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Atherosclerosis and Inflammation

1.4 Manidipine Inhibits the Release of Interleukin-6 (Il-6) Induced by Modified Lipoprotein and by TNF-Alpha in Culture Human Endothelial Cells

S. Costa (1), M. Pedrelli (1), N. Ronda (2), M. Adorni (1), F. Bernini (1), G. Cremonesi (3)

(1)Università di Parma, Dipartimento Scienze Farmacologiche, Biol. e Chim. Applicate, Parma, Italy, (2)Università di Medicina Clinica Nefrologica Scienze della Prevenzione, Parma, Italy, (3)Chiesi Farmaceutici S.p.A., Parma, Italy

Introduction. The vascular inflammation is a critical event in the formation of atherosclerotic lesions. The exposure of endothelial cells to oxidized lipoproteins or other stress like hypertension, induce the expression of pro-atherogenic cytokines including interleukin-6 (IL-6). Drugs act by targeting one of the many factors involved in these processes can have direct antiatherosclerotic effect enhancing the beneficial effect of a reduction of cardiovascular risk factors such as high cholesterol level and hypertension.

Aim. In this study we assessed t he ability of a lipophilic calcium antagonist Manidipine to reduce the release of IL-6 induced by modified lipoprotein or tumour necrosis factor-α (TNF-alpha) in human endothelial cells.

Methods. The endothelial cells isolated from human umbilical vein (HUVEC) were incubate d with acetylated LDL (AcLDL) 50 μg/ml or oxidized LDL (OxLDL) 100 μg/ml or with TNF-alpha 2 ng/ml, and treated with Manidipine 1-20 μM for 48 hours. The release of IL-6 in the media was determined by ELISA analysis.

Results. Our results showed that both AcLDL and OxLDL stimulate the secretion of IL-6 by 100% and 134% respectively. Treatment of cells with Manidipine 1 μM reduces the secretion of IL-6 from 211.6 ± 11.5 pg/ml to 122.4 ± 11.8 pg/ml ($p < 0.001$) and from 1300.29 ± 39.5 pg/ml to 649.39 ± 22.4 pg/ml ($P < 0.01$), in the presence of ACLDL or OxLDL respectively. Incubation of endothelial cells with TNF-alpha increased IL-6 secretion by 56% and treatment with Manidipine 20 μM abolished this effect by 74% (TNF-alpha 437.8 ± 51.6 pg/ml and Manidipine 115.1 ± 4.7 pg/ml, $p < 0.05$). Manidipine did no show toxicity at all the concentrations tested.

Conclusions. Manidipine is able to inhibit the release of IL-6 induced by modified lipoprotein and by TNF-alpha in culture human endothelial cells, suggesting a potential antiatherosclerotic effect of this drug.