summary

We have carried out studies to investigate the role of endothelium for the initiation, progression and prevention of the intimal hyperplasia following endothelial removal. Endothelial cells are known to produce/release endothelin-1 and endothelium-derived relaxing factor (EDRF/NO). Therefore, we focused on the physiological roles of endothelin-1 and EDRF/NO. we have reported that (1) EDRF/NO is an antiaggregating substance which may also modulate the release of platelet-derived growth factor, (2) there is a strong inverse correlation between the intimal hyperplasia following endothelial removal and the amount of EDRF/NO produced/released by endothelial cells, (3) endothelin-1 is involved in the neointima formation after endothelial removal and the ET_A receptors would not play a role in this process and (4) the accumulation of endogenous inhibitors (N^G-monomethyl-L-arginine: NMMA and asymmetrical N^G,N^G-dimethyl-L-arginine: ADMA) for nitric oxide synthesis and decreased L-arginine content, as a substrate for the NO biosynthesis, are associated with the decreased EDRF/NO production/release from endothelial cells and neointima formation.

The present experiments were performed to investigate the effect of chronic high salt diet on the neointimal formation following endothelial removal in connection to the changes in parameters described above. The intimal hyperplasia was attenuated in the high salt diet group which had been fed with diet containing 3% salt for 12 weeks (from 6 weeks before to 6 weeks after the endothelial removal). It was demonstrated that the attenuation of the intimal hyperplasia by the chronic high salt diet would occur in association with the restoration of the decreased production/release of EDRF/NO, the increased endothelin-1 content, the increased NMMA and ADMA content, and of the decreased content of L-arginine. However, the precise mechanism attenuating intimal hyperplasia by the high salt diet remains to be investigated.