Effects of LPS and TNFα on the histamine responsiveness of vascular endothelial cells

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Patients with chronic spontaneous urticarial (CSU) are often resistant to treatment with H1 antihistamines and have an increased response to intradermal injection of histamine. In this study, we evaluated the changes of responsiveness of vascular endothelial cells treated with Lipopolysaccharide (LPS) and Tumor necrosis factor (TNF)-α, known as exacerbating factors of CSU, to histamine using the impedance sensor, which can analyze the gap formation of cells in real time. Umbilical cord blood-derived vascular endothelial cells (HUVECs) were used as human vascular endothelial cells. HUVECs were cultured on the electrodes of sensor and the effects of LPS and TNFα treatment on the gap formation of cells in response to histamine were monitored. Moreover, the effects of H1 antihistamines on the gap formation of LPS- or TNF- treated HUVECs were examined. When LPS and TNFα were added simultaneously with histamine, the response of HUVECs to histamine did not increase. On the other hand, when LPS and TNFα were added a day before measurement of impedance, the responsiveness to histamine was increased and the response became difficult to be suppressed by H1 antihistamines. The increase of histamine responsiveness in vascular endothelial cells by LPS and TNFα may contribute to resistance to antihistamines in patients with CSU.