

Effectiveness of Levofloxacin in Community Acquired Pneumonia in Adult Bangladeshi Population

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Abstract

Community-acquired pneumonia (CAP) is a common condition with a significant mortality. Levofloxacin is recommended for the empiric management of CAP in inpatient and outpatients. The present study conducted to find out the effectiveness of Levofloxacin in CAP among Bangladeshi Population. Total 50 Patients aged more than 18 years, diagnosed pneumonia based upon clinical features of respiratory tract infection and radiological changes, were included in this study. The study consists of four visits: first one for screening and enrollment. Second visit on day 2-4 during which patient on therapy, third visit 5-7 day after the last dose of the drug and fourth visit 28 days after the last dose of the drug. The mean # SD of age of the respondents was 34.3# 19.1 years with a range of 18-100 years. Among the respondents 62.0% were male and 38.0% were female. Most of the respondents presented with fever (98.0%) and cough (100.0%) and chest pain was present in 66.0% cases. Ninety six percent respondents presented with productive cough and only 4.0% respondents with dry cough. Consolidation in left lower zone was the most common findings (32.0%) followed by consolidation in right mild zone (30.0%). Among the respondents 32.0% were treated with oral form and 68.0% were treated with injectable form of levofloxacin. About 92.0% were improved with the treatment. Levofloxacin monotherapy is well tolerated, cost-effective treatment for patients with CAP. Further large scale multi-centered study will help to strengthen this outcome.

Keywords: Community-acquired pneumonia (CAP); Levofloxacin.

Introduction

Community-acquired pneumonia (CAP) is defined as signs and symptoms of an acute infection of the pulmonary parenchyma in a previously healthy patient who acquired the infection in the community^{1,2}. The diagnosis of CAP is based primarily on clinical factors: a combination of signs and symptoms such as cough, fever, chills, sputum production, dyspnea, pleuritic pain, tachypnea, tachycardia, hypoxemia, features of consolidation on auscultation, and a new infiltrate on chest imaging³. CAP is a common and potentially serious illness with considerable morbidity worldwide and places a large burden on medical and economic resources^{4,6}. It is the leading cause of death in the world and remains a common and serious illness despite the availability of potent new anti-microbials and effective vaccines^{7,8}. The mortality rate of pneumonia patients in out-patient settings is low, in the range of one to five per cent, but among patients who require admission to ICU it approaches 25%⁹⁻¹². Despite the availability of effective antimicrobial agents, CAP remains a significant cause of morbidity and mortality worldwide, especially among elderly individuals and individuals with coexisting disease^{8,13}. Today, physicians must choose an optimal therapeutic regimen that eradicates the respiratory infection effectively, minimizes the risk of development of resistance, and does not compromise the safety of the patient⁶. Treatment of patients with CAP is often empiric. Any agent selected for empirical therapy should have good activity against pathogens associated with CAP, a favorable tolerability profile and be administered in a simple dosage regimen for good compliance⁴. Strategies for the empirical treatment of CAP are complicated by shifting etiologies and the emergence of drug-resistant pathogens¹⁴. Streptococcus pneumonia has been identified as the commonest organism causing CAP all over the world^{6,8,14-20}. But some studies, over the last three decades, have reported of increased incidence of pneumonia due to "atypical" and gram-negative organisms^{10,14,19,21-24}. Previously effective therapy for CAP has traditionally been accomplished with B-lactam antibiotics, macrolides, trimethoprim/ sulfamethoxazole and tetracyclins. However, increasing antibiotic resistance has been observed for several common pathogens in CAP including *S. pneumonia*, *H. influenza*, *M. Catarrhalis*, *S. aureus* and gram negative bacteria¹⁰. Increased prevalence of drug-resistant strains remains a primary

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concern in the treatment of CAP⁶. The respiratory fluoroquinolones have gained a reputation as a highly effective and well-tolerated option for the first-line treatment of CAP^{6-8,25}. Levofloxacin is a fluoroquinolone antibacterial agent with a broad spectrum of activity against Gram-positive and Gram-negative bacteria and atypical respiratory pathogens. It is active against both penicillin-susceptible and penicillin-resistant *Streptococcus pneumoniae* and recommended for the empiric management of CAP in inpatients and outpatients^{7,8,25-27}. Some studies showed that in the treatment of CAP Levofloxacin alone is comparable to or better than combination therapy like injectable 3rd generation Cephalosporin plus Macrolides⁵. Levofloxacin was effective in treating patients infected with *S. pneumoniae* that was nonsusceptible (intermediately resistant or resistant) to Penicillin⁶. Levofloxacin was also a beneficial treatment for CAP from a pharmacoeconomic perspective^{7,8,28}. Several published articles provide data from clinical trials measuring the efficacy and safety of levofloxacin used in the treatment of CAP and CAP-related infections⁶. So far we know there are limited data about efficacy of levofloxacin in the treatment of CAP in Bangladeshi population. The present study conducted to find out the effectiveness of Levofloxacin in CAP among Bangladeshi population.

Materials and Methods

This prospective observational study was conducted from February to November in 2010 at Uttara Adhunik Medical College Hospital. The study consists of four visits: first one for screening and enrollment, other 3 visits for assessment of safety and effectiveness. Second visit on day 2-4 during which patient on therapy, third visit 5-7 days after the last dose of the drug that is post therapy visit and fourth visit 28 days after the last dose of the drug that is post study follow-up. Approximately 6 weeks needed to complete the study. Total 50 patients aged more than 18 years, diagnosed pneumonia based upon clinical signs and symptoms of lower respiratory tract infection including at least 2 of fever, cough, greenish-yellow sputum, chest pain, shortness of breath, or evidence of decreased lung function during the physical examination, has a chest x-ray findings consistent with acute pneumonia, previously received antibiotics for pneumonia if the duration of therapy was <24 hours were included in the study. Patients having allergic or serious adverse reaction to any antibiotic similar to those used in this study or to penicillin, collection of pus in the cavity between the lung and the membrane that surrounds it, cystic fibrosis, severe kidney failure, decreased in white blood cell count, seizure disorder or any unstable psychiatric condition were excluded from this study. Those fulfilled the diagnostic criteria were enrolled in the study and treated with oral Levofloxacin 750mg once daily for 10 days or injectable Levofloxacin 500mg once daily for same duration. Data were collected by face to face interview with a

predesigned questionnaire. Data were analysed with statistical software and presented in frequency and percentage in tabulated form.

Results

The mean \pm SD of age the respondents was 34.32 \pm 19.12 with a range of 18-100. Among the respondents 31 (62.0%) were male and 19(38.0%) were female. The male and female ratio was 1.63:1. Among the respondents 13(26.0%) were in the age group of less than 20 years, 15(30.0%) were in the age group of 21-30 years, 5(10.0%) were in the age group of 31-40 years, 7(14.0%) were in the age group of 41-50 years and rest 10 (20.0%) were in the age group of more than 50 years. Among the respondents 3 (6.0%) were diabetic and 10(20.0%) were hypertensive. Most of the respondents presented with fever (98.0%) and cough (100.0%) and chest pain was present in 66.0% cases. 48 (96.0%) respondents presented with productive cough and rest 2 (4.0%) respondents presented with productive with dry cough (table I).

Table- I: Distribution of characteristics of the respondents

Variables	Frequency	Percentage
Age group		
20	13	26.0
21-30	15	30.0
31-40	05	10.0
41-50	07	14.0
>50	10	20.0
Mean \pm SD	34.32 \pm	19.12 (18-100)
Sex		
Male	31	62.0
Female	19	38.0
Male : Female		1.63:1
Co morbid condition		
DM	03	06.0
HTN	05	10.0
Clinical features		
Fever	49	98.0
Chest pain	33	66.0
Cough		
Dry	02	04.0
Productive	48	96.0

Mean \pm SD of total counts of WBC was 15.13 \pm 6.71 per cmm. Mean \pm SD of differential counts of neutrophils, lymphocytes eosinophils and monocytes were 78.00 \pm 10.46, 15.50 \pm 8.53, 2.50 \pm 1.60 and 3.26 \pm 1.24 respectively. Mean \pm SD of ESR was 58.58 \pm 29.97 in first hour with a range of 9.00-125.00 in first hour (table II).

Table- II: Distribution of the clinical Laboratory findings of the respondents (n=50)

Laboratory findings	Mean \pm SD	Range
TC	15.13 \pm 6.71	4.10-31.70
Platelet count	223.14 \pm 42.77	100.00-320.00
ESR	58.58 \pm 29.97	9.00-125.00
Neutrophils	78.00 \pm 10.46	45.00-92.00
Lymphocytes	15.50 \pm 8.53	5.00-50.00
Eosinophils	2.50 \pm 1.60	1.00-9.00
Monocytes	3.26 \pm 1.24	1.00-600

Consolidation in left lower zone was the most common findings in left lower zone was the most common findings (32.0%) followed by Consolidation in right mild zone (30.0%). Other findings were consolidation in right lower zone, consolidation in left mild zone and consolidation in right upper zone were 20.0%, 08.0% and 6.0% respectively (table III).

Table- III: Distribution of the findings of the chest X ray of the respondents (n=50)

ChestXrayP/Avie	Frequency	Percent
Consolidation in Rt Mild zone	15	30.0
Consolidation in Lt lower zone	16	32.0
Consolidation in Rt Penililas	01	02.0
Consolidation in Rt Lower zone	10	20.0
Consolidation in Lt Mild zone	04	08.0
Consolidation in Rt Upper zone	03	06.0
Consolidation in Lt Upper zone	01	02.0
Total	50	100.0

Among the respondents 16 (32.0%) were treated with oral form and 34 (68.0%) were treated with injectable form the levofloxacin (table IV).

Table- IV: Distribution of study population according to form of medicine taken (n= 50)

Form of medicine taken	Frequency	Percent
Oral	16	32.0
Injection	34	68.0
Total	50	100.0

Among the 50 respondents 46 (92.0%) were improved with the treatment and rest 4 (8.0%) were not improved with the treatment (table V).

Table- V: Distribution of the respondents according to the response of the treatment (n=50)

Clinical features	Frequency	Percent
Improved	46	92.0
Not- improved	04	8.0
Total	50	100.0

Discussion

In the present study the mean \pm SD of age of the respondents was 34.3 \pm 19.1 years and 31(62.0%) were male and 19(38.0%) were female. The male and female ratio was 1.63:1. Advanced age has become a well-recognized risk factor for death in patients with pneumonia. It may also be associated with reduced symptom reporting, raising the possibility that diagnosis and treatment may be delayed in older patients²⁹. Marrie *et al.* (1996) in their study consisted of 149 Patients found a mean age (\pm SD) of 41 \pm 15 years and 36.0% of whom were men¹⁰. Kahn *et al.* (2004) retrospective reviewed 661 Levofloxacin-treated patients with pneumococcal CAP in 9 studies and found the mean age of patients was 53.4 years. Approximately one - third of patients were > 65 years old in their study¹³. Patients with CAP often present with cough, fever, chills, fatigue, dyspnea, rigors, and pleuritic chest pain. Depending on the pathogen, a patient's cough may be persistent and dry, or it may be productive^{20,30}. The sputum is usually yellowish or greenish in colour, Sometimes containing flecks of blood²⁰. In the present study most of the respondents presented with fever (98.0%) and cough (100.0 %) and chest pain was present in 66.0% cases. Ninety six percent respondents presented with productive cough and rest only 4.0% respondents presented with dry cough. Metlay *et al.* (1997) in a study showed that respiratory and nonrespiratory symptoms are less commonly reported by older patients with pneumonia²⁹. Mean \pm SD of total counts of WBC was 15.13 \pm 6.71 per cmm. Mean \pm SD of differential counts of neutrophils, lymphocytes eosinophils and monocytes were 78.00 \pm 10.46, 15.50 \pm 8.53, 2.50 \pm 1.60 and 3.26 \pm 1.24 respectively. Mean \pm SD of ESR was 58.58 \pm 29.97 in first hour with a range of 9.00-125.00. Melbye *et al.* (1992) in a study showed that those with radiological evidence of pneumonia had a higher mean

white blood cell count (WBC)³¹. But a WBC of ≥ 10.4 was not helpful in predicting radiologically defined pneumonia unless symptoms had been present for seven days or more. In CAP due to *Streptococcus pneumoniae*, the commonest organism, leukocytosis is common and early in the disease, chest X-ray findings may be normal, but later, they may show classic lobar pneumonia²⁰. Chest radiography (posteroanterior and lateral views) has been shown to be a critical component in diagnosing pneumonia. According to the latest American Thoracic Society (ATS) guidelines for the diagnosis and treatment of adults with CAP, "all patients with suspected CAP should have a chest radiograph to establish the diagnosis and identify complications (Pleural effusion, multilobar disease)." Chest radiography may reveal a lobar consolidation, which is common in typical pneumonia; or it could show bilateral, more diffuse infiltrates commonly seen in atypical pneumonia. However, chest radiography performed early in the course of the disease could be negative³⁰. In the present study consolidation in left lower zone was the most common findings (32.0%) followed by consolidation in right mild zone (30.0%) Other findings were consolidation in right lower zone, consolidation in left mild zone and consolidation in right upper zone were 20.0%, 08.0% and 6.0% respectively. Broad-based, national surveillance studies have demonstrated that clinical isolates of *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* in the United States continue to be highly susceptible to levofloxacin (>99% of isolates)³²⁻³⁴. Many clinical trials support the effective and safe use of levofloxacin for the treatment of CAP and CAP-associated infection⁶. In the present study 32.0% were treated with oral form and 68.0% were treated with injectable form the levofloxacin. About 92.0% were improved with the treatment. Kahn *et al.* (2004) in their retrospective review of 661 levofloxacin-treated patients showed that the overall clinical success rates for patients with CAP due to penicillin-resistant or macrolide-resistant *S. pneumoniae* were 94.7% (18 of 19 patients) and 96.9% (31 of 32 patients), respectively¹³. Dunbar *et al.* (2003) in their study showed that the majority (99%) of pathogens identified at study entry were fully susceptible to levofloxacin *in vitro*¹⁴.

Levofloxacin monotherapy is well tolerated, cost-effective treatment for patients with CAP. Further large scale multi-centered study will help to strengthen this outcome.

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