168 Filgrastim in Non-neutropenic Immunocompromised Patients with Bacterial Infections

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Background: Effectiveness of filgrastim in neutropenic patients is well established. However, its role in non-neutropenic patients isn't clarified. Objective: To evaluate efficacy of Filgrastim (G-CSF) in non-neutropenic immunocompromised patients with severe bacterial infections. Design: Open-label prospective follow-up study has been conducted. Materials and Methods: A total of 27 immunocompromised patients aged 21 – 63 were involved. Among them 13 were HIV infected patients, 8 patients were on cytotoxic treatment and the other 6 were immunocompromised patients with various genesis. All patients had severe bacterial infections or sepsis. Absolute neutrophil count in all patients was more than 1,500/mm^3 on admission. Diagnosis of bacterial infections was made by clinical signs and symptoms and confirmed with laboratory investigations. Patients were divided into the two groups. 14 patients (1st group) were treated with antibacterials and Filgrastim and 13 patients (2nd group) were treated with antibacterials without Filgrastim. Filgrastim was administered subcutaneously 5 micrograms/kg daily for 5 consecutive days. Results: In the 1st group patients Filgrastim significantly reduced the severity and duration of bacterial infections compared to the 2nd group patients. Mortality due to the bacterial complications, duration of antibacterial treatment and hospital days were also less in Filgrastim-treated patients. Type and genesis of immunodefficiency didn't influence the results. Filgrastim was well tolerated in all patients. Conclusions: Filgrastim seems to be effective and safe for the treatment of infections in non-neutropenic immunocompromised patients. It holds promise to decrease infection related morbidity and mortality in immunucompromised patients. Further studies are required to optimize treatment regimen.

169 Safety and Efficacy Comparison of Clarithromycin Extended Release with Trovafloxacin in Community-Acquired Pneumonia

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Background: Community-acquired pneumonia (CAP) is the sixth leading cause of death in the U.S. The objective of this study was to compare the safety and efficacy of clarithromycin extended release (CLA ER) and trovafloxacin (TROVA). *Methods:* The study was a double-blind, randomized, parallel-group, multicenter study in ambulatory patients with CAP who received either CLA ER, 1000 mg QD for 7 days (n=90), or TROVA, 200 mg QD for 7 days (n=86). Efficacy evaluations were done up to Test-of-Cure Visit (Days 14-21). Safety was assessed by clinical laboratory tests, physical examinations, vital signs, and monitoring adverse events. *Results:* There were no statistically significant differences between CLA ER and TROVA groups in the clinical cure rates, bacteriological cure rates, pathogen eradication rates, and radiographic success rates in the clinically and bacteriologically evaluable patients. *Conclusions:* CLA ER was comparable to TROVA in treating patients with CAP. Both treatments were effective in eradicating target pathogens, resolving clinical signs and symptoms of pneumonia, and resolving/improving radiographic evidence of pneumonia. Both the treatments were well tolerated by the patients with CAP.

	Clarithromycin ER	Trovafloxacin
Clinical Cure Rate	89% (42/47)	97% (29/30)
Bacteriological CureRate	89% (42/47)	93% (28/30)
Overall Pathogen Eradication Rate	88% (58/66)	95% (39/41)
Radiographic Success Rate	94% (44/47)	93% (28/30)

170 Community Acquired Pneumonia: Changing Practice Over 5 Years and Role of Levofloxacin.

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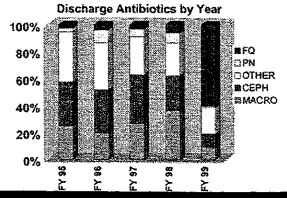
Introduction: We retrospectively collected data for Community Acquired Pneumonia (CAP) patients over a 5-year period and analyzed changes in diagnostics, initial and discharge antibiotic (Abx) choice, days to switch from IV to PO, and length of stay (LOS). Methods: We reviewed medical records of patients (pts) with CAP (DRGs 79/80/89/90) discharged during FY 95-99. Those requiring intubation were excluded. Severity of illness score and risk class were calculated (Fine MJ, NEJM). Results: Of 1095 pts, 300 were excluded because of transfer from other hospitals, recent hospitalization, or immune deficits, leaving 795 pts. Although hospital Case Mix Index increased ($p<0.001$), CAP LOS decreased from 5.1 days in Oct 94 to 3.7 days in Sept 99 ($p=0.004$), without change in mortality or 30-day readmission rate. CAP severity of illness did not increase significantly. The drop in CAP LOS occurred at a faster rate than overall hospital LOS ($p=0.007$). In FY95-98 74% of pts received Ceftriaxone within the first 24 hours, with a macrolide or other Abx added in 19% and 9% of these cases. Prescribing patterns were largely unchanged in this period, although IV to PO switch declined from 3.7 to 3.2 days ($p=0.06$). In FY99 Levofloxacin (Levo) became the dominant initial Abx choice (50% Levo in FY99). Similarly, fluoroquinolone use at discharge increased 14-fold, from 4% to 61%. Use of all other types of discharge Abx dropped 35-87% (Figure). Prescribing patterns for a known etiologic diagnosis also changed—in FY95-98 pts were more likely to be discharged with Penicillin when *S. pneumoniae* was identified (OR=25, $p<0.001$). This changed in FY99 (OR=1.1), when use of generic discharge Abx decreased 85%. In multivariate analysis, severity of illness, initial and discharge Abx choices, and elimination of 24-hr observation after PO switch affected LOS. Time to first Abx had less impact ($p=0.099$). Discussion: LOS decreased from FY95-99 without decline in quality of care, as reflected by stable mortality and 30-day readmission rates. In an environment of increasing pneumococcal resistance, treatment practices changed dramatically in FY99 when Levo became available. This resulted in a more uniform, empiric approach to therapy, with diminishing influence of diagnostic studies.



171 A Randomized Open-label Comparative Trial of Levofloxacin 750 mg Once-daily versus IV Ticarcillin/clavulanate with or without Amoxicillin/clavulanate for the Treatment of Complicated Skin and Skin Structure Infections.

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This study compared the safety and efficacy of levofloxacin 750 mg qd (oral, iv, or iv/oral) (LVX) to ticarcillin/clavulanate (iv) alone or followed by amoxicillin/clavulanate (oral) (TC/AC) for the treatment of complicated bacterial skin and skin structure infections. The 750 mg dose, higher than that usually prescribed for pneumonia or urinary tract infections, has been shown to be safe and to have excellent skin penetration in healthy volunteers. In this multicenter, open-label study, 399 subjects were randomized on a 1:1 basis. Of the clinically evaluable subjects, 116/138 (84.1%) in the LVX group and 106/132 (80.3%) in the TC/AC group were deemed clinical successes (95% CI = -13.3,5.8). Of the 98 microbiologically evaluable subjects in each group, LVX eradicated 84.0% of infections and TC/AC eradicated 71.0% [95% CI = -24.3, -0.2]. For the most common pathogens isolated (*Staphylococcus aureus, Streptococcus agalactiae, Enterococcus faecalis, and Proteus mirabilis*), clinical success rates were 67% to 90% for LVX-treated subjects and 58% to 78% for TC/AC-treated subjects. Among the small number of subjects with pseudomonal infections, clinical success rates for the treatment arms were ~ (6/7 LVX; 6/6 TC/AC). Incidence of adverse events was ~ for LVX and TC/AC, with gastrointestinal adverse events the most common for both groups. Conclusion: Levofloxacin 750 mg qd (oral, iv, or iv/oral) was well tolerated and as effective as iv ticarcillin/clavulanate 3.1 mg q4-6h alone or followed by oral amoxicillin/clavulanate for treatment of complicated skin and skin structure infections.

172 LEVOFLOXACIN IN THE TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA DUE TO PENICILLIN-RESISTANT AND -SUSCEPTIBLE PNEUMOCOCCI AND OTHER PATHOGENS

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Streptococcus pneumoniae remains the most common cause of community-acquired pneumonia (CAP) and is responsible for substantial mortality and morbidity. Widespread concern about drug-resistant pneumococci has prompted clinicians to seek other therapeutic options for CAP. A recent US surveillance study demonstrated penicillin resistance in 35% of *S. pneumoniae* isolates, with high-level resistance in 13% of strains. LEVAQUIN®(levofloxacin)(L) recently received a clinical claim for the treatment of penicillin-resistant *S. pneumoniae* in CAP (penicillin MIC ≥2 μg/ml). The current open-label, non-comparative, multicenter trial was designed to recruit additional patients with infections due to penicillin-resistant *S. pneumoniae*(PRSP). As of April 17, 2000, more than 1800 cases of CAP have been enrolled to the study, including 7 patients with CAP due to high-level PRSP and 24 cases due to strains with intermediate-level penicillin resistance (PISP)(MIC = 0.12-1μg/ml). Data from 1377 patients have been analyzed to date (3 PRSP and 11 PISP evaluable cases are part of this analysis). The overall clinical success rate (including all pathogens (N=219); *S. pneumoniae, S. aureus, H. influenzae, M. catarrhalis, K. pneumoniae,* and *H. parainfluenzae*) was 95% (83% cured, 12% improved). The clinical success rate in patients with *S. pneumoniae*(N=137) was 95% with eradication of the organism in 95% of the cases. All three patients with CAP due to high-level PRSP were clinically cured and the organism eradicated. Similarly, in the 11 patients with CAP due to PISP, all cases were considered clinical successes (7 cured, 4 improved) with all organisms eradicated. Nó isolates were resistant to (L). The most commonly reported treatment-emergent adverse events deemed related to study therapy were nausea (0.7%), rash (0.7%), abdominal pain (0.3%), and diarrhea (0.3%). Although the clinical significance of PRSP remains a subject of debate, this study confirms that L, 500mg once daily, is highly effective against most common respiratory pathogens, including penicillin-resistant strains of *Streptococcus pneumoniae.*

173 Risk factors for infection or colonization by levofloxacin-resistant Streptococcus pneumoniae in Hong Kong

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Background: The rate of levofloxacin-resistant *Streptococcus pneumoniae* (LRSP) was found to increase from <0.5% in 1995 to 5.5% in 1998 in Hong Kong. Objectives: This study aims to identify risk factors associated with the isolation of LRSP. Methods: A case-control study was conducted to identify and quantify potential risk factors associated with LRSP colonization/infection. A case patient was defined as a patient who was admitted to one of the three hospitals during the period of 1 July 1998 to 30 Nov 1999, and then was either clinically infected with/colonized by LRSP. The two consecutive patients that followed each case, with levofloxacin-susceptible *S. pneumoniae* were used as the controls. Results: Twenty-seven cases were found in 3 hospitals A (9), B (12) and C (6). Cases were older (median age; interquantile range in years) than the controls (75; 70-85 versus [vs.] 72.5; 62.3-78.3; P=0.01). Male sex predominated in both groups (24/27 vs. 43/54) and their *S. pneumoniae* were associated with a ~ proportion of syndromes including acute exacerbation of chronic obstructive pulmonary disease, COPD (10/27 vs. 30/54), pneumonia (11/27 vs. 9/54) and colonization (6/27 vs. 15/54). Risk factors (odds ratio [OR]; 95% CI) for LRSP by univariate analysis ($P<0.05$) were living in old age home, OAH (7.2; 2.4-21.6), having COPD (5.9; 2.2-16.3), isolation >2 days after admission (5.7; 2.1-15.6), recent (4.6; 1.7-12.3) and multiple (4.4; 1.6-11.8) hospitalizations, prolonged hospitalization >7days (2.9; 1.1-7.5), and exposures to fluoroquinolone (10.6; 2.8-41.8) and β-lactam (8.6; 1.8-40). Logistic regression model showed that OAH residency (OR 5.5; 95% CI, 1.3-22.9; P=0.02), isolation >2 days after admission (OR 10.9; 95% CI, 2.0-60.2; P=0.006), having COAD (OR 14.8; 95% CI, 2.7-80.2; P=0.002) and exposure to β-lactams (OR 7.2; 95% CI, 1.3-39.0; P=0.02) were risk factors associated with LRSP infection/colonization. Conclusions: Institutionalized COPD patients appear to be an important reservoir of LRSP. Selection of resistant mutant and nosocomial transmission in this group of patients might contribute to the emergence of levofloxacin-resistant among drug-resistant S. pneumoniae in Hong Kong.