Microbial Safety of Ceftiofur and its Metabolites: Instability in the Right Places

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Introduction

Ceftiofur is a late-generation, injectable cephalosporin developed solely for veterinary therapeutic use. During the 12 years of field use, surveys suggest that the incidence of veterinary and food-borne pathogens with decreased susceptibility to ceftiofur is still very low. This paper assesses the microbiological safety of ceftiofur with respect to current susceptibility patterns of pathogens, and inherent chemical and biological factors that aid in maintaining its effectiveness.

Materials and Methods

Surveys of ceftiofur minimum inhibitory concentrations (MICs) for target and food-borne pathogens are summarized. Fate and metabolism studies, monitored by HPLC and microbiological cylinder plate assays are summarized.

Results and Conclusions

The incidence of susceptibility to ceftiofur among target respiratory pathogens for cattle has remained at 100% in our surveys. Target pathogens are very sensitive to ceftiofur and its principal metabolite, desfuroylceftiofur. Minimum inhibitory concentration (MIC) values for these organisms have remained 4- to 133-fold lower than the clinical susceptibility breakpoint (MIC value ≤2.0 μg/ml) approved by the National Committee for Clinical Laboratory Standards. Plasma concentrations of active metabolite well exceed the MIC_{100} of target pathogens over the 24-hour dosing interval. Thus, the pharmacokinetic properties of ceftiofur likely work to minimize resistance emergence during the course of therapy. Another important attribute of ceftiofur is its instability upon elimination from the animal. Only inactive metabolites are observed to be excreted in feces of treated cattle. Urinary residues are inactivated readily in bovine excreta incubated aerobically ($T_{1/2}$=6-24 h, n=6). Ceftiofur inactivation also occurs rapidly ($T_{1/2}$=30-120 min, n=11) upon anaerobic incubation in human fecal slurries. Finally, ceftiofur is inactivated via hydrolytic and photolytic mechanisms, and is rapidly transformed and mineralized to carbon dioxide in soils. This instability of ceftiofur upon excretion is a desirable quality for any antibiotic, and may have played a pivotal role in the low- or no-incidence of ceftiofur resistance observed to date among bovine pathogens.