Research and Reviews: Journal of Veterinary Medicine and Allied Science

Extended Abstract
Vol. 3, Iss. 4
2019

Pharmacokinetics study and efficacy evaluation of Ceftriaxone and Tazobactam combination in ESBL E. coli infected diarrhoeic poultry birds

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Abstract :

The infections caused by ESBL strains of E. coli were often related to diarrhea in poultry birds. The present research work was undertaken to study the pharmacokinetic profile of Ceftriaxone and Tazobactam in healthy and ESBL E. Coli infected with diarrheal birds (broiler, Rhode Island red, Haringhata black) after a single intramuscular administration of the combination Ceftriaxone Tazobactam (8: 1) at 28.125 mg kg-1. The efficacy of the Ceftriaxone Tazobactam combination has been evaluated for ESBL-producing E. coli infection in birds (Broiler, Rhode Island Red, Haringhata Black) at a predetermined dosing schedule supported by a pharmacokinetic study. For induction of infection in experimental broiler, Rhode Island Red and Haringhata Black birds, 56 × 108 CFU / ml of the bacterial culture was orally inoculated. Broiler chickens developed severe diarrhea on the 7th day after oral inoculation of 1 ml of E. ESBL-producing coli, while moderate diarrhea occurred in Rhode Island Red birds on the same day. Due to failure of initial challenge, Haringhata Black birds were again inoculated orally with a higher second dose (112Ã—108 CFU/ml sub culture) after 21 days of first oral inoculation. Ultimately, moderate diarrhea was induced in Haringhata Black birds on the 8th day after the 2nd inoculation. A single dose combination of ceftriaxone tazobactam (8: 1) 28.125 mg kg-1 was administered intramuscularly to healthy, diarrheal broilers, Rhode Island Red and Haringhata Black in six groups (Gr BCT & BCT -D, RCT & RCT-D, HCT & HCT-D) each containing six birds and blood samples were taken at predetermined time intervals. Ceftriaxone and Tazobactam concentrations from plasma were analysed by HPLC to evaluate pharmacokinetic profile. Following induction of diarrhea Ceftriaxone-Tazobactam combination was given twice daily (at 12 hours interval) for 3 days at 28.125 mg kg-1 intramuscularly. In diarrheic birds of all the three breeds, Ceftriaxone persisted up to eight hours in presence of Tazobactam and highest plasma concentration was recorded at 0.08 hours. Tazobactam also persisted up to 8 hours while the peak plasma concentration was recorded at 0.25 hour. Longer elimination halflife (tÂ½ Î²: 3.72Â±0.24 hours) associated with higher levels of Tazobactam were evident at 2, 4, 6 and 8 hours in diarrheic Broiler birds in presence of Ceftriaxone. Significantly increased body clearance (ClB: 12.34Â±0.58 L kg-1 h-1) of Ceftriaxone in healthy Haringhata Black birds in presence of Tazobactam compared to a mean ClB value of 10.19Â±0.57 L kg-1 h-1 in diarrhoeic birds was observed. It was also observed that Tazobactam undergoes rapid absorption in diseased Haringhta Black birds (Ka: 18.77Â±1.73 h-1) compared to healthy birds (Ka: 11.91Â±1.39 h-1) in presence of Ceftriaxone. Diarrhea began to subside on 2nd day of treatment in all the birds of three groups and a complete recovery was noticed on 3rd day of treatment.

Pseudomonas aeruginosa is an opportunistic microorganism with the ability to respond to a wide variety of environmental changes, exhibiting a high intrinsic resistance to a number of antimicrobial agents. This low susceptibility to antimicrobial substances is primarily thanks to the low permeability of its outer membrane, efflux mechanisms and therefore the synthesis of enzymes that promote the degradation of those drugs. Cephalosporins, particularty ceftazidime and cefepime are effective against P. aeruginosa, however, its increasing resistance has limited the usage of those antibiotics. Encapsulating antimicrobial drugs into unilamellar liposomes is an approach that has been investigated so as to beat microorganism resistance. In this study, antimicrobial activity of liposomal ceftazidime and cefepime against P. aeruginosa ATCC 27853 and P. aeruginosa SPM-1 was compared thereto of the free drugs. Liposomal characterization included diameter, encapsulation efficiency and stability. Minimum Inhibitory Concentration (MIC) decided for free of charge and liposomal sorts of both drugs. Minimum Bactericidal Concentration (MBC) decided at concentrations 1, 2 and 4 times MIC. Average diameter of liposomes was 131.88 nm and encapsulation efficiency for cefepime and ceftazidime were 2.29% end 5.77%, respectively. Improved stability was obtained when liposome formulations were prepared with a 50% molar ratio for cholesterol in reference to the phospholipid.

Numerous drug interactions with methotrexate have been identified, which can lead to serious life-threatening effects. Up to 90% of methotrexate is excreted unchanged within the urine with primary excretion hooked in to organic anion transport within the renal proximal tubule. The two pathways liable for methotrexate secretion are organic anion transport 1 and primarily organic anion transport 3. Penicillins undergo tubular secretion via organic anion transport, and cephalosporins are believed to also possess an identical risk when administered with methotrexate; however, there are not any human studies observing this interaction with cephalosporins and methotrexate. Ceftriaxone undergoes biliary clearance and has low affinity for an equivalent organic anion transports as methotrexate; therefore, ceftriaxone features a low potential to interact with methotrexate. Cefepime is primarily secreted by organic cation transport N2, and also features a low potential to interact with methotrexate. This case report describes the pharmacokinetic effect of concomitant beta-lactam therapy during a patient receiving high-dose methotrexate.

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This work is partly presented at Veterinary Surgeons and Veterinary Medicine Congress, October 02-04, 2017 Philadelphia, USA