

Original Article



Comparison of Efficacy of Moxifloxacin and Ceftriaxone in Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Author's Contribution

^{1,2,5}Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work, Final approval of the version to be published.³Drafting the work or revising it critically for important intellectual content, ⁶data collection, manuscript writing

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ABSTRACT

Objective: To compare the efficacy of Moxifloxacin and Ceftriaxone in acute exacerbation of chronic obstructive pulmonary disease.

Methodology: This randomized trial was conducted in the Pulmonology Department, PIMS, Islamabad, between August 2018 and February 2019. Patients were screened from the OPD department, and before randomization, their sputum was collected over 24 hours in a solid, sterile plastic (60 mL) bottle at room temperature. They were randomized equally into two treatment groups using a lottery method. Group A received Moxifloxacin 400 mg orally once daily for five days, and group B received Ceftriaxone 1 g (IV infusion) once daily for five days. All the measurements (dyspnea grading, sputum volume, and character) were taken after five days of antibiotic therapy.

Results: The mean age was 60.79 ± 13.34 years in Moxifloxacin and 59.86 ± 12.72 years in the Ceftriaxone group. In Moxifloxacin group, there were 49(68.06%) male and 23(31.94%) females and in the Ceftriaxone group, there were 49(68%) males and 23(31.94%) female cases. In Moxifloxacin, a total of 68(94.4%) cases recovered, while 4 (5.6%) cases did not achieve efficacy, whereas, in the Ceftriaxone group, 54 (75.0%) cases achieved efficacy and 18 (25.0%) were therapy failures. The efficacy of the oral Moxifloxacin group was significantly better than the oral Ceftriaxone group (p-value, < 0.05).

Conclusion: The efficacy of Moxifloxacin was better than Ceftriaxone in acute exacerbation of chronic obstructive pulmonary disease.

Keywords: Acute exacerbation, chronic obstructive pulmonary disease, Moxifloxacin, Ceftriaxone, efficacy, complications.

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Introduction

Acute exacerbations of chronic bronchitis (AECB), which include lung disease (AECOPD), are a significant health burden for patients, resulting in decreased lung function, increased morbidity and mortality, & long-term quality of life damage. Moxifloxacin is a 4th generation fluoroquinolone with broad activity against microorganisms isolated from AECB, including Gram-positive and Gram-negative bacteria, unusual pathogens, and bacteria.

Individuals afflicted with chronic obstructive pulmonary disease (COPD) are susceptible to infective exacerbations, clinically characterized by increased dyspnea, augmented

cough, and sputum production, prompting affected individuals to seek medical intervention.¹ The management of these exacerbations can take place in either outpatient or inpatient settings, contingent upon the severity of the infectious exacerbation or the seriousness of an underlying condition. In most cases, outpatient care suffices. The goals of COPD exacerbation treatment are to minimize the impact of the current exacerbation while also preventing the development of subsequent exacerbations.²

More than 80% of exacerbations can be treated ambulatorily with antibiotics.³ The use of antimicrobial drugs in COPD exacerbations is based on placebo-controlled studies and retrospective observational studies that discovered that antibiotics enhance clinical outcomes

in many COPD exacerbations.³⁻⁵ Based on these studies, most clinical practice guidelines recommend antibiotic treatment for moderate to severe infective exacerbations. The optimal antibiotic regimen for treating exacerbations of COPD has not been determined,⁶ *Pseudomonas aeruginosa* and *Enterobacteriaceae* can occur in patients with advanced COPD.⁷ Minov J. and colleagues conducted a comparison of eight antibiotics utilized for outpatient management of COPD exacerbations. The effectiveness of doxycycline ranged from 69.8 percent to 80.9 percent, comparable to the success achieved with Moxifloxacin. Regarding the time required for symptom relief, Moxifloxacin exhibited a range from 5.6 days to 6.30 days, while this extended slightly to 6.30 days when using Amoxicillin/clavulonic acid. Notably, relapses were observed within the initial 20 days among group treated with Doxycycline, Azithromycin, and Ciprofloxacin.⁸

Chuchalin A, et al. assessed the efficacy of Moxifloxacin dose (once daily, 400 mg) in patients with acute exacerbations of COPD. They found that symptom improvement was reported after an average of 3.40 ± 1.40 days or after 5.0 days, 93.21% of patients stated improvement in the cardinal symptoms.⁹ In another study, Sankar V, et al compared the efficacy of 1.0 gm Ceftriaxone IV infusion BD & oral 500.0 mg levofloxacin OD for 5.0 days depending on clinical parameters in patients with acute exacerbations of COPD. They found that ceftriaxone was significantly more in efficacy compared to levofloxacin. Ceftriaxone's efficacy was 76.5%, with a treatment failure rate of 23.5%.¹⁰

Acute infective exacerbation in COPD patients can differ in severity and may require hospitalization, but most mild to moderate exacerbations can be managed in primary care settings. The present study is designed to compare two different antibiotic regimens in our population to treat moderate to severe exacerbations in admitted patients. This can help the physicians identify the best antibiotic regimen in our population, which can subsequently be offered to those patients to reduce the severity of the current exacerbation and prevent the growth of future exacerbations.

Methodology

This randomized controlled trial was conducted in the Department of Pulmonology, PIMS, Islamabad, from August 2018 to February 2019. The Institutional Review Board approved the study, and written informed consent was obtained from all patients. The sample size of 144 patients was included in both groups, with 72 cases in each

group with a 95% level of confidence and 5% margin error and an anticipated population proportion 1 (Moxifloxacin=93.2%) and anticipated population proportion 2 (Ceftriaxone=76.5%).

Patients present with the age of 35 to 80 years and cases with COPD with an acute infective exacerbation in any of the following three cardinal symptoms: 1: Dyspnea increases (shall be diagnosed through history) 2: Sputum production increases in volume. 3: Sputum character changes (which shall be diagnosed through history) were included in the study.

Those patients who received recent antibiotic treatment (30 days previous) and had other lower tract infections like pneumonia and TB were detected clinically. Patients who require concomitant antibiotics with a range of activity comparable to that of the study drugs, pregnant and lactating women, and known psychiatric illnesses were excluded from the study.

All patients underwent a thorough history, clinical examination, and spirometry on the presentation day. Dyspnea severity was assessed as per Borg's score. Sputum shall be collected over 24 hours by all the patients before randomization in a strong, sterile plastic (60.0 mL) bottle at room temperature. Patients were instructed to empty the contents of their mouths before they expectorated to ensure that there was minimal contamination by saliva. The 24.0-h sputum volume and character shall be graded as the questionnaire depicts. All the patients were randomized equally into two treatment groups by lottery method. Group A was given Moxifloxacin 400 mg once daily orally for five days and group B was given Ceftriaxone 1 g (IV infusion) once daily for five days. All the patients were followed up after 5 days. All the measurements (dyspnea grading, sputum volume, and character) were taken after 5 days of antibiotic therapy in each group, and efficacy was determined per the operational definition. The researcher entered all the data in predesigned performa, attached as Annexure-IV.

Data was entered in SPSS 21. Age, dyspnoea score, sputum volume, and character score were presented as mean & SD. Categorical data such as gender, smoking, history, and efficacy treatment were presented as frequencies & percentages. The treatment efficacy was compared in both groups by applying the chi-square test and a *P*-value < 0.05 was considered significant.

Results

The study included 144 patients in two groups. Group A (Moxifloxacin) were 49 males (68.1%) and 23 females (31.9%), while Group B (Ceftriaxone) were 47 males (65.2%) and 25 females (34.8%). The average age was 60.79 ± 13.34 years for Group A and 59.86 ± 12.72 years for Group B. (Table I)

Table I: Distribution of Age and Gender. (n=72)

	Group A (Moxifloxacin)	Group B (Ceftriaxone)
Age (years)		
Mean \pm SD	60.7 \pm 13.3	59.8 \pm 12.7
Gender		
Male	49 (68.1%)	47 (65.2%)
Female	23 (31.9%)	25 (34.8%)

Table II: Comparison of Dyspnea (Borg Score), Sputum Volume score, and character Score between two groups. (n=72)

	Group A (Moxifloxacin)	Group B (Ceftriaxone)	p-value
Mean \pm SD			
Dyspnea (Borg Score)	7.54 \pm 1.70	7.57 \pm 1.65	0.69
Sputum Volume Score	4.44 \pm 1.14	4.57 \pm 1.07	0.31
Sputum Character Score	5.94 \pm 1.41	6.01 \pm 1.43	0.29

In Table II, the Dyspnoea scores were 7.54 ± 1.70 and 7.57 ± 1.65 in the Moxifloxacin and Ceftriaxone groups, respectively. The pre-treatment sputum volume scores were 4.44 ± 1.14 and 4.57 ± 1.07 in the Moxifloxacin and Ceftriaxone groups, respectively. The given table compared Dyspnoea (Borg Score), Sputum Volume score, and character Score between the two groups (n=72).

In Moxifloxacin, 68(94.4%) cases had efficacy, and 4(5.6%) cases did not. In the Ceftriaxone group, a total of 54(75%) cases had efficacy, and 18(25%) patients did not have efficacy; the frequency of effectiveness was

statistically higher in Moxifloxacin group as compared to Ceftriaxone group, p-value < 0.05. (Table III)

In the age group of 35-55 years, in Moxifloxacin a total of 28(100%) cases had efficacy. In the Ceftriaxone group, a total of 26(83.9%) cases had efficacy, the frequency of efficacy was statistically higher in Moxifloxacin group as compared to Ceftriaxone group, p-value < 0.05. In the age group of 56-80 years of age group in Moxifloxacin, a total of 40(90.9%) cases had efficacy. In the Ceftriaxone group, a total of 28(68.3%) cases had efficacy, the frequency of efficacy was statistically higher in Moxifloxacin group as compared to Ceftriaxone group, p-value < 0.05. Gender and smoking had efficacy in both groups as shown in Table IV.

Table III: Comparison of efficacy between study groups. (n=72)

		Study groups		p-value
		Moxifloxacin	Ceftriaxone	
Efficacy	Yes	68 (94.4%)	54 (75.0%)	0.001
	No	4 (5.6%)	18 (25%)	

Discussion

This study highlights that oral moxifloxacin is better than oral ceftriaxone in the treatment of patients with acute exacerbation of COPD. The rational use of antibiotics has always been a grave concern in treating various infectious diseases.¹¹ Antimicrobials are widely used and their role and selection in treating COPD exacerbations have been debated. Antimicrobials are provided to most COPD patients with acute exacerbations; however, their efficacy has been questioned. Though antimicrobials benefit moderate to severe COPD exacerbations, there is significant debate on which antimicrobials to use, particularly for initial empirical therapy.¹²

Because most exacerbations are treated without acquiring sputum bacteriology, such initial empirical choices for antibiotic usage in exacerbations usually become the only

Table IV: Comparison of Efficacy in both study groups. (n=72)

		Study Groups		p-value
		Moxifloxacin	Ceftriaxone	
Age	35-55	Yes	28(100%)	0.026
		No	0 (0.0%)	
	56-80	Yes	40(90.9%)	0.009
		No	4(9.1%)	
Gender	Male	Yes	46(83.9%)	0.861
		No	3(6.1%)	
	Female	Yes	22(95.7%)	0.020
		No	1(4.3%)	
Smoking	Yes	Yes	26(92.9%)	0.042
		No	2(7.1%)	
	No	Yes	42(95.5%)	0.013
		No	2(4.5%)	

option. The findings of antimicrobial comparative trials should help to guide recommendations about proper empirical antibiotic research in exacerbations. Even though many such trials have been done, most show that antimicrobial choice does not affect clinical outcomes.¹³

Most antibiotic clinical studies were conducted for regulatory approval and were planned to show comparability instead of differences among antibiotics. While antibiotics are more effective than placebo in treating acute COPD exacerbations, more research is needed to compare different antibiotic classes in particular clinical situations.¹⁴ Clinical efficacy must be examined more rigorously in studies based on a classification method (Anthonisen criteria) that can help choose patients most likely to benefit from an antibiotic.¹⁵

Ceftriaxone was chosen based on clinical resolution experience in the area. Levofloxacin was selected as studies have demonstrated that fluoroquinolones' in vitro microbiological advantage translates to increase in vivo effectiveness. It also achieves significant drug concentrations in the lungs. Short-course drug therapy (5 days) was used instead of traditional therapy (7 days) because it enhanced compliance, reduced expense and waste, had fewer adverse effects, and reduced the risk of antimicrobial resistance. In CB and COPD, five-day levofloxacin is equally effective as ten-day levofloxacin.¹⁶ Five-day cephalosporin medication is similarly effective in individuals with different respiratory tract infections as ten-day therapy.¹⁷

In the current study, in Moxifloxacin a total of 68(94.4%) cases had efficacy and 4(5.6%) cases did not. In the Ceftriaxone group a total of 54(75%) cases had efficacy and 18(25%) cases did not have efficacy, the frequency of efficacy was statistically higher in Moxifloxacin group as compared to Ceftriaxone group, with p-value < 0.05. Chuchalin A, et al assessed the efficacy of Moxifloxacin dose (once daily 400 mg) in patients with acute exacerbations of COPD. They found that symptom improvement was described after an average of 3.39 ± 1.39 days and after five days, 93.1% of patients stated improvement in the cardinal symptoms.⁹

Sankar V, et al. examined the efficacy of 1 gm Ceftriaxone IV infusion BD & oral 500 mg levofloxacin OD for five days in patients with acute COPD exacerbations using clinical parameters. They found that Ceftriaxone was significantly beneficial in efficacy compared to levofloxacin. Ceftriaxone's efficacy was 76.5%, with a

treatment failure rate of 23.5%.¹⁰ We also found that Ceftriaxone was more effective.

Another study examined Moxifloxacin efficacy & safety in acute exacerbations of chronic bronchitis or disruptive pulmonary disease. Clinical success at early follow-up was the primary outcome. The result stated that eleven randomized controlled studies were considered. In an intention-to-treat analysis, there has been no difference in treatment success between moxifloxacin and comparator drugs (ITT) [OR =1.1], clinically evaluable (CE) (OR=1.130) patients, or general adverse effects (OR=1.0). As a result, Moxifloxacin was shown to be clinically & bacteriologically comparable to antibiotic schedules commonly used in patients with AECB & AECOPD.¹⁸

Likewise, in another study of patients with acute COPD exacerbations, a recent retrospective trial was conducted to evaluate the efficacy of oral moxifloxacin therapy over other IV antibiotics. Group A received moxifloxacin 400 mg/day from the start, whereas group B received various IV antibiotics first and later the comparable oral medication. There were no significant variations in the gender, age, or comorbidity distributions among the 287 patients in the trial (120 in group A & 167 in group B). As a result, the researchers concluded that ab initio oral moxifloxacin is a useful alternative in managing COPD exacerbations requiring admission to a short-stay emergency outpatient clinic.¹⁹

Conclusion

The efficacy of Moxifloxacin was better than Ceftriaxone in patients with acute exacerbation of chronic obstructive pulmonary disease. The efficacy of Moxifloxacin is even proven in all age groups and smokers, too. So, in the future, the clinical and therapeutic efficacy of Moxifloxacin can be utilized to treat patients' acute exacerbation of chronic obstructive pulmonary disease.

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