Effects of Cadmium and Lead on the Release of Fibrinolytic Proteins from Vascular Endothelial Cells, Vascular Smooth Muscle Cells and Fibroblasts

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Introduction

Vascular endothelial cells produce and release fibrinolytic proteins such as tissue plasminogen activator (t-PA) and its inhibitor type 1 (PAI-1) and regulate the fibrinolytic system in normally circulating blood. Vascular smooth muscle cells (SMC) and fibroblasts also are capable of producing t-PA and PAI-1 and are postulated to regulate the fibrinolysis when vascular endothelial cell layer is damaged or the vascular tissue disrupted. Cadmium and lead have been shown experimentally and epidemiologically to induce vascular disorders such as atherosclerosis and hypertension. The present study was undertaken to determine the effects of cadmium and lead on the release of t-PA and PAI-1 from vascular-composing cells.

Methods

Human umbilical vein endothelial cells, human aortic SMC and human fetal lung fibroblasts (IMR-90) were cultured until confluent and incubated at 37°C for 24 h in serum-free ASF 301 medium in the presence of cadmium chloride or lead chloride. The antigens of t-PA and PAI-1 (t-PA: Ag and PAI-1: Ag, respectively) were determined by enzyme immunoassay.

Results

In endothelial cells, cadmium significantly enhanced the release of PAI-1: Ag without change of the t-PA: Ag release.¹⁾ However, the release of either t-PA: Ag or PAI-1: Ag from SMC was strongly suppressed by cadmium.²⁾ In fibroblasts, the t-PA: Ag release was significantly enhanced by cadmium but the PAI-1: Ag release was unaffected by the metal.²⁾ On the other hand, lead suppressed the t-PA: Ag release without change of the PAI-1: Ag release in endothelial cells.³⁾ The release of either t-PA: Ag

or PAI-1: Ag from SMC was significantly suppressed by lead.⁴⁾ In fibroblasts, the release of t-PA: Ag was significantly suppressed but that of PAI-1: Ag was significantly enhanced by lead.⁴⁾ The effects of cadmium and lead on the fibrinolytic protein release were not necessarily similar to those of calcium ionophore A23187.^{4,5)}

Discussion

The findings revealed in the present study are summarized as follows: (1) the response of vascular-composing cells to cadmium and lead differs among endothelial cells, SMC and fibroblasts. (2) The alterations in t-PA and PAI-1 release from vascular-composing cells after exposure to cadmium and lead are not necessarily coupled. (3) The effects of cadmium on the release of fibrinolytic proteins in endothelial cells and fibroblasts are different from those of lead. (4) The effects of cadmium on the release of fibrinolytic proteins are postulated to be mediated by the intracellular calcium-independent pathway. The variety of perturbation of the fibrinolytic protein release induced by cadmium and lead appeared to be useful in understanding the pathogenesis of vascular lesions caused by these heavy metals.

References

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