P9 EFFECTS OF RUSSELL'S VIPER VENOM PROINFLAMMATORY CYTOKINE PRODUCTION IN CULTURED HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS

Sopit Thamaree[1], Visith Sitprija[2], Pravit Akarasereenont[3], Narumol Puckmanee[2], Orawan Khow[2], Nongnuch Thaworn[1]

[1]Department of Pharmacology Faculty of Medicine, Chulalongkorn University, [2]Queen Saovabha Memorial Institute, The Thai Red Cross Society, [3]Department of Pharmacology Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

ABSTRACT

Hemodynamic alterations in Russell's viper envenomation are the result of interactions of various vasoactive mediators and perhaps proinflammatory cytokines. Since vascular endothelium is likely to be exposed to high concentrations of the venom and endothelial cell itself not only plays an important role in physiologic control of the circulation, but also play a role in inflammation with the synthesis and secretion of proinflammatory cytokines. It is therefore, the objective of this study to determine the effects of Russell's viper venom (RVV) on proinflammatory cytokine production by cultured human umbilical vein endothelial cells (HUVEC). Endothelial cells were isolated from freshly obtained human umbilical cords and grown in tissue culture to confluence as a homogeneous population. Cells were then incubated at 37 °C under 5 % CO_2 with RVV (0.2, 1.0, 5.0, and 25.0 μg/ml) or lipopolysaccharide (LPS, 10 μg/ml) for 3,6,12 and 24 hours. After indicated time, the levels of tumor necrosis factor- α (TNF-α); interleukin-1β (IL-Iβ) ; and interleukin-6 (IL-6) in supernatants were measured by using ELISA or EIA. The effect of RVV or LPS on cell viability was also measured using MTT assay. The results showed slight increase of IL-1β level together with TNF-α level indicating that endothelial cell activation by LPS or RVV is not sufficient per se to elevate levels of the major endothelial cell-derived cytokine. The level of endothelial cell-derived cytokine. The level of endotherial cell-derived IL-6 was higher than that of TNF-α. Endothelial cell-derived IL-6 may be produced through other way apart from production via a cascade of cytokines. However, TNF-α and IL-6 productions were not different among these groups. The levels of IL-1β were very low, although IL-1β was detectable in the group treated with RVV at concentration of 25.0 μg/ml. In conclusion, RVV upto 25.0 μg/ml has no effect on prominent proinflammatory cytokine production by HUVEC. However, In the body and blood circulation, EC is not the single type of cells that produce cytokines. The major sources of cytokines are monocyte-macrophage lineage cells. It is possible that RVV which contains various constituents may activate the production of cytokines from those cells other than the EC and subsequently induce production of other mediators of inflammation that are responsible for the pathogenesis of RVV-induced toxicity.