Inhibitory Effect of Pooled Human Immunoglobulin on Cytokine Production in Peripheral Blood Mononuclear Cells

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摘要

Abstract

Human intravenous immunoglobulins (IVIG) are widely used as immunomodulators because of their ability to modify the course of various immune-mediated diseases. We investigated the mechanisms responsible for the regulatory effects of IVIG on in vitro human peripheral blood mononuclear cell (PBMC) cytokine production. Pre-incubation of PBMCs with IVIG inhibited lipopolysaccharide (LPS) and phorbol 12-myristate 13-acetate (PMA)/ionomycin stimulated cytokine secretion. Pre-incubation of PBMCs with IVIG induced a significant inhibition of LPS-stimulated (IL-6) secretion (p = 0.045); the effect on tumor necrosis factor-alpha (TNF- alpha) secretion was not significant (p = 0.234). Pre-incubation of PBMCs with IVIG inhibited IL-6 secretion (p = 0.033) stimulated with anti-CD14 antibody cross-linking but had no significant effect on TNF-alpha secretion (p = 0.125). PBMC pre-incubation with anti-CD14-blocking antibody induced a significant reduction (p = 0.042) in LPS-stimulated TNF - alpha secretion in comparison with a non-significant reduction (p =0.256) noted with IVIG pre-treatment. In contrast, pre-incubation of PBMCs with anti-CD14 antibody did not induce a significant reduction in LPS- stimulated IL- 6 secretion (p = 0.166) in comparison with a significant reduction (p = 0.001) induced with IVIG pre-treatment. Our data suggest that the immunoregulatory properties of IVIG may rely on several mechanisms, some of which may be independent of CD14. Our data also showed that cross-linking cell membrane-bound IVIG with anti-human kappa- and lambda- chain antibodies resulted in cytokine secretion levels similar to those elicited by LPS. In addition, intracellular DNA staining results did not support the involvement of apoptosis in the regulatory mechanisms of IVIG. This data may further our understanding of the immunoregulatory effects exerted by IVIG on the production of inflammatory- response mediators.