

# EVALUATION OF THE EFFICACY OF SEQUENTIAL INTRAVENOUS-ORAL ADMINISTRATION OF PEFLOXACIN IN COMMUNITY-ACQUIRED LOWER RESPIRATORY TRACT INFECTIONS IN PATIENTS WITH UNDERLYING CONDITIONS

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## ABSTRACT

*We studied the efficacy of sequential intravenous-oral pefloxacin therapy in community-acquired lower respiratory tract infection in 24 patients with one or more underlying conditions. Twenty-eight patients were enrolled into the study but only 24 patients were evaluated. There were 16 males and 8 females with a mean age of 66.9±11.2 years (mean±SD, range 46 to 87 years). The underlying conditions present were bronchiectasis, chronic obstructive lung disease and diabetes mellitus. Patients who were older than 70 years but without any underlying condition were also enrolled. All received 4 days of intravenous pefloxacin 400 mg twice a day followed by oral pefloxacin 400 mg twice a day for another 10 days. Assessment of success was based on clinical, microbiological and radiological improvement. Pefloxacin produced 79.2% clinical cure rate. Another 8.3% showed improvement. Pefloxacin was well tolerated. There were few adverse effects and none of the patients required a change of antibiotic. Pefloxacin was an effective and well tolerated treatment for respiratory tract infection and had the advantage of broad in-vitro antibacterial activity, twice daily dosing and sequential availability in an intravenous and oral formulation.*

*Keywords: community-acquired pneumonia, underlying conditions, pefloxacin*

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## INTRODUCTION

The introduction of fluoroquinolone represents a major advance in the development of antibiotics as it allows effective oral therapy of serious infection caused by a wide range of bacteria<sup>(1-3)</sup>. The pharmacokinetic behaviour of fluoroquinolone is impressive. The long half life allows easy administration, twice a day. Its gastrointestinal absorption is high. In the case of pefloxacin, oral bioavailability reaches almost 100% and this allows oral pefloxacin as a cost effective replacement for parenteral antibiotics<sup>(4)</sup>. Penetration of most tissues is excellent and this contributes to the success of eradicating difficult to treat infections.

A number of studies have shown the efficacy and safety of pefloxacin in serious bacterial respiratory tract infection<sup>(5,6)</sup>. In this study, we report the results of the efficacy of pefloxacin in community-acquired lower respiratory tract infection in patients

with one or more underlying conditions.

## PATIENTS AND METHOD

We studied patients who were admitted into the Departments of Respiratory Medicine and General Medicine between April 1992 to October 1992 for community-acquired pneumonia. Bacterial lower respiratory tract infection is presumed if patients had symptoms of cough, fever, pleurisy or sputum production and had compatible clinical signs of a temperature greater than 38°C, consolidation, effusion or crepitations. In addition, investigations should show opacities in their chest roentgenogram and raised total white blood cell count greater than  $10 \times 10^9/L$ .

Patients with symptoms and signs of lower respiratory tract infection were enrolled into the study if they had one or more of the following underlying conditions: chronic obstructive lung disease, alcoholism, diabetes mellitus, bronchiectasis, chronic renal failure, malignancy, or those on oral steroid therapy ( $\geq 10$  mg/day). Patients who were older than 70 years but without any underlying condition were also enrolled. They were excluded if they were under 18 years of age, pregnant, breastfeeding, allergic to quinolones, terminally ill, G6PD deficient, had any central nervous system diseases, liver failure or neutropenia. All patients gave informed oral consent.

## Antibiotic administration

Pefloxacin was administered in a sequential intravenous-oral manner. The patients received intravenous pefloxacin 400 mg twice a day for 4 days. They were then assessed on the fifth day for clinical response and continued on oral pefloxacin 400 mg twice a day for another 10 days if clinical assessment showed improvement.

## Clinical monitoring

Chest X-ray films and total white cell counts with its differentials were monitored before, on day 5 of, at the end of and 14 days after therapy. Sputum was sent for gram staining. Sputum and

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blood cultures were performed before therapy and repeated if they showed bacterial growth. Susceptibility of pathogen to pefloxacin was not performed. All patients were monitored daily for adverse drug reaction; and a daily record of the physical examination and of fever, cough and sputum production was maintained.

#### Evaluation of antibiotic therapy

A clinical cure was defined as achievement of afebrile for at least 72 hours, resolution of all clinical signs and symptoms, including disappearance of the purulent sputum and major improvement of the X-ray. The patient was considered improved if he became afebrile with amelioration of respiratory signs and symptoms without complete cure but not requiring the prescription of another antibiotic during the follow-up period. Clinical failure was defined as a lack of clinical response or worsening of the bronchopulmonary infection. A relapse was considered to be present if there was recurrence of clinical signs and symptoms during the follow-up period.

#### RESULTS

Twenty-eight patients were enrolled into the study and of these, only 24 were evaluated. Four were not evaluated for the following reasons: defaulted follow-up (2), died of acute myocardial infarction (1), and confirmed pulmonary tuberculosis (1). There were 16 men and 8 women with a mean age of 66.9±11.2 years (mean±SD, range 46 to 87 years). Fourteen patients had one underlying disease, while nine had two underlying diseases. The remaining patient had 3 medical conditions (Table I). Chronic obstructive lung disease and bronchiectasis were common (Table II). One-third of the patients were above 70 years of age. Three of these did not have any underlying medical condition. Thirteen patients had less than one day of other antibiotics before they were started on the pefloxacin study.

**Table I - Characteristics of patients**

Patients enrolled:	28
Patients evaluated:	24
Age (years) mean±SD:	66.9±11.2
range:	46-87
Sex:	16M, 8F
Number of underlying conditions:	
one	14
two	9
three	1

**Table II - Underlying conditions in patients treated with pefloxacin**

	No. of Patients
Bronchiectasis	10
Chronic obstructive lung disease	9
Diabetes mellitus	6

#### Clinical response

A clinical cure was achieved in 19 of the 24 patients (79.2%), while 2 patients (8.3%) showed improvement but did not require another antibiotic during the follow-up period.

Three patients did not respond to pefloxacin (12.5%). The first patient was an 82-year-old male whose chest X-ray film showed deterioration after 4 days of intravenous pefloxacin. The antibiotic was changed to amoxicillin/clavulanate and he responded. The second patient was a 82-year-old female with a right lower lobe pneumonia. The infective changes in her chest

X-ray increased on the fifth day. The pneumonia cleared with ampicillin/sulbactam. The last patient was a 65-year-old female with underlying bronchiectasis. She remained febrile after one week of pefloxacin. Fever subsided with erythromycin. None of the patients had relapsed during the follow-up period.

All patients with successful response became afebrile within 4 days of treatment. Half of the patients stopped coughing by the fifth day. The same number had either decreased sputum production with an improvement in colour of their sputum or stopped producing sputum within the same period.

#### Bacteriological response

Sputum gram staining was performed in only 7 patients. Sputum cultures from these patients did not grow any organism. *Klebsiella* species were cultured in the sputum of 2 patients, one with clinical cure and the other one with failure requiring a change of antibiotic. All repeat sputum cultures were cleared of *Klebsiella* subsequently. All blood cultures performed did not show any bacterial growth.

#### Radiological response

There were 12 cases of single lobe pneumonia. The remaining had either multiple lobes or bilateral lung involvement. Radiological clearing were seen in 13 patients by the end of the therapy. The rest of the successfully treated patients had radiological clearing during the follow-up period.

#### Adverse effects

Pefloxacin was well tolerated by all patients except for 5 (20.8%). The side effects encountered were nausea with resultant loss of appetite (12.5%) and giddiness (8.3%). None of the patients required a change of antibiotic. Nine patients with chronic obstructive pulmonary diseases and who were also on oral theophylline did not develop any side effect. Hence theophylline level was not done.

#### DISCUSSION

Our data revealed parenteral followed by oral pefloxacin 400 mg twice a day to be effective and safe for community-acquired pneumonia in patients with one or more underlying diseases. Overall, 87.5% of patients showed cure or improvement of acute infective episodes. The good clinical outcomes were confirmed by clinical, microbiological and radiological improvements. The results obtained were comparable to other studies<sup>(7-11)</sup>.

Studies have shown that 98% of gram-negative bacilli and 73% of gram-positive cocci were sensitive to 2 or less mg/l of pefloxacin<sup>(1)</sup>. The exceptions were anaerobic (minimum inhibitory concentration [MIC]: 2-64 mg/l) and streptococcal organisms, in particular *Streptococcus pneumoniae* (MIC: 4-16 mg/l)<sup>(2,3)</sup>. *Streptococcus pneumoniae* is a common pathogen found in community-acquired pneumonia, even in those with underlying medical conditions; however we found that the high *in-vitro* MIC did not interfere with the action of the drug *in vivo*. The reason for this may be related to the unique property of pefloxacin in penetrating tissue compartments<sup>(11-20)</sup>. The fluoroquinolones penetrate well into bronchial lining and achieve high concentration in the lung, bronchial mucosa and sputum.

Oral pefloxacin with its excellent bioavailability, good tissue penetration and minimal side effects, will play a major role in the treatment of various respiratory tract infections. We had found it useful in the treatment of pneumonia in patients with chronic obstructive lung disease and bronchiectasis. *Haemophilus influenzae*, *Branhamella catarrhalis* and other gram negative bacteria are more important in these groups of patients. These bacteria have a low *in-vitro* MIC to pefloxacin. Atypical community-acquired pneumonia caused by *Legionella*

*pneumophila* is also susceptible to pefloxacin. It is useful in treating respiratory tract infection in the elderly patients as they are often due to gram-negative and staphylococcal organisms<sup>(10)</sup>. The increased incidence of gram negative pneumonia in the elderly is probably related to more frequent use of antibiotics, pre-existing chronic disease, crowded institutional care, silent aspiration, ageing immune and physical lung defences. Due to its predominantly extra-renal elimination, the pharmacokinetics of this drug are unchanged in patients with renal insufficiency; thus no dosage adjustment is usually recommended in elderly subjects who often resemble patients with slight to moderate renal impairment. Pefloxacin can be used in the diabetics and alcoholics who have a higher propensity for developing gram-negative chest infections than the general population.

It is known that fluoroquinolone may impair hepatic theophylline metabolism and therefore an increased blood level of theophylline may cause some side effects such as nausea and vomiting. Pefloxacin may increase the level by 30% but in this trial, none of those on oral theophylline had any side effect. Hence the level was not checked.

Our study demonstrated the effectiveness and potential cost savings of this sequential regime and we would also recommend oral pefloxacin in treating community-acquired pneumonia in this group of patients on an outpatient basis if appropriate.

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