Scholars Academic Journal of Pharmacy (SAJP)
Abbreviated Key Title: Sch. Acad. J. Pharm.
©Scholars Academic and Scientific Publisher
A Unit of Scholars Academic and Scientific Society, India
www.saspublisher.com

ISSN 2347-9531 (Print)
ISSN 2320-4206 (Online)

Medicine

Levofloxacin versus Co-Amoxiclav in the Management of Acute Exacerbation of Chronic Bronchitis

Alaa Ryalat*
Pharmacist the Royal Medical Services, Jordan

Original Research Article

***Corresponding author**
Alaa Ryalat

Article History
Received: 10.04.2018
Accepted: 23.04.2018
Published:30.06.2018

DOI:
10.21276/sajp.2018.7.6.6

Abstract: Chronic bronchitis is a relatively common infection among patients suffering from chronic obstructive pulmonary disease (COPD). Usual management includes pulmonary hygiene, bronchodilators, and antimicrobial therapy. This study will be conducted to compare the efficacy of Levofloxacin and Co-Amoxiclav in the management of chronic bronchitis among ambulatory patients with COPD in King Hussein Medical Centre (KHMC) at the Royal Medical Services (RMS) in Jordan/Amman. A prospective observational study will be performed on patients each in Levofloxacin and Co-Amoxilav group, who are receiving treatment for chronic bronchitis. Demographic and clinical data will be taken from the patients' medical records. The clinical success rates were superior in 89.3% of patients in the Levofloxacin group versus 61.8% of those in the Co-Amoxiclav group. The pulmonary function test (PFT) significantly increased in Levofloxacin study group compared with Co-Amoxiclav group (P value 0.033). A 7-day course of levofloxacin was convenient with once daily dose, and found to be therapeutically superior to Co-Amoxiclav in terms of clinical effectiveness for the treatment of AECB patients.

Keywords: COPD, sputum, Levofloxacin, Co-Amoxiclav, Chronic bronchitis.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is expected to be the third most common reason of death and fifth most common reason of disability worldwide by 2020. COPD is an overarching diagnosis that brings together a range of clinical syndromes linked with airflow restriction and damage of the lung parenchyma [1].

COPD is associated with a number of co-morbidities, e.g. Ischemic Heart Disease (IHD), Hypertension (HTN), diabetes Mellitus (DM), Congestive Heart Failure (CHF) and Malignancy, proposing that it may be fragment of a generalized systemic inflammatory process [2]. Patients with COPD handle severely respiratory infections, which are frequently the precipitating reason of acute exacerbations of the disease. Nevertheless, it is less obvious whether infection is accountable for the progressive airflow limitation that make distinctive of disabling COPD [3]. Acute exacerbations of COPD (AECB) are defined as a deteriorating of COPD symptoms generally characterized by decline in forced expiratory volume (FEV_1), increases in cough with sputum, purulence, and dyspnea. Recent epidemiological data from the literature show that AECB is the most common cause of morbidity and mortality in COPD patient. AECB is associated with recurrent calls to physicians, and increase in the number of hospitalizations [4]. The most common detected bacteria in sputum include *H. influenzae, Haemophilus parainfluenzae, S. pneumoniae*, and *M. catarrhalis.* The influences of these four bacteria can rely on the seriousness of primary airway disease. In general, during AECB, several of the same organisms that are detected in the airways throughout clinically stable periods are existing but at greater colony counts [5]. Treatment should be focused on three chief aims: resolution of symptoms, inhibition of transitory loss of pulmonary function (can increase morbidity), and review of the infection in an effort to lessen the risk of any future exacerbations. Pharmacologic therapy should be intended at reducing the exertion of breathing, lessening airway inflammation, depressing the organism's burden at the lower respiratory tract, and managing hypoxia [6]. Levofloxacin is a fluoroquinolone antibacterial with activity against numerous micro-organisms causing AECB, and is commonly recommended for the management of AECB, along with other antibacterial including macrolides, ß-lactam/ß-lactamase inhibitors, and second-generation or third-generation cephalosporins [7]. The role of antibacterial therapy in the management of AECB is debated even though abundant therapeutic studies of antibacterials in the last decades. Most comparative trials have found equivalence in the use of antimicrobials. Differences in study end points,

differences in patient groups studied, and variations in antibiotics used have made the comparison of these studies difficult. Not all antibacterials prescribed to manage AECB have the same spectrum of activity or pharmacokinetic properties. Consequently, various aspects should be taken in consideration when choosing an antibacterial agent [8]. Antibacterial should have both in vitro and in vivo activities against the most commonly associated organisms detected in AECB. In particular subgroups of patients suffering from severe obstructive disease, coverage may require to be extensive to cover other organisms such as *S. aureus*, *Pseudomonas aeruginosa*, species in the Enterobacteriaceae family, and atypical microorganisms. The efficacy of Levofloxacin compared with other antibacterials is infrequently examined. Levofloxacin has been verified to be successful compared with ß-lactam/ß-lactamase inhibitor in various clinical trials [(9)]. For that reason, we designed a prospective observational study to compare the efficacy of Levofloxacin versus Co-Amoxiclav in the treatment of chronic bronchitis among ambulatory patients with COPD.

PATIENTS AND METHODS

This prospective parallel-group prospective observational study was carried out in King Hussein Medical Centre (KHMC) at the Royal Medical Services (RMS) in Jordan/Amman. In total, 83 men and women older than 18 years with AECB were included in the study. Patients were between 18 and 78 years of age and they were 15 or more smoking pack yearly or they were ex smoking and had a history of chronic bronchitis characterized by cough and sputum production for 2 consecutive years and for most days in a consecutive 3-month period in every year. Primary chest X-Ray was examined by radiologists, and those patients who had confirmation of pneumonia, bronchiectasis, cystic fibrosis, or lung malignancy were excluded from the study. Patients with serious renal impairment, a history of epilepsy, a history of allergy to fluroquinolone, cephalosporins, or penicillins, a history of antibacterial treatment in the last 2 days, on an existing schedule of systemic corticosteroids at a dose of >10 mg/day, , pregnancy or possibility of pregnancy, and nursing mothers were also excluded. All patients were diagnosed to suffer from mild, moderate, or severe AECB by pulmonologist, and received Levofloxacin or Co-Amoxiclav. Patients in the Levofloxacin group (Group 1) were treated with a once-daily dose of 500 mg for seven days and those in the Co-Amoxiclav group (Group 2) were treated for seven days with one 625 mg tablet every 8h for 7 days. Ethical approval has been obtained from the IRB committees at the JRMS.

Outcomes and follow-up

Patients attended the pulmonolgy clinic for evaluation at screening (day 0) and at long-term follow-up (days 28 to 35). The patients considered for inclusion in the study were assessed in the first clinic visit, in which clinical histories were documented, full physical examinations were done, laboratory tests were performed including full blood count, ESR, CRP, renal function tests, and liver enzymes, plain chest X rays were performed, and spirometry was performed. Lung function test results and screened symptoms were evaluated in accordance to the Global Initiative for Obstructive Lung Disease (GOLD) criteria and were employed to classify a patient's severity of disease. The outcome measure was clinical success of antibiotic therapy. Clinical response was graded as cure, improved, or failure, and a clinical response of cure and improved at the second visit were defined as clinical success.

STATISTICAL ANALYSIS

Data analysis was conducted using SPSS version (22). Descriptive analyses were reported as were reported as Mean ± standard deviation (SD), and percentage. The lower limit of the 95% confidence interval for a difference in clinical success (success rate of levofloxacin group – success rate of Co-Amoxiclav group) of −10% was defined as the criterion for non-inferiority.

RESULTS

Baseline characteristics

Of 97 patients screened, 83 were eligible for the study. Figure (1) displays a flow chart for the study groups and patients recruitment. Medical care team included two pulmonologist and one fellow resident in pulmonology specialty.

Table (1) shows the baseline characteristics of the subjects. There was no notable difference between the two groups in terms of gender, age, smoking status, and severity of exacerbation.

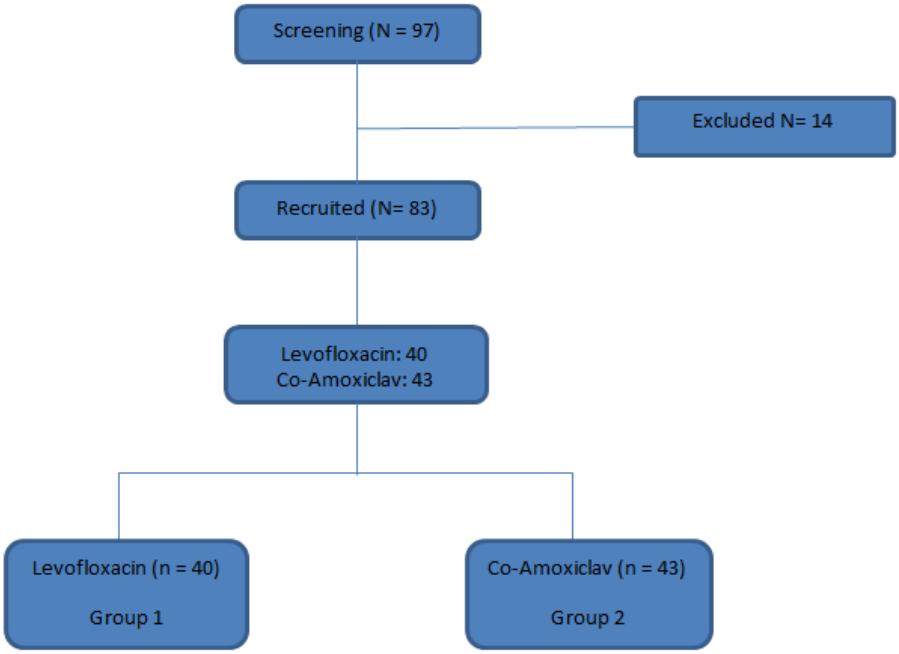

Fig-1: Flow chart of the study procedure

Table-1: Characteristics of enrolled patients

Characteristic	Levofloxacin (n = 40) [1] Group 1	Co-Amoxiclav (n= 43) [1] Group 2	*P-value*
Gender: Female Male	 4 (10) 36 (90)	 6 (14) 37 (86)	 0.71
Age (years): Mean± SD	 69.84 ± 7.79	 71.13 ± 8.01	 0.29
Smoking Habit : Active smoker Former smoker Never smoked	 29 (72.5) 8 (20) 3 (7.5)	 33 (76.7) 7 (16.3) 3 (7)	 0.21
Severity of exacerbation, n (%) Mild Moderate Severe	 17 (42.5) 8 (20) 15 (37.5)	 21 (48.8) 9 (20.9) 13 (30.3)	 0.54

SD, standard deviation

1: Percent out of patients in mentioned group.

Clinical Success Rates

Clinical response as assessed by pulmonologists at the last visit was superior in group 1. Clinical success was achieved in 89.3% of patients in the Levofloxacin group and 61.8% of those in the Co-Amoxiclav group. The minimum and maximum value for the 95% confidence interval of the difference between the groups was 8.2 and 11.4, respectively, confirming that the clinical success rate of levofloxacin was superior to that of Co-Amoxiclav.

Table 2 shows the smoker patients in group 1 and group 2 and the effect of smoker on the improvement of AECB. 70.7% of patients in group 1 and 76.7% in group 2 are active smokers while the remainders are ex-smoker or never smoked. By using Chi square the P value is < 0.05 which indicates that there is significance in improvement between smoker and ex-smoker patients who using oral levofloxacin and Co-Amoxiclav

Table-2: The improved patients in smokers and ex-smokers in both groups

Group	Smoking Status		Improved	P value within the same group	P value between The two study groups
Group 1	Smoker	29	28 (68%)	0.021	0.041
	Ex-Smoker/never smoked	11			
Group 2	Smoker	33	24 (55.8%)	0.038	
	Ex-smoker/never smoked	10			

Table 3 shows the effect of gender on the improvement of the AECB in both study groups. This table shows no significant effect of gender on the improvement of AECB among those taking the drug.

Table-3: the distribution of improved patients according to sex

Study Group	Sex	Improved	Not imp.	P-value within the same group	P-value between The two study groups
Group 1	Male (n=36)	25	9		
	Female (n=4)	3	1	0.061	0.053
Group 2	Male (n=37)	20	17		
	Female (n=6)	4	2	0.058	0.064

Table (4): 66 patients performed the pulmonary function tests (PFT), 33 from each group. All those patients show impairment in the PFT and repeated the test at the end of treatment as illustrated in table 4.

Table-4: The PFT in both groups (n= for each group)

Group	FEV1 increased >15%	FEV1 increased 10-15%	FEV1 increased <10%
Group 1	20	10	3
Group 2	12	8	13
Total	34	18	16
P value	0.033	0.078	0.095

DISCUSSION

In this prospective observational study, Levofloxacin 500 mg daily for 7 days was more effective clinically in the management of AECB than Co-Amoxiclav 625 mg three times daily.

The GOLD guidelines recommend antibacterial regimen for patients showing signs and symptoms of acute bronchitis [10]. Thus, this study was not designed to evaluate the benefit of antibacterial management versus no treatment in AECB but rather to compare the efficacy of the Levofloxacin versus Co-Amoxiclav in cases where antibacterial treatment would be considered proper and in line with presently established guidelines.

In this study all patients had criteria of chronic bronchitis with history of at least two episodes of exacerbation. Both groups had male predominance and this was compatible to other studies, this might reflect the high incidence of smoker's habit among male than female, especially in Jordan.

The improvement in both study groups was significant in currently and ex-smokers patients, with a statistical significance in improvement between smokers and ex-smokers and this might reflect that the airways of patients with chronic bronchitis are chronically colonized with bacteria. The termination of smoking is vital in the management of AECB because the smoking can cause further impairment in cilliary function.

Approximately 70 % of patients in the current study performed pulmonary function test had an FEV1 of > 50%. This would propose that patients enrolled in this study were moderately to severely ill, and consequently more likely to respond to management plan. After the use of antibacterial regimen the improvement in FEV1 was most likely because of decrease of inflammatory changes and edema of bronchial mucosa with improvement of airways narrowing.

A variety of factors should be taken in consideration when selecting antibacterial for the management of patients with AECB [11]. Worth

mentioning among these aspects are the spectrum of activity, the expected rate of bacterial resistance, convenient dosage regimen and sufficient penetration into pulmonary secretions. A range of antibacterial is used in the managing acute exacerbation of most frequently implicated in community-acquired respiratory infections [13].

Fluoroquinolones (levofloxacin, moxifloxacin, and gemifloxacin) show a broad spectrum activity against most organisms detected in AECB. Fluoroquinolones have been recommended as first-line treatment for AECB in patients with chronic bronchitis complicated by co-morbid illness, severe COPD with a FEV1 < 50%, patients >65 years, or recurrent exacerbations [(12)]. Clinical researches have shown greater effectiveness for short-course, 7-day Levofloxacin administration to that of standard therapy in AECB, as measured by both clinical and bacteriological outcomes. In a randomized, double-blind study of a 7-day course of 500 mg Levofloxacin regimen in 532 patients with AECB, the clinical success rates in the PP analysis were 82.8% for the 7-day schedule compared with 61% in patients treated with Co-Amoxiclav regimen 625 3 times per day [14].

CONCLUSION

Levofloxacin reveal great activity against a variety of organisms infecting the respiratory tract. Current data support the use of these agents in treatment of lower respiratory tract infections; particularly AECB. A rising body of evidence supports respiratory fluoroquinolones as first-choice antibacterial for the treatment of high-risk AECB.

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