IMMUNOMODULATION, CYTOKINES AND ANTIBIOTICS

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Antimicrobial drugs can interact directly with the immune system of man and animal. A growing evidence can be found in literature that some antimicrobials exert their beneficial effects not only by killing or inhibiting the growth of bacterial pathogens but also indirectly by immunomodulation and by influencing the cytokine production. Aspects of the immune system which are reported to be influenced by chemotherapeutics and antibiotics are: phagocytosis, apoptosis, chemotaxis, lymphocyte proliferation, cytokine expression, antibody formation, hypersensitivity reaction, opsonisation, intracellular killing and PMN penetration.

Several studies in different species were undertaken to quantify and compare the immunomodulatory properties of antimicrobial agents. It is remarkable from the reported results that statements hereby are very diverse and sometimes even controversial for a particular active substance or class of antibiotics.

Concerning phagocytosis, positive effects were seen for cephalosporins, carbapenems, amphotericin B, florfenicol and clindamycin, while negative effects were rather observed for erythromycin, azithromycin, tetracycline, ampicillin and gentamicin.

Lincomycin, clindamycin and imipenem induce chemotaxis, whereas rifampicin and cefotaxime should decrease this cell activity. Regarding lymfocyte proliferation, macrolides would have a strong stimulating effect while tetracyclines have a negative effect. Erythromycin, broad spectrum penicillins and amphotericin B appear to stimulate production of the anti-inflammatory types of cytokines.

Reduction of IL-6 and a clear anti-inflammatory result of tobramycin and ceftazidime could be demonstrated in pigs with endotoxin shock. Endotoxin neutralization has been reported for polymyxin E in the same animal species.

The anti-inflammatory properties of macrolides and triamilides in chronic inflammatory pulmonary disease were several times documented. These group of antimicrobial substances should also establish an adjunctive treatment to β-lactams by their immunomodulatory properties in man.

Bactericidal antibiotics such as rifampicin, clindamycin and aminoglycosides kill pathogens and prevent at the same time that high quantities of pro-inflammatory cell wall components are released.

It has been shown that fluoroquinolones can induce growth factor IL-2 synthesis *in vitro* and at the same time hamper the secretion of pro-inflammatory IL-1β and TNF-α. This potential of immunomodulatory effects of these broad-spectrum antibacterial chemotherapeutics could be of great interest in patients confronted with immunosuppression and chronic inflammatory diseases.

For most antimicrobial agents, however, the number of studies reported seems at the moment to be too scarce to be conclusive for an ultimate interpretation of their effects on cytokine production.

Also the direct immunomodulation effect of antimicrobial agents should be interpreted carefully with regard to possible therapeutic implication.