IN VITRO IMMUNOREGULATORY EFFECTS OF ANTIDEPRESSANTS IN HEALTHY VOLUNTEERS

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Major depression is accompanied by an activation of the inflammatory response system (IRS) and antidepressants may have immunoregulatory activities.

This study was carried out to compare the effect of imipramine, mianserin and lithium on the in vitro production of Th1-like cytokines, such as IL-2, IFN-γ, lymphotoxin and Th2-like cytokines such as IL-4, IL-10 as well as IL-12 and TGF-β. Peripheral blood mononuclear cells (PBMC) of 16 healthy volunteers were stimulated with polyclonal activators (phytohemagglutinin with lipopolysaccharide PHA + LPS) with or without incubation with imipramine, mianserin (1 µM) or lithium (1 mM). Imipramine and mianserin exhibited similar activities enhancing unstimulated IFN-γ and IL-10 production. In PHA + LPS-stimulated PBMC both antidepressants inhibited IFN-γ, IL-2 and lymphotoxin production (Th1-like cytokines) as well as IL-12 and IL-4 production. Under the same in vitro conditions, both antidepressants stimulated production of negative immunoregulatory cytokines such as IL-10 and TGF-β. Lithium differed significantly from imipramine and mianserin, as it enhanced IL-2, IFN-γ, IL-10 and TGF-β production and inhibited only IL-4. All three examined antidepressants reduced IFN-γ/IL-10 ratio. None of the antidepressants at the used concentrations induced apoptosis in PBMC so those changes in cytokine production were not the result of selective killing of certain cell subpopulations. Imipramine and mianserin at high concentrations negatively influenced reactive oxygen species (ROS) production in neutrophils, however, at concentrations in the therapeutical range none of the antidepressants used influenced “oxidative burst” in neutrophils. The results indicate that antidepressants exert immunoregulatory effects on human leukocyte functions, especially on cytokine production.

Key words: antidepressants, imipramine, mianserin, lithium, peripheral blood leukocytes, cytokines, reactive oxygen species