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CHRONIC BRONCHITIS;

EFFECTIVENESS OF MOXIFLOXACIN COMPARED WITH CLARITHROMYCIN IN THE TREATMENT OF ACUTE EXACERBATION OF CHRONIC BRONCHITIS

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ABSTRACT… Chronic bronchitis is chronic inflammation of the airways resulting from exposure to noxious particles and gases which is slowly progressive and accentuated by episodes of acute exacerbation. These exacerbations tend to become more frequent and more severe as the underlying disease advances resulting in increased morbidity. More than half of these exacerbations are due to bacterial infections and use of antibiotics in such cases result in early recovery. Moxifloxacin is a newer fluoroquinolone that is very effective against respiratory pathogens including atypical organisms and even in resistant pathogens as compared to beta lactams and macrolides. **Objectives:** To compare the effectiveness of Oral Moxifloxacin compared with Oral clarithromycin in the treatment of acute exacerbation of chronic bronchitis. **Study Design:** Randomized control trial. **Setting:** Department of Pulmonology Multan Medical and Dental College Tertiary care hospital, Multan. **Period:** Six months, from October 2017 to March 2018. **Materials and Methods:** 64 patients with acute exacerbation of chronic bronchitis were included in the study. Patients were diagnosed on history of smoking and chronic productive cough with recent onset increase in shortness of breath, sputum amount and purulence. Patients were divided into 2 equal groups A and B containing 32 patients each. Group A was given oral clarithromycin 500mg daily for 7 days and Group B was given oral moxifloxacin 400mg daily for 5 days. Response to this treatment was assessed before treatment and at 14 days by an improvement in both the breathlessness on Borg dyspnea scale and by decrease in sputum purulence on sputum microscopy. **Results:** There were 64 patients in our study. Females were 12 (18.75%) while 52 (81.25%) were males. Mean age of the patients was 52. 19 + 6.37 years. Mean number of Pack years was 24.8 + 9.32. Mean age for group A patients was 51.09 + 7.56 years. There were 7 (21.87%) females and 25 (78.13%) males. Mean number of pack years was 24.47 + 9.88. Oral moxifloxacin was found to be effective in 30 (93.75%) patients in comparison with oral clarithromycin which was effective in 27 (84.37%) patients (p-value = 0.23). **Conclusion:** Oral Moxifloxacin is not more effective than oral clarithromycin in the treatment of AECB in our local population of COPD patients.

Key words: AECB, Clarithromycin, COPD, Borg Dyspnea Scale, Moxifloxacin.

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INTRODUCTION

Chronic bronchitis is defined as chronic cough with production of sputum for at least three consecutive months over two consecutive years.[1] Most of the patients affected by this chronic condition are also suffering from dyspnea and are labeled to have chronic obstructive pulmonary disease (COPD).[2] Chronic bronchitis is considered as a progressive disease characterized by episodes of acute exacerbations which tend to become more frequent and more severe as the underlying disease advances leading to increased morbidity. The characteristic symptoms during these episodes are cough, dyspnea and changes in sputum volume and purulence. Most patients have between 1–4 acute exacerbations annually.[3] The most common risk factors for exacerbation are continuing cigarette smoking, advancing age, and low baseline lung function.[4]

Treatment of Acute exacerbation of chronic bronchitis is multifactorial including smoking cessation, oxygen supplementation, appropriate hydration, bronchodilators, parenteral steroids and antibiotic therapy. Infectious agents are involved in upto 80% of the exacerbations. Of these 50%–70% are estimated to be caused by bacterial agents.[5] The most frequently cultured

bacterial agents found during AECB are Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pneumoniae.[5] Previously the antibiotics recommended for the treatment of AECBs were ß-lactams and macrolides.[6] However, more recently updated guidelines of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) have recommend the use of the new respiratory fluoroquinolones like moxifloxacin for the treatment of patients with severe exacerbations of chronic bronchitis,[7] because resistance continues to increase not only among the traditional antibional antibiotic groups but also among the entire fluoroquinolone class.[8] One study, oral moxifloxacin was compared with clarithromycin for the treatment of acute exacerbation of chronic bronchitis and was found to have higher success in resolution of clinical symptoms and bacterial eradication at 90.1% as compared to 64.2% for that of the clarithromycin.[9,10] Our study will help us identify the success rates of oral moxifloxacin in comparison with oral clarithromycin which will enable us select appropriate antibiotic in our patients with acute exacerbations.

To compare the effectiveness of Oral Moxifloxacin compared with Oral clarithromycin in the treatment of acute exacerbation of chronic bronchitis.

Acute exacerbation of chronic bronchitis was diagnosed when all of the following three standard criteria of an exacerbation were found positive by the researcher during clinical evaluation of the patients: recent history of doubling of the daily amount of sputum reported by the patient; recent increase in sputum purulence from white to yellow/green and recent worsening of shortness of breath.[1]

Effectiveness of treatment were defined as clinical improvement in all of the three above mentioned symptoms. Decrease in sputum volume was assessed by directly questioning the patient. Decrease in sputum purulence was quantified by at least 50% reduction in number of pus cells in sputum microscopy at day 14 as compared to that checked at day 0. Improvement in shortness of breath was quantified by at least 50% decrease in score on Borg dyspnea scale at day 14 from that before the commencement of therapy at day 0.

Borg dyspnea scale is a 10 score tool widely used for subjective evaluation of dyspnea, at zero end the patient has no dyspnea while at 10 score patient has maximal dyspnea.

Hypothesis
Oral moxifloxacin is more effective in improving the symptoms of acute exacerbation of chronic bronchitis as compared to oral clarithromycin.

MATERIAL AND METHODS

Setting
Department of Pulmonology Multan Medical and Dental College Tertiary care hospital of 600 beds.

Study Design
Randomized controlled trial

Sample Size
64 patients divided in two equal groups.

Sample Technique
Non-probability purposive

Inclusion Criteria
Patients of both genders in age group 35-60 years with history of smoking>10 pack years and having acute exacerbation of chronic bronchitis were included in the study.

Exclusion Criteria
Pregnant women and patients with clinical or radiographic evidence of pneumothorax, pneumonia, bronchiectasis, renal failure, chronic liver disease or those with history of use of antibiotics within last 2 weeks were excluded from the study.

Data Collection Procedure
64 patients with acute exacerbation of chronic bronchitis from outpatient department of Pulmonology department of Multan Medical and dental college were included in this study. Permission was taken from the ethical committee

of the hospital. Written informed consent was taken from the patients. Confounding variables like age and gender were controlled by stratification. Patients were diagnosed on history and examination, having history of smoking and chronic productive cough with recent onset increase in shortness of breath, sputum amount and purulence. Chest x-ray was done in all patients to exclude pneumonia and underlying structural lung disease such as bronchiectasis. Shortness of breath and functional status of the patient were assessed by using Borg Dyspnea Scale before the commencement of treatment and at 14 days. Sputum samples were assessed for gross amount and color as well as sputum microscopy for pus cells before and at the end of treatment. Patients were divided in 2 groups A and B by envelop method, each containing 32 patients. Group A patients were given oral clarithromycin 500mg twice daily for 7 days and Group B patients were given oral moxifloxacin 400mg daily for 5 days. Effectiveness of treatment was assessed at 14th day and was entered as yes/no in the attached proforma.

RESULTS

There were 64 patients in our study. Females were 12 (18.75%) while 52 (81.25%) were males (Fiugre-1). Mean age of the patients was 52. 19 + 6.37 years. Patients ranged in age from a minimum of 39 years to a maximum of 63 years. Mean number of Pack years was 24.8 + 9.32. Pack years ranged from a minimum of 10 pack years to a maximum of 50.

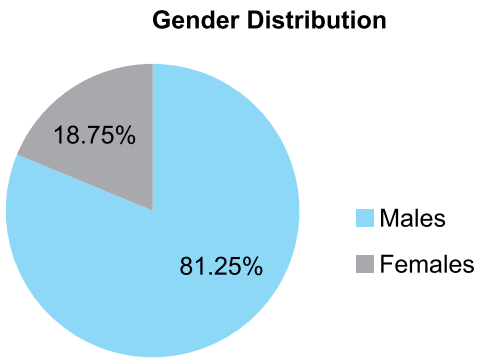

Figure-1. Gender distribution in the study population

Mean age for group A patients was 51.09 + 7.56 years from a minimum of 39 to a maximum of 63 years. There were 7 (21.87%) females and 25 (78.13%) males. Mean number of pack years was 24.47 + 9.88 with a minimum of 10 to a maximum of 50. Mean age for group B patients was 53.28 + 4.77 years with a minimum of 39 to a maximum of 59. There were 5 (15.6%) females and 27 (84.37%) were males. Mean number of pack years was 25.19 + 8.8 (Table-I).

	Group A	Group B
Mean age	51.09 + 7.56 years	53.28 + 4.77 years
Males	25 (78.13%)	27 (84.37%)
Females	7 (21.87%)	5 (15.6%)
Mean pack years of smoking	24.47 + 9.88	25.19 + 8.8
Effectiveness of treatment	30/32 (93.75%) p value = 0.23	27/32 (84.37%) p value = 0.23

Table-I. Comparison of characteristics of group A and B patients

Oral Moxifloxacin was given to 32 patients and out of 25 males and 7 females, moxifloxacin was found to be effective in 24 (96%) males and 6 (85.7%) females. Overall it was found to be effective in 30 (93.75%) patients. Group B patients were treated with oral clarithromycin 500mg twice daily for 7 days. Among 27 males and 5 females given clarithromycin, treatment was effective in 23 (85.18%) males and 4 (80%) females. Overall this treatment was effective in 27 (84.37%) patients (Figure-2). When chi-square test was applied it was noted that this difference is statistically non-significant with a p-value = 0.230.

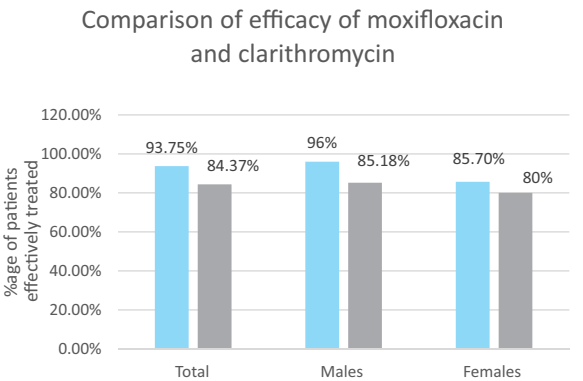

Figure-2. Comparison of efficacy of moxifloxacin and clarithromycin in the study population

In patients treatment group A there were 19 patients < 55 years of age and 18 (94.7%) were

found to be responsive to the treatment while in treatment group B there were 19 patients with age < 55 years and 17 (89.4%) were found to be treated effectively with clarithromycin (p-value = 0.54). In group A there were 13 patients > 55 years of age and moxifloxacin was effective in 12 (92.3%) patients while there were 13 patients > 55 years of age and 10 (76.9%) were found to be treated effectively with clarithromycin (Graph 3). When chi-square test was applied to see the effect of age on treatment effectiveness p-value was found to be 0.27 which is statistically non-significant.

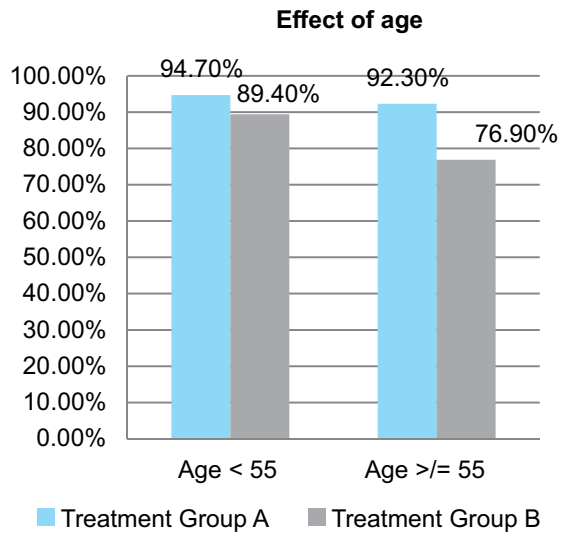

Figure-3. Effect of age on effectiveness of moxifloxacin and clarithromycin

DISCUSSION

Moxifloxacin has been widely studied for its effectiveness in the treatment of AECB as compared to the conventional antibiotics. There are four major studies which compared the effectiveness and safety of moxifloxacin with clarithromycin in 2381 patients who were having exacerbation of Chronic Bronchitis.[10] The success rate were similar between the two but there was an improved bacteriological success rate with moxifloxacin treatment compared with clarithromycin treatment. Both had similar eradication rates of S. pneumoniae and M. catarrhalis but moxifloxacin showed better eradication against H. influenzae.[11] Overall moxifloxacin showed clinical success rate of 89% and a bacteriological eradication rate of 87%.[10] Bacterial eradication with moxifloxacin has been described to be better than macrolides. In one trial which compared moxifloxacin with macrolides in eradicating H. influenzae, moxifloxacin was found to be effective in 93% (133/143) compared with 73.2% (109/149) with macrolides, p = 0.001.[11]

There were 64 patients in our study. Females were 12 (18.75%) while 52 (81.25%) were males. Males outnumbered in our study because COPD is much more common among males in our society than females. This trend probably is due to the fact that smoking, which is the most common cause of COPD, is much more common among males in our society. Mean age of the patients was 52. 19 + 6.37 years. Patients ranged in age from a minimum of 39 years to a maximum of 63 years. This mean age correlates with the age of onset of symptoms in COPD. Oral Moxifloxacin was given to 32 patients in Group A and was found to be effective in 30 (93.75%) patients. Group B patients were treated with oral clarithromycin 500mg twice daily for 7 days. This treatment was effective in 27 (84.37%) patients. Moxifloxacin was thus not found to be more effective in the treatment of AECB as compared to clarithromycin in our study as the difference in effectiveness was small and statistically non-significant with a p-value of 0.23.

One possible reason for these results is that the microbial resistance patterns in our local population is different from those of the European populations, where most of the above mentioned researches had been conducted. This needs to be further confirmed by conducting a larger trial where bacterial cultures can be concomitantly obtained which will help us identify the causative pathogens, their sensitivity and resistance patterns to various antibiotics and the microbiologic eradication spectra of various antibiotics. These were the limitations in our study. Bacterial cultures of the sputum of patients would have provided us with a more confident diagnosis of bacterial etiology of the exacerbation. They were not possible because of limited resources, expense and lack of easy availability of the test. No pre-exacerbation status of the patient was available to compare the severity of their underlying COPD. Also, there were no long term follow up possible,

which could have allowed us to compare the 'exacerbation prevention' characteristics of moxifloxacin versus clarithromycin.

CONCLUSION

There was an only small benefit in effectiveness with oral moxifloxacin over clarithromycin but this was statistically non-significant (p-value= 0.230). Oral Moxifloxacin is not found to be more effective than oral clarithromycin in the treatment of AECB in our study population.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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