PL6 Hyperhomocysteinemia and atherosclerosis: role of chemokine and adhesion molecules

A/Prof Karmin O, Department of Pharmacology, Faculty of Medicine, University of Hong Kong, Hong Kong

Introduction: Hyperhomocysteinemia is regarded as an independent risk factor for cardiovascular and cerebral vascular disorders. The stimulatory effect of homocysteine (Hcy) on monocyte chemoattractant protein-1 (MCP-1) expression *in vitro* has been suggested to play an important role in Hcy-mediated atherosclerosis. We previously reported that Hcy stimulated MCP-1 expression in endothelial cells, in vascular smooth muscle cells and in monocyte-derived macrophages. The objective of the present study was to investigate whether such stimulatory effect occurred *in vivo* leading to monocyte adhesion to the endothelium.
Methods: Hyperhomocystenemia was induced in Sprague-Dawley rats after four weeks of high-methionine diet (serum Hcy levels 4-5 fold higher than the control).
Results: The number of monocytes present on the surface of aortic endothelium was significantly elevated in hyperhomocysteinemic rats. There was a significant increase in the expression of MCP-1, vascular cell adhesion molecule-1 (VCAM-1) and E-selectin in the endothelium. Antibodies recognizing MCP-1, VCAM-1 or E-selectin could abolish the enhanced monocyte binding to the aortic endothelium of hyperhomocysteinemic rats.
Conclusions: These results suggest that hyperhomocysteinemia alone stimulates the expression of chemokine and adhesion molecules *in vivo* leading to increased monocyte adhesion to the aortic endothelium. Such effect may contribute significantly to the development of atherosclerosis by facilitating monocyte infiltration into the arterial wall.

This study was supported by grants (HKU7346/00M and HKU7249/02M) from the Research Grant Council of Hong Kong.