Effects of Moxifloxacin on Neutrophil Phagocytosis, Burst Production, and Killing as Determined by a Whole-Blood Cytofluorometric Method

Intact function of polymorphonuclear phagocytes (PMN) is the most important component of the nonspecific immune response against invading microorganisms. As the number of immunosuppressed patients requiring antibiotic treatment is increasing, the impact of antibacterials on the nonspecific immune system has become of increasing interest. Investigations of newer quinolones showed that these antibacterials exert heterogenous effects on the immune system (1, 3, 6, 7, 8, 11). Moxifloxacin is a new 8-methoxyquinolone that has potent antimicrobial activity against both gram-negative and gram-positive bacteria and anaerobes (2, 4). The aim of this study was to evaluate the influence of moxifloxacin on PMN function using a whole-blood flow-cytometric method. The assay, which has been described previously (5, 9, 10) is designed to investigate effects on the phagocytosis of *Candida albicans* and *Staphylococcus aureus* (the percentages of phagocytosing PMN were determined), the percentage of PMN producing respiratory burst, and the percentage of *C. albicans* that has been killed by PMN. All three parameters were measured at multiple time points: for phagocytosis and burst, at 0, 2, 4, 6, 8, 10, 15, 20, and 25 min; for killing, at 0, 5, 10, 15, 20, 30, and 40 min.

Blood samples of 12 healthy volunteers were incubated with three different moxifloxacin concentrations (1, 10, and 100 µg/ml) and compared to a drug-free control. Phagocytic capacity was assessed by measuring the uptake of calcin-labeled yeasts or SYTO-9-labeled bacteria. Reactive burst after phagocytosis of yeasts or bacteria was estimated by the amount of dihydroethidium converted to ethidium by PMN intracellularly. Killing of *C. albicans* was analyzed by the specific uptake of ethidium homodimer 1 by nonviable yeasts. Therefore, PMN lysing was necessary to count the killed and liberated yeasts as free, red particles.

The results of investigations with the antibacterial-resistant pathogen *C. albicans* showed that moxifloxacin has no significant influence on PMN functions. Even the high moxifloxacin concentration of 100 µg/ml (maximum concentration in serum after oral administration of 400 mg, 1 to 10 µg/ml) did not lead to an impairment in any functional parameters studied (Fig. 1). In contrast, for the moxifloxacin-susceptible *S. aureus* (MIC at which 90% of the isolates are inhibited, 0.03 µg/ml) a mild dose-dependent decrease in phagocytic capability was detectable. However, respiratory burst remained unaffected. As intact viable intracellular bacteria are a prerequisite for accurate determination of the phagocytosis rate with flow cytometry, it can be suggested that the decreased phagocytosis rate is attributable to the specific interaction between the antibiotic and the bacteria and not a direct moxifloxacin effect on PMN.

Investigating the quinolones ofloxacin, ciprofloxacin, sparfloxacin and temafloxacin, Aoki et al. (1) found that quinolones differ in their immunomodulating effects. For ofloxacin as well as ciprofloxacin they found burst-increasing attributes, but in contrast, burst-decreasing properties were observed for sparfloxacin and temafloxacin. In the present study we demonstrated that moxifloxacin did not affect oxidative burst...
activity. Thus, immunmodulating properties of an individual quinolone do not represent a general class effect.

In summary, this in vitro study indicates that moxifloxacin does not impair phagocytic function with yeasts as test organisms. The results obtained with *S. aureus* showed only a mild reduction in phagocytic capacity with no effect on burst production.

REFERENCES


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