Abstracts

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There was a significant reduction in chest pain after treatment from day 3 onwards which improved by 1.0% by 10th day from baseline.

Post-treatment, dyspnea was significantly reduced by 35.1% by day 3 and 78.1% by day 10. After the treatment, productive cough was significantly reduced to 62.2% by day 3 and 14.4% by day 10. After the treatment, on day 3, 36.8% had mucous sputum and on day 10, 80% had mucous sputum. 84% cases showed complete to marked improvement after treatment on physician's overall assessment. 97% patients showed good resolution of the X-ray findings of the Chest. 15.2% of the total number of patients reported adverse events leading to modification of the treatment. Conclusion: Cefdinir was effective and safe in the treatment of Lower respiratory tract infections.

Clinical Implications: Cefdinir is an important addition to orally active, third generation cephalosporins and especially effective in lower respiratory tract infections.

P2680
Penetration of piperacillin and tazobactam into pneumonic human lung-tissue measured by in-vivo microdialysis
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Objectives: The pharmacokinetic profile of antibiotics at the site of anticellactive is one of the most important determinants of drug response. We studied the clinical feasibility of a new microdialysis-based approach to measure antibiotic penetration into the extracellular space fluid of pneumonic human lung.

Patients and Methods: Lung penetration of Piperacillin/Tazobactam was measured in five patients suffering from pneumonic/severe septicemia. Microdialysis was performed by intubation and microdialysis probes were inserted into pneumonic lung tissue. Serum and microdialysis samples were collected in 20-minute intervals for at least 8 hours.

Results: The mean interstitial concentration profiles of Piperacillin in infected lung tissue as compared to plasma showed a massive tissue concentration (Cmax) of 215.0 ± 41.1 μg/mL and 296.0 ± 15.8 μg/mL, respectively. The AUC (area under the curve)-values of infected lung tissue (684.0 ± 307.0 μg·h·mL−1) compared to plasma (323.0 ± 95.8 μg·mL−1) revealed no significant differences (p > 0.05). Intravascular Wilcoxon matched pairs rank signed test for Piperacillin revealed a significant difference between AUC (muscle) and AUC (plasma) (p = 0.043), and also between the respective higher values obtained from the two probes in each lung and skeletal muscle (p = 0.043).

Conclusion: The first clinical application of peri- and postoperative microdialysis in patients with pneumonia operated on for metapneumonic empyema, enabled continuous tissue pharmacokinetic measurement of free, unbound anti-infective agents in pneumonic lung tissue. The present data corroborate the use of Piperacillin/Tazobactam, but demonstrate a widespread distribution profile of Piperacillin in the interstitial space of pneumonic lung tissue.

P2681
Bronchopulmonary pharmacokinetic (PK) profile of moxifloxacin in older adults undergoing diagnostic bronchoscopy
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Background: Ensuring optimal treatment of lower respiratory tract infections requires adequate drug concentrations at the site of infection. The objective of this study is to characterize the drug penetration of moxifloxacin (MXF) into the extracellular compartment of the lung, as assessed in the epithelial lining fluid (ELF), compared to that of the plasma.

Methods: Eight volunteers, 66 ± 12 years old, scheduled to undergo a diagnostic bronchoscopy, were enrolled in this randomized, open-label, multicenter study. Subjects received five days of MXF (400 mg orally, once daily, with the last dose given at either 4th, 12th or 24th before the scheduled bronchoscopy. At the time of bronchoscopy, plasma and BAL aliquots were obtained and assayed by a validated HPLC procedure to assess drug concentrations in the plasma and the ELF. Results: The mean plasma and ELF concentrations at specified time points were as follows: 4h: plasma 2.9 mg/L, ELF 7.9 mg/L; 12h: plasma 2.1 mg/L, ELF 8.6 mg/L; 24h: plasma 0.9 mg/L, ELF 5.9 mg/L.

Conclusions: The concentration at the site of infection (ELF) well exceeded that of the plasma at every time point studied and exceeded the MIC90 for common community-acquired respiratory pathogens over the entire dosing period.

P2682
Bacterial agents of community-acquired lower respiratory tract infections: observational study on antimicrobial drugs susceptibility
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In recent years, antibiotic resistance has increased alarmingly in several bacterial species that are common causes of community acquired lower respiratory tract infections (CA-LRTIs). The aim of this observational study was to determine the antibiotic resistance of antimicrobial agents isolated from patients with CA-LRTIs. Subjects recruited were day-hospital and hospitalized patients. Overall, 1190 consecutive patients (72.9% male, mean age 58.1 ±16.8 years) with CA-LRTIs were observed during a eight years period (1994-2001). A total of 480 pathogenic microbial strains were isolated and tested for their in vitro susceptibility to six common antimicrobial drugs. Among all isolated, the four most frequent pathogens were Pseudomonas aeruginosa (140 isolates, 29%), Staphylococcus aureus (137 isolates, 30%), Escherichia coli (31 isolates, 7%), and Klebsiella pneumoniae (26 isolates, 6%). The mean susceptibility of Pseudomonas aeruginosa was 60.7% to cefazidime, 64.7% to ciprofloxacin, 25.9% to ceftriaxone, 70.2% to levofloxacin, and 72.6% to piperacillin. The susceptibility of others Gram-negative isolates was 76.3% to cefazidime, 82.6% to ciprofloxacin, 71% to ceftriaxone, 80.5% to levofloxacin, and 80.1% to piperacillin. The susceptibility of Gram-positive isolates was 88% to amoxicillin/clavulanate, 85.5% to ciprofloxacin, 77.8% to ceftriaxone. These trends analysis evidenced a increasing prevalence of Pseudomonas aeruginosa and other gram negative bacteria to all antimicrobial drugs tested (ranged from 16.3% to 36.8%). The lowest resistance rate was reported for piperacillin. We don't reported, instead, a conclusive pattern of increasing resistance for gram positive bacteria. We conclude that an increasing antimicrobial drugs resistance is evident for gram negative bacteria.

P2683
Exposure to sub-lethal levels of penicillin G and high osmotic potential leads to stable antibiotic resistance in Staphylococcus aureus
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Background: Bacteria may lose all or part of their cell walls under certain environmental conditions, including the presence of cell wall-active antibiotics. Cell wall-deficient bacteria (CWDB) are hard to detect by light microscopy or culture, but can proliferate in vivo on specialized media. We investigated whether cell wall-deficiency confers stable resistance to penicillin. Method: Staphylococcus aureus was recultured repeatedly with sub-lethal levels of penicillin G on various media, including one that we found to be optimal for CWDB. Minimum inhibitory concentration (MIC) assays were performed at regular intervals and Gram staining and transmission electron microscopy (TEM) at various stages. After 45 passages on CWDB optimal media, bacteria were recultured 7 times with or without penicillin. MICs were then determined. Results: CWDB were Gram-negative on light microscopy, showed no cell wall and indistinct margins on TEM and different colony morphology. The MIC for penicillin increased following serial passages, particularly on CWDB optimal media (32μg/mL compared with 1 μg/mL on DST medium, after 12 passages). After 7 passages without penicillin the cell wall was regained, but penicillin resistance was maintained. Conclusion: In the presence of sub-lethal levels of antibiotics and media optimal for CWDB, Staphylococcus aureus rapidly develops a high degree of stable penicillin resistance. We propose that loss of the cell wall, though rarely demonstrated in clinical microbiology laboratories, is an important cause of antimicrobial resistance. This could have profound implications for the prescription of cell wall-active antibiotics.

288. Genetics of hyperreactivity and IgE markers for inflammatory airways disease

P2684
Replication study for a locus modulating total serum IgE on chromosome 14q13.24 in families with asthma
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To validate a locus modulating total serum IgE on 14q13.24-32, we performed a linkage and association study between total serum IgE and a panel of seven microsatellites spanning the 14q13.24 region. Using the 14q13.24-32 region with asthma recruited from Leeds, UK. Non-parametric, multipoint, sib-pair analysis showed no evidence of genetic linkage. However, we observed significant association between locus D14S631 (14q23) and total serum IgE (p=3.8x10-3). Allelic analysis showed association of low total IgE with allele 157 of D14S631 (p=0.01, OR=0.63, 95%CI=0.44-0.90). Modelling of allele 157 genotypes as a continuous covariate indicated evidence of a significant inverse linear trend across the three genotypes, where homozygotes of allele 157 (157/157 genotype) demonstrated the lowest mean log IgE (p=0.015).