volume 30 | number 2 | pages 101–166 | April 2010

Autonomic & Autacoid Pharmacology

WILEY-BLACKWELL

ISSN 1474 8665 (Print)
ISSN 1474 8673 (Online)

PLENARY LECTURES

Autonomic & Autacoid Pharmacology
2010, 30, 101–165

Innate immunity and immunoregulatory mechanisms of polybacterial immunomodulators

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Innate immunity is extremely important as an immediate defence mechanism, but today it is clear that it also takes the central stage in activation and regulation of the adaptive immune response. Cellular elements of natural resistance are key participants in this process.

Respivax (BulBio-NCIPD Ltd.) is an oral polybacterial immunomodulator intended for treatment and prevention of non-specific respiratory tract infections (NSRTI). We studied for the first time its effects on the inductive mechanisms of innate immunity, in the course of 3 consecutive cycles of treatment [one tablet (50 mg) daily for 20 days, followed by a 10-days pause] in 25 patients with NSRTI by means of flow cytometry.

Our results show that prolongation of respiratory infections is connected with decreased expression on phagocytes of: CD11b receptor responsible for the transendothelial migration, TLR2 for the gram (+) bacteria recognition, the complex TLR4/CD14 on monocytes, decreased oxidative burst level in Gr in weak stimulation response.

Respivax increased the effectiveness of phagocytes as it restored the ability for: endothelial adhesion and transmigration (increasing the expression of CD62L and CD11b), recognition of Gram (+) and Gram (−) bacteria with high sensitivity. The preparation restored the oxidative processes in response to low-dose stimulations. It increased the resistance to viral infections as: increased the percentage and the resistance of NK cells and the relative share of plasmocytoid dendritic cells. NSRTI are characterized with deficiency of the antigen-presenting (AP) functions of the immune system: decreased expression of HLA-DR and CD86 co-stimulator on monocytes, decreased percentage of precursors of dendritic cells (CD14+16+), disturbance of the maturation of dendritic cells (lower ratio CD86low/CD86hi).

Respivax restored the AP potential of the immune system as it stimulated: phagocytosys, AP capacity of circulating monocytes, differentiation and AP ability of dendritic cells and decreased the portion of the inhibitory regulatory CD4+ CD25hiFoxP3+ population.

NSRTI are connected with prevalence of second type cytokines (decreased ratio IFN-g / IL-4) and very low values of IL-10 regulatory cytokine. Respivax restored the flexibility of the immune system as it modulated the extreme deviations in cytokine levels and potentated Th1 immune responses without over stimulation of the pro inflammatory mechanisms.

We conclude that Respivax treatment restores the inductive function of innate immunity at three key levels: antigen recognition and presentation, co-stimulation of naïve T cells, and Th1/Th2 balance. This results, at least in part, from a differential modulation effect on the expression of different pathogen-recognition receptors (TLRs).