Ecological impact of antibiotic treatment on human normal microflora

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ABSTRACT

The skin and the mucosal surfaces of humans are colonized with microorganisms, which are often referred to as the normal microflora. There is a biological balance between the human host and the normal microflora in health. The extensive use of antibiotics in both humans and animals has caused the development of many resistant bacteria. Administration of antibacterial agents can cause disturbances in the ecological balance between the host and microorganisms.

Cefotiboprole is a new broad-spectrum cephalosporin active against methicillin-resistant Staphylococcus aureus. Twelve healthy volunteers received cefotiboprole. Plasma and fecal samples were collected according to the study design for analysis. Plasma concentrations of cefotiboprole were 14.7–24.5 mg/l. No measurable concentrations of cefotiboprole were found in feces. There were minor to moderate changes in the numbers of enteric bacteria, enterococci, Candida albicans, bifidobacteria, lactobacilli, clostridia and Bacteroides spp. No Clostridium difficile strains and no new colonizing bacteria were found.

Ciprofloxacin is a well-known fluoroquinolone active against Gram-negative and Gram-positive bacteria. Thirty-six healthy female volunteers according to the study design received either the extended release formulation of ciprofloxacin or the immediate release formulation. Mean fecal concentrations were 453 mg/kg and 392 mg/kg, respectively. The numbers of Escherichia coli were significantly suppressed while the enterococci decreased moderately in both treatment groups. No toxigenic C. difficile strains were found.

Telavancin is a new glycopeptide for the treatment of Gram-positive infections. Thirteen healthy volunteers received telavancin. Fecal and urine samples were collected according to the study design. There were no measurable concentrations of telavancin in feces. No significant effects on the number of Enterobacteriaceae, enterococci, C. albicans, bifidobacteria, lactobacilli, clostridia and Bacteroides spp. were observed in the study. No C. difficile strains and no new colorizing Gram-positive bacteria were found.

Thirty-four healthy volunteers were included and received either doxycycline or placebo for 16 weeks. Plasma, saliva and fecal samples were collected according to the study design. The plasma concentrations of doxycycline in the doxycycline group were 0.20–1.49 mg/l. The fecal concentrations of doxycycline in the doxycycline group were 0–4.10 mg/kg. Minor effects on the oropharyngeal microflora were observed in both groups. There were minor changes in the number of enterococci and E. coli in both groups. No C. difficile strains were isolated.

This thesis shows that intravenous administration of antibiotics (cefotiboprole and telavancin) had less impact on the intestinal microflora. Both antibiotics caused minor disturbance on the normal microflora indicating a low risk to develop C. difficile infection. Ciprofloxacin had impact on the microflora regardless of the formulation of the drug. Doxycycline sub-antimicrobial dose had minor effect on the normal microflora and development of resistance.

Keywords: Cefotiboprole, Ciprofloxacin, Telavancin, Doxycycline, Oropharyngeal microflora, Intestinal microflora, Ecological impact, Normal flora, Health, Subantimicrobial dose, Antibiotic resistance.