ORIGINAL ARTICLE

Intravenous Followed by Oral Ofloxacin in the Treatment of Community Acquired Lower Respiratory Tract Infections in Adults Requiring Hospitalisation

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Summary

Forty patients were treated with ofloxacin for community acquired lower respiratory tract infections. Eighteen pathogens were isolated in sputum; *Streptococcus pneumoniae* (4) and *Haemophilus influenzae* (4) were the most common, followed by *Klebsiella pneumoniae* (3), *Klebsiella spp.* (2), *Staphylococcus aureus* (2), *Pseudomonas spp.* (2), and *Pseudomonas aeruginosa* (1). Ofloxacin 200 mg every 12 hours was administered for an average of 3.7 days intravenously followed by 5.4 days orally. Response to therapy was judged to be cure in 38 (95%; 95% C.I., 85% - 95%) patients, failure in one (2.5%) and "indeterminate" in one (2.5%).

Key Words: Lower respiratory tract infections, Ofloxacin, Switch therapy

Introduction

Patients with community acquired lower respiratory tract infections (LRTIs) can often be treated by "switch therapy", in which parenteral administration of an antibiotic is prescribed for the early period of treatment, followed by an oral antibiotic after the patient has begun to show clinical improvement and is able to tolerate oral medications[1,2]. Ofloxacin is a fluoroquinolone antibiotic with broad spectrum *in vitro* activity against respiratory pathogens which include Gram-positive aerobic cocci, Gram-negative aerobic bacteria and organisms causing atypical pneumonia such as *Mycoplasma pneumoniae, Legionella spp.* and *Chlamydia pneumoniae*[3,4]. The bioavailability of oral ofloxacin is equivalent to that of the intravenous (IV) formulation which allows conversion from IV to oral administration of the drug while maintaining equivalent potency[4]. This study was conducted to assess the efficacy and tolerability of IV followed by oral ofloxacin in the treatment of LRTIs in patients aged 18 years and above requiring hospitalisation.

Materials and Methods

This was an open and non-comparative study conducted in the University of Malaya Medical Centre and the Institute of Respiratory Medicine, Kuala Lumpur Hospital from August 1997 to May 1998. Baseline evaluations consisting of physical examination, chest radiography, sputum culture, two blood cultures obtained one hour apart, full blood count and blood biochemistry were performed on admission before the commencement of ofloxacin. Bacteria isolated were tested for susceptibility to ofloxacin using the disk

diffusion method. Serological testing for infection by *Mycoplasma pneumoniae* but not *Chlamydia pneumoniae* and *Legionella* was routinely performed.

The dose of ofloxacin was 200 mg given by slow IV infusion over 30 minutes every 12 hours followed by 200 mg orally every 12 hours, for a combined duration of up to 14 days. The clinical criteria for IV to oral switch included (i) subsidence of fever for at least 8 hours, (ii) improvement of cough and respiratory distress, and (iii) no abnormal gastrointestinal absorption. Laboratory parameters at baseline and at the end of ofloxacin therapy were compared using paired Student's *t* test.

Results

Forty patients consisting of 22 males and 18 females were treated with ofloxacin for community acquired LRTIs. The clinical profile of the patients and their underlying diseases are shown in Table I. Bacteria were isolated in the sputum specimens of only 18 patients (Tables II and III). These included *Streptococcus pneumoniae* from four patients (all sensitive to ofloxacin), *Haemophilus influenzae* from four (all sensitive to ofloxacin), *Klebsiella pneumoniae* from three (2 isolates sensitive to ofloxacin, one resistant to ofloxacin), *Klebsiella spp.* from two (all sensitive to ofloxacin), *Staphylococcus aureus* from two (all sensitive to ofloxacin), *Pseudomonas spp.* from two (all sensitive to ofloxacin), and *Pseudomonas aeruginosa* from one patient (sensitive to ofloxacin). No pathogen was isolated in any of the blood samples taken. Serology for *Mycoplasma pneumoniae* was positive in one patient with pneumonia in whom no pathogen was isolated from the sputum.

Table I
Clinical Profile of Patients

Number of Patients	40
Age (year)	
Mean (S.D.)	56.7 (17.8)
Range	18 - 91
	Number of Patients
Type of lower respiratory tract infection	
Pneumonia	32
Acute infectious exacerbation of chronic obstructive pulmonary disease	7
Bronchiectasis with superimposed bacterial infection	1
Underlying disease	
Chronic obstructive pulmonary disease	13
Bronchiectasis	5
Diabetes mellitus	5
Chronic asthma	4
Ischaemic heart disease	2
Congestive heart failure	1
Old pulmonary tuberculosis	1
None	9

Ofloxacin 200mg every 12 hours was administered for an average of 3.7 (±1.3) days (range, 2 - 7 days) intravenously followed by 5.4 (±2.0) days (range, 3 - 11.5 days) orally. The mean duration of ofloxacin therapy was 9.0 (±2.2) days (range, 5 - 14 days). Response to ofloxacin therapy was judged to be cure in 38 (95%; 95% C.I., 85% - 100%) patients and failure in one (2.5%). One patient whose sputum did not grow any pathogen improved with 6 doses of IV ofloxacin and was switched to the oral formulation and discharged following which he defaulted follow-up. His response to treatment could not be assessed and was classified as "indeterminate". The patient who failed to respond to 9 doses of IV ofloxacin had diabetes mellitus and his sputum grew *Klebsiella pneumoniae* which was resistant to ofloxacin. He responded to a combination of cefuroxime and gentamicin.

Treatment with ofloxacin was well tolerated by all the patients. None of the patients experienced any hypersensitivity rash, dizziness, light-headedness, nausea, headache, vomiting, diarrhoea, abdominal pain, injection site inflammation, or significant changes in serum creatinine or transaminases. The white blood cell count [mean (±S.D.)] decreased from 13.1 (±4.3) x 10^9/L to 9.0 x 10^9/L=4.0 (95% C.I.; 2.7, 5.4) x 10^9/L ($P<0.001$) at the end of ofloxacin therapy.

Discussion

The results of this study show that switch therapy with IV followed by oral ofloxacin given at the same dose was very effective and well tolerated by patients with community acquired LRTIs requiring hospitalisation who have no associated risk factors for increased

Table II
Distribution of Bacterial Isolates According to Type of Lower Respiratory Tract Infection

Organism	Pneumonia	Acute Infective Bronchitis	Bronchiectasis with Superimposed Bacterial Infection	Total
Streptococcus pneumoniae	3	1	0	4
Haemophilus influenzae	3	0	1	4
Klebsiella pneumoniae	3	0	0	3
Klebsiella spp.	2	0	0	2
Staphylococcus aureus	2	0	0	2
Pseudomonas spp.	2	0	0	2
Pseudomonas aeruginosa	1	0	0	1
None	16	6	0	22
Total	32	7	1	40

Table III
Distribution of Bacterial Isolates According to Underlying Disease

Organism	Underling Disease								
	COPD	Bronchiect-asis	Diabetes Mellitus	Chronic Asthma	Ischaemic Heart Disease	Congestive Heart Failure	Old Pulmonary TB	None	Total
Streptococcus pneumoniae	1	0	0	0	0	0	0	3	4
Haemophilus influenzae	3	1	0	0	0	0	0	0	4
Klebsiella pneumoniae	0	1	1	0	0	0	0	1	3
Klebsiella spp.	1	1	0	0	0	0	0	0	2
Staphylococcus aureus	0	0	1	0	0	0	1	0	2
Pseudomonas spp.	1	0	0	0	1	0	0	0	2
Pseudomonas aeruginosa	0	1	0	0	0	0	0	0	1
None	7	1	3	4	1	1	0	5	22
Total	13	5	5	4	2	1	1	9	40

morbidity and mortality. On the average, the patients could be safely switched from IV to oral ofloxacin therapy after the third or fourth hospital day and probably would not have benefited from continued hospitalisation after the fourth hospital day. The economic benefits of switch therapy by replacing IV antibiotics with effective oral antibiotics include lower acquisition and administration costs of oral antibiotics as well as shortened hospitalisation[1,2]. Potential problems associated with maintaining an IV line such as local cellulitis, abscess formation, septic thrombophlebitis, line sepsis and endocarditis are avoided[2].

Streptococcus pneumoniae and *Haemophilus influenzae* were the two most frequent bacterial isolates in our patients with community acquired LRTI. COPD was the most common underlying disease in our patients. In keeping with published data, the organisms isolated in our patients with underlying COPD included *Haemophilus influenzae, Streptococcus pneumoniae, Klebsiella spp.*, and *Pseudomonas spp*[5]. However, the microbiology of sputum specimens is often difficult to interpret especially when Gram-negative bacilli are isolated.

In conclusion, switch therapy with IV followed by oral ofloxacin given at the same dose is very effective in the treatment of community acquired LRTIs. For non-bacteraemic LRTI patients it is possible to convert from IV to oral ofloxacin by day 3 or 4 of treatment and the patient can be discharged from the hospital. The economic benefits of switch therapy make ofloxacin an attractive alternative for the treatment of LRTIs and if infection by an atypical pathogen is a likely possibility. However, it is not absolutely necessary to switch from the parenteral to the oral formulation of the same antibiotic or even the same class of antibiotic.

References

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