PHARMACOKINETIC/PHARMACODYNAMIC OF MACROLIDES IN AN IN VIVO MODEL OF *CHLAMYDIA PNEUMONIAE'*S PNEUMONIA

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The treatment of acute *Chlamydia pneumoniae* infection with beta-lactamase, macrolides or fluoroquinolones markedly decreased the positive culture of the organisms in lung tissue, but neither DNA nor antigens are been totally eradicated with any of these antimicrobial agents. The PK and PD parameters may be used in the selection of an appropriate dosing regimen in order to provide important information for maximizing bacteriologic and clinical efficacy.
The aim of our work was to evaluate the pharmacokinetic and pharmacodynamic profile of Azithromycin (AZM) and Clarithromycin (CLA) in a *C. pneumoniae* pneumonia model since, in vivo, no data are available on the pharmacodynamics of macrolides against intracellular pathogens.
Methods. BALB/c mice were treated for 3 days with AZM or CLA, 4 days after intranasal inoculation of 1 x 10^6 inclusion-forming units (IFU) of *Chlamydia pneumoniae*, strain CWL029 (ATTC VR-1310). The regimen of AZM and CLA consisted of daily doses ranging from 4 to 200 mg/kg divided into one, two, or four administrations. Twenty-four hours after the last injection, the animals were sacrificed and lungs removed. For each lung, ten slices were taken, two every ten sections. *C. pneumoniae* IFU, evaluated by immunofluorescence assay, were counted in double blind by two independent observers, using a Zeiss Axioplan microscope with a Zeiss Plan-Neofluar 40x ocular.
Results. MICs for Azithromycin and Clarithromycin were 0.25 and 0.031, respectively. PK studies exhibited non-linear response both for AZM and CLA. For Clarithromycin, T>MIC% (R^2 0,8867) correlated better than AUC/MIC ratio (R^2 0,8452). The data obtained with Azithromycin showed that AUC/MIC ratio (R^2 0,8102) correlates with clinical efficacy, while there is no clear relationship between T>MIC% and antimicrobial activity of this azalide.
Conclusion. The data obtained suggest that AUC/MIC was the best predictive PK/PD parameter for Azithromycin while T>MIC% was the best for Clarithromycin even also AUC/MIC correlated with efficacy of treatment. On the basis of our results the best efficacy of AZM will be obtained increasing the daily dose while the best efficacy of CLA will be obtained dividing the daily dose in two or three administrations.