

Efficacy of Levofloxacin in Hospital admitted cases of Community Acquired Pneumonia (CAP)

MUHAMMAD AZAM, MUHAMMAD AFTAB, TARIQ SULEMAN, ALI SHUAIB ASHRAF, FARAH SHAFI

ABSTRACT

Objective: To determine the efficacy of Levofloxacin in hospital admitted cases of community acquired pneumonia.

Methods: Three hundred patients of CAP fulfilling the inclusion criteria admitted in medical Unit-1 of Services Hospital over a period of six months were included in this descriptive case series study.

Results: 201 patients out of 300 met the efficacy criteria of Levofloxacin in the treatment of community acquired pneumonia. The clinical success rate was 67%.

Conclusion: It is concluded that Levofloxacin with adequate activity against respiratory pathogens, represents an important and convenient treatment option for patients with community acquired pneumonia in terms of treatment as a monotherapy, cost effectiveness, shorter duration of hospital stay and with less chances of microbial resistance.

Keywords: Community acquired pneumonia, Fluoroquinolones, Levofloxacin.

INTRODUCTION

Pneumonia is defined as an inflammation of the substance of the lungs. It is usually caused by bacteria. Clinically it presents as an acute illness characterized in majority of cases by the presence of cough, purulent sputum and fever together with physical signs or radiological changes compatible with consolidation of the lungs. Pneumonia is typically classified as being either community acquired or hospital acquired (health care associated) pneumonia¹. Community acquired pneumonia is common infectious disease in primary care practice. It is associated with high rates of morbidity and mortality particularly in elderly and immune compromised patients². The most common bacterial pathogen identified in community acquired pneumonia is streptococcus pneumonia, accounting for approximately more than two third of the cases of CAP. Other causative pathogens include, Haemophilus influenzae, Mycoplasma Pneumoniae, Chlamydia pneumoniae, staphylococcus aureus, Neisseria meningitidis Moraxella catarrhalis, klebsiella pneumoniae, other gram negative rods and legionella species^{3,4}. There is no optimal therapy for CAP. Community acquired pneumonia may be treated with monotherapy or combination therapy. Effective monotherapy antibiotics include respiratory quinolones e.g., levofloxacin, doxycyclin or tigeaycline^{5,6,7}. Combination Therapy Usually consists of Ceftriaxone plus doxycyclin, azithromycin or

respiratory quinolone. As a class, the respiratory fluoroquinolones e.g., levofloxacin has a very favourable pharmacokinetic and pharmacodynamic profile. Pharmacodynamic criteria suggest that levofloxacin is more potent against streptococcus pneumoniae. In clinical trials levofloxacin is generally well tolerated and is a first line option for the treatment of hospitalized patients of community acquired pneumoniae^{8,9,10}.

MATERIAL AND METHODS

This descriptive case series study was conducted in medical unit-1 Services Hospital, Lahore. Three hundred patients of community acquired pneumonia were enrolled for study. Sampling technique was non probability purposive sampling. All male and female patients between 18 to 70 years with community acquired pneumonia as per operational definition were included in the study. Based on history and clinical examination all of the following patients were excluded from the study.

- Diagnosed case of neoplastic disease.
- Patients having any clinical or laboratory evidence of liver disease.
- Patients of congestive heart failure
- Patients having cerebrovascular disease.
- Patients suffering from chronic kidney disease.

Three hundred patients meeting the inclusion and exclusion criteria admitted through emergency and outdoor of Services Hospital, Lahore were enrolled for study. Informed consent was taken from the patients. Data collection included patients demographic profile, like name, age, sex and hospital

Department of Medicine, Services Institute of Medical Sciences/Services Hospital, Lahore.

*Correspondence to Dr. Muhammad Azam, Assistant Professor
Email: muhammadazamgojra@gmail.com cell:0333-4226603*

member. The drug levofloxacin in a dose of 500mg daily was given to the patients I/V for 7 days. The patients were followed and assessed daily according to the operational definition. The patients who did not respond to levofloxacin were excluded from the study and managed according to the hospital protocol. All information was collected through a specially designed Performa. All the data was entered and analyzed using SPSS version 10. The quantitative variables like age were presented as mean± SD. The qualitative variables like gender and efficacy were presented as frequency and percentages. Data was stratified for age to address effect modifier

RESULTS

Three hundred patients of community acquired pneumonia fulfilling the inclusion criteria were selected for this trial. In this study majority of the patients 64(21.3%) were between 41-50 years of age. Age distribution of rest of the patients is shown in table (I). Mean age was 3.81 and standard deviation 1.594. Out of 300 patients 177 (59%) were males and 123(40%) were females (Table 2) Out of 300 cases 132(44%) patients had fever between 99 to 100° F, 99(33%) had fever between 101 to 102° F and 69 (23%) had fever between 103 and 104° F. Out of 300 patients 273(91.0%) patients presented with productive cough and 27(9%) patients presented with dry cough. Out of the 300 admitted patients 184 (61.3%) had respiratory rate between 36-38 breaths per minute, 23(7.7%) had respiratory between 33-35 per minute, 82(27.3%) had respiratory rate between 30-32 breaths per minute and 11(3.7%) had respiratory rate greater than 38 breaths per minute. Thirty (10%) patients had bronchial breathing on clinical examination of the chest.

At day 7, 254 out of 300 patients (84.7%) had fever equal or less than 99°F. Out of 254, 201 patients (79.2%) met the efficacy criteria of levofloxacin (Table 3,6).

At day 7, 277 out of 300 patients (92.3%) had dry cough including 27 patients who had dry cough at day 1. So 250 patients had change from productive to dry cough. Out of these 250 patients 201(80.4%) patients met the efficacy criteria of levofloxacin (Table 4,7). At day 7, 203 patients out of 300 (67.7%) had respiratory rate equal or less than 25 breaths per minute. Out of these 201 (67%) patients met the efficacy criteria of the drug. (Table 5,8).

Table 1: Association of community acquired pneumonia by age

| Age Group | No. of Cases | Percentage |
|-----------|--------------|------------|
| 18-20 | 29 | 9.7 |
| 21-30 | 46 | 15.3 |
| 31-40 | 47 | 15.7 |
| 41-50 | 64 | 21.3 |
| 51-60 | 59 | 19.7 |
| 61-70 | 55 | 18.3 |
| Total | 300 | 100.0 |

Mean age: 3.81

Standard deviation: 1.594

Table 2: Association of community acquired pneumonia by gender

| Gender | No. of Cases | Percentage |
|--------|--------------|------------|
| Male | 177 | 59.0 |
| Female | 123 | 41.0 |
| Total | 300 | 100.0 |

Table 3: Distribution of cases by efficacy of Levofloxacin in community acquired pneumonia setting of fever less than 99°F at day 7

| Fever | No. of Cases | Percentage |
|--------|--------------|------------|
| ≤99° F | 254 | 84.7 |
| >99° F | 46 | 15.3 |
| Total | 300 | 100.0 |

Table 4: Settling of cough from productive to dry at day 7

| Cough | No. of Cases | Percentage |
|------------|--------------|------------|
| Dry | 277 | 92.3 |
| Productive | 23 | 7.7 |
| Total | 300 | 100.0 |

Table 5: Decrease in respiratory rate less than 25 breaths per minute at day 7

| Respiratory Rate in breaths per min | No. of Cases | Percentage |
|-------------------------------------|--------------|------------|
| ≤ 25 | 203 | 67.7 |
| > 25 | 97 | 32.3 |
| Total | 300 | 100.0 |

Table 6: Distribution of cases by efficacy *setting of fever less than 99° F

| Efficacy | Setting of fever less than 99°F | | Total |
|--------------|---------------------------------|--------|-------|
| | ≤ 99°F | > 99°F | |
| Efficacy Yes | 201 | 0 | 201 |
| No | 53 | 46 | 99 |
| Total | 254 | 46 | 300 |

Pearson CHI-square = 1.103

P-value=0.000 (Significant)

Table 7: Efficacy * settling of cough from productive to dry

| Efficacy | Setting of Cough From Productive to Dry | | Total |
|----------|---|------------|-------|
| | Dry | Productive | |
| Yes | 201 | 0 | 201 |
| No | 76 | 23 | 99 |
| Total | 277 | 23 | 300 |

Pearson chi-square = 50.574 P-value=0.000(SIGNIFICANT)

Table 8: Efficacy*decrease in respiratory rate less than 25 breaths per minute

| Efficacy | Decrease in Respiratory Rate less than 25 breaths per minute | | Total |
|----------|--|------|-------|
| | ≤ 25 | > 25 | |
| Yes | 201 | 0 | 201 |
| No | 02 | 97 | 99 |
| Total | 203 | 99 | 300 |

Pearson chi-square = 3.000 P-value = 0.000 (significant)

Table 9: Distribution of cases by efficacy of levofloxacin

| Efficacy | No. of Cases | Percentage |
|----------|--------------|------------|
| Yes | 201 | 67.3 |
| No | 99 | 33.0 |
| Total | 300 | 100.0 |

Over all 201 (67%) patients out of 300 met the efficacy criteria of the drug levofloxacin in the treatment of patients with community acquired pneumonia. Remaining 99(33%) patients did not meet the efficacy criteria of the drug (Table 9)

DISCUSSION

Community acquired pneumonia is one of the leading causes of morbidity and mortality in adult population^{11, 12}. The incidence is high and it is more severe in elderly and immunocompromised patients¹³. Initial antimicrobial treatment for patients with community acquired pneumonia should provide appropriate coverage against the most common causative organisms including resistant strains¹⁴.

Levofloxacin has the advantage of being able to cover gram-positive pathogens, including penicillin-resistant streptococcus pneumoniae, gram-negative and atypical pathogens with a single agent, generally given once a day^{15,16,17}.

This study was carried out to measure the efficacy of levofloxacin in hospital admitted cases of community acquired pneumonia in terms of decrease in respiratory rate to less than 25 breath per minute, settling of cough from productive to dry and settling of fever to less than 99° F.

Patients were given 500mg of levofloxacin intravenously daily. Patients were followed up and assessed daily for improvement in temperature, respiratory rate and cough for the efficacy levofloxacin. At day7 after levofloxacin administration,

84.7% had fever equal or less than 99° F and out of these 79.2% met the efficacy criteria of levofloxacin. 91.6% of the patients had dry cough at day 7 and 80.4% met the efficacy criteria of levofloxacin. At day7, 67.7% patients had respiratory rate equal or less than 25 breaths per minute and 67% met the efficacy criteria of levofloxacin.

According to the results of the study 201 out of 300 patients met the efficacy criteria of levofloxacin in hospital admitted cases of community acquired pneumonia. The clinical response rate was 67%. Several studies mentioned below have evaluated the efficacy of levofloxacin in community acquired pneumonia. These studies have advocated that the levofloxacin monotherapy is equal or more effective than combination regimens in clinical and microbiological responses.

In a study conducted by Linty et al, efficacy of 500 mg daily of levofloxacin was compared with the efficacy of combination of Amoxicillin/ clavulanate (500mg/100mg) thrice a day and clarithromycin 500mg twice daily. In this randomized, open label study, the clinical response rate of levofloxacin was 69.2% and hospital stay 7.4±3.1 days¹¹.

Van Ransburg DJ et al conducted a study on efficacy and safety of nemoxacin versus levofloxacin for community acquired pneumonia. The clinical cure rate assessed by settling of fever for levofloxacin was 91.1%¹².

In a retrospective study conducted by Ye X et al in outdoor patients with community acquired pneumonia, rates of treatment failure were assessed with levofloxacin as compared with macrolides. Rates of treatment failure with levofloxacin was 21-1% which was significantly lower than with macrolides¹³. In a study conducted by Hurst M et al the clinical response rate with levofloxacin in community acquired pneumonia was between 86 to 95%¹⁴.

The efficacy of levofloxacin in CAP was also assessed by Bru JP et al, in 5 large clinical trials. Success rate with levofloxacin ranged from 70.6% to 84.2%. In proved cases of pneumococcal pneumonia success rate with levofloxacin was 67%¹⁵.

In another study conducted by shorr et al eradication rates in microbiologically evaluable population were 87.5% with levofloxacin¹⁶.

Most of the above mentioned studies showed cure rate with levofloxacin ranging from 69 to 91%. Where as the cure rate in our study was 67% after 7 days of treatment. There could be few reasons for this difference in results. Some of the patients developed respiratory failure because of severe nature of pneumonia. Mechanical ventilation is required in such patients and in our setup this option is not easily available.

Other reason for lower success rate in our study was late presentation of the patients in the hospital resulting in severe forms of pneumonia.

There was also a possibility of drug resistance in our set up because of the injudicious use of the drugs prior to this disease. Another reason could be lack of easily available serological tests and polymerase chain reaction required for the detection of atypical pneumonial organisms.

CONCLUSION

It is concluded from this study that treatment of patients of community acquired pneumonia with levofloxacin, as a monotherapy, is associated with better clinical out come, improved patient survival, lower mortality rate, lower treatment failure rate, low total hospital cost for patients admitted to the hospital. Levofloxacin is well tolerated, represents an important and convenient treatment option for patients with community acquired pneumonia. Thus, levofloxacin is a valuable antimicrobial agent that has activity against a wide range of bacterial pathogens. However, its use should be considered with caution so that the Potential resistance can be minimized and its usefulness in community acquired pneumonia and against a range of penicillin and macrolide resistant pathogens can be maintained.

REFERENCES

1. Kumar P, Clark M. Respiratory disease. In: Clinical medicine, a textbook for medical students and doctors.6th ed. London: W.B.Saunders 2005;873-956.
2. Gutierrez F, Masia M, Rodriguez JC, Mirete C, Soldan B, Padallis S, et al. The influence of age and gender on the population-based incidence of community acquired pneumonia caused by different microbial pathogens. *J Infect* 2006;53:166-74.
3. Chesnutt MS, Murray JA, Prendergast TJ. Pulmonary disorders. In: Tierney LM, Mcphee SJ, Papadakis MA, editors. Current medical diagnosis and treatment.45th ed. New York: Mcgraw-Hill medical publishing Division2008;203-279.
4. Butt T, Rafi N, Ahmad RN, Salman M, Mirza SH. Community acquired bacterial pneumonias in Rawalpindi. *Pak J Pathol* 2005;16(1)14-16.
5. Boselli E, Breilh D, Rimmelé T, Djabarouti S, Saux MC, Chassard D, et al. Pharmacokinetics and intrapulmonary diffusion of levofloxacin in critically ill patients with severe community acquired pneumonia. *Crit Care Med*. Jan 2005;33(1):104-9.
6. Chokshi R, Restrepo MI, Weeratunge N, Frei CR, Anzueto A, Mortensen EM, et al. Monotherapy versus combination antibiotic therapy for patients with bacteremic *Streptococcus pneumoniae* community-acquired pneumonia. *Eur J Clin Microbiol Infect Dis*. Jul 2007;26(7):447-51.
7. Mokabberi R, Haftbaradaran A, Ravakhah K. Doxycycline vs. levofloxacin in the treatment of community-acquired pneumonia. *J Clin Pharm Ther*. Apr 2010;35(2):195-200.
8. Dunbar LM, Khashab MM, Kahn JB, Zadeikis N, Xiang JX, Tennenberg AM, et al. Efficacy of 750-mg,5 day levofloxacin in the treatment of community acquired pneumonia caused by atypical pathogens. *Curr Med Res Opin* 2004;20:555-63.
9. Hurst M, Lamb HM, Scott LJ, Figgitt DP. Levofloxacin: an updated review of its use in the treatment of bacterial infections. *Drugs* 2002;63:2127-67.
10. Fish DN, Chow AT. The clinical pharmacokinetics of levofloxacin. *Clin Pharmacokinet* 1997;32:101-19.
11. Lin TY, Lin SM, Chen HC, Wang CJ, Wang YM, Chang ML, et al. An open label, randomized comparison of levofloxacin and amoxicillin/clavulanate plus clarithromycin for the treatment of hospitalized patients with community acquired pneumonia. *Chang Gung Med J*. 2007 Jul-Aug;30(4):321-32.
12. Van Rensburg DJ, Perng RP, Mitha IH, Bester AJ, Kasumba J, Wu RG, et al. Efficacy and safety of nemonoxacin versus levofloxacin for community-acquired pneumonia. *Antimicrob Agents Chemother*. 2010Oct;54(10):4098-106.
13. Ye X, Sikirica V, Schein JR, Grant R, Zarotsky V, Doshi D, et al. Treatment failure rates and health care utilization and costs among patients with community-acquired pneumonia treated with levofloxacin or macrolides in an outpatient setting: a retrospective claims database analysis. *Clin Ther*. 2008 Feb;30(2):358-71.
14. Hurst M, Lamb HM, Scott LJ, Figgitt DP. Levofloxacin: an updated review of its use in the treatment of bacterial infections. *Drugs*. 2002;62(14):2127-67.
15. Bru JP. Update on the role of levofloxacin in the management of acute community acquired pneumonia. *Presse Med*. 2002 Jun 15;31(21 Pt 2):S19-22.
16. Hurst M, Lamb HM, Scott LJ, Figgitt DP. Levofloxacin: an updated review of its use in the treatment of bacterial infections. *Drugs* 2002; 63:2127-67
17. Fish DN, Chow AT. The clinical pharmacokinetics of levofloxacin. *Clin Pharmacokinet* 1997;32:101-19.