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ORIGINAL ARTICLE

Comparison of Mean duration of Hospital Stay in COPD patients with Acute Exacerbations Treated with and without Prophylactic Azithromycin

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ABSTRACT

Introduction: Acute exacerbations of chronic obstructive pulmonary disease (AECOPDs) can lead to high frequencies and duration of hospitalization and mortality. Azithromycin is a class of antibiotic that possess both antimicrobial and anti-inflammatory properties. The aim of this study was to compare the mean duration of hospital stay in COPD patients presenting with acute exacerbations treated with and without prophylactic azithromycin.

Objective: To compare the mean duration of hospital, stay in COPD patients presenting with acute exacerbations treated with and without prophylactic azithromycin

Setting: Department of Pulmonology, Military Hospital, Rawalpindi.

Study Design: Randomized controlled trial.

Duration of study: Was 6 months from 1st Oct 2019 1st March 2020.

Subject & Methods: All patients who fulfill the inclusion criteria and admitted in the department of Pulmonology, Military Hospital, Rawalpindi were included in the study. After taking informed written consent history was taken, clinical examination was done and patients were divided into two groups group A (prophylactic Azithromycin) & C (control without prophylactic Azithromycin). Outcome was checked by comparing both the groups for mean duration of hospital stay.

Result: Out of 122 AECOPDs patients 77 (63.1%) were males & 45 (36.9%) were female with the mean age 43.1830+10.8170 years. The mean duration of hospital stay in group A was 4.2787+1.880 days while in group C it was 9.4262+2.224 days.

Conclusion: Azithromycin prophylaxis therapy could effectively reduce the duration of hospital stay among patients with AECOPDs. However, it may bring increased adverse events and the emergence of resistance. A recommendation for its prophylactic use should weigh both the advantages and disadvantages.

Keywords: chronic obstructive pulmonary disease, hospital stay, azithromycin.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and that is caused by an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. COPD is a major cause of morbidity and mortality worldwide and results in an economic and social burden that is both substantial and increasing. COPD prevalence, morbidity, and mortality vary across countries.[1-3]

Exacerbations have a significant and prolonged impact on health status and outcomes, and negative effects on pulmonary function. A significant proportion of exacerbations are unreported and therefore left untreated, leading to a poorer prognosis than those treated. COPD exacerbations are heterogeneous, and various phenotypes have been proposed which differ in biologic basis, prognosis, and response to therapy. Identification of biomarkers could enable phenotype-driven approaches for the management and prevention of exacerbations. For example, several biomarkers of inflammation can help to identify exacerbations most likely to respond to oral corticosteroids and antibiotics, and patients with a frequent exacerbator phenotype, for whom preventative treatment is appropriate. Reducing the frequency of exacerbations would have a beneficial impact on patient outcomes and prognosis. Preventative strategies include modification of risk factors, treatment of comorbid conditions, the use of bronchodilator therapy with long-acting β_2-agonists or long-acting muscarinic antagonists, and inhaled corticosteroids.[4-6]

Chronic obstructive pulmonary disease (COPD) is a poorly reversible disease of the lungs and one of the major causes of morbidity and mortality worldwide. In the United States, it is the fourth leading cause of death after heart disease, cancer, and cerebrovascular disease[7,8]. By 2020, it was projected to become the third leading cause of death worldwide.[9] Contrary to trends for other major chronic diseases in the United States, the prevalence of and mortality from COPD have continued to rise;[10] the death rates doubled between 1970 and 2002,[11] and for the first time in 2000, mortality figures for women surpassed those for men.[12] In the United States, 12 million patients are currently diagnosed with COPD, but there is believed to be at least an equal number of individuals with impaired lung function suggestive of COPD who are undiagnosed.[13] Given that the majority of COPD cases are caused by smoking, it is primarily a preventable disease.

COPD comprises a diverse group of clinical syndromes that share the common feature of limitation of expiratory airflow.[14] The American Thoracic Society defines COPD in terms of chronic bronchitis and emphysema.[15] Chronic bronchitis is characterized by the clinical symptoms of excessive cough and sputum production; emphysema refers to chronic dyspnea resulting from enlarged air spaces and destruction of lung tissue. The GOLD initiative defines COPD as "a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases."[16] Asthma is also characterized by airflow obstruction and inflammation; however, the reversibility of functional deficits in asthma differentiates it from COPD.[15]

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MATERIAL AND METHODS

Study design: It was a randomized controlled trial.

Setting: Department of Pulmonology, Military Hospital, Rawalpindi.

Duration of Study: Was 6 months from 1st October 2019 to 1st March 2020.

1. Sample size: Sample size of 122 cases (61 in each group) is calculated with 80% power of test and level of significance

5% while taking expected mean duration of hospital stay among the patients presenting with acute exacerbations treated with and without prophylactic azithromycin to be 6.5 ± 4.7 days vs. 10.4 ± 9.8 days respectively.[6]

Sampling Technique: Non probability consecutive sampling

Sample Selection:

Inclusion criteria:

1. Patients with ages in the range of 18-70 years presenting with acute exacerbation of COPD as per operational definition.
2. Patients who sign written informed consent to participate in the study.

Exclusion criteria:

1. Patients with valvular heart disease or ejection fraction < 40% on echo as per clinical record.
2. Patients with renal failure (serum creatinine > 4mg/dl), or CLD liver cirrhosis on ultrasound with ascites.
3. Patients who have undergone pneumonectomy HIV positive on ELISA, or proven lung malignancy or secondary's or have taken chemo or radiotherapy in past 8 weeks as per history and clinical record.

Data Collection: After approval from ethical review committee of the hospital, 122 cases (61 in each group) patients who present in the Pulmonology Department, Military Hospital, Rawalpindi and who fulfill the above criteria was counseled and explained the details of the study. Written informed consent and detailed history was taken from each patient. COPD patients who presented in the OPD of the department were prescribed 250mg of azithromycin once per day on every alternate day of the week for 12 weeks at least. The patients who were present in the Pulmonology department with acute exacerbation of COPD was divided into two groups base on the clinical record that had they been advised to take azithromycin or not in following groups.

- Group-A: Prophylactic Azithromycin
- Group-C: Control Without Prophylactic Azithromycin

These patients were managed as per hospital protocol with low flow oxygen, anti-biotics along with bronchodilator therapy with long-acting β_2-agonists or long-acting muscarinic antagonists I/V or inhaled corticosteroids and use of CPAP or ventilatory support as per clinical condition of the patient, ABG's report and oxygen saturation on pulse oximeter. There daily progress was monitored and observed by the consultant of the department. Patient was discharged once the discharge criteria was met. The duration of the hospital stay was noted as per operational definition. All the data was noted and recorded into the attached proforma along with demographic details of the patient. All the drugs used were given of the same company to eliminate bias and confounding variables were controlled by exclusion.

Data analysis: All the collected data was entered and analyzed into SPSS version 21.

1. Numerical variables i-e age, and mean duration of hospital stay was presented by mean ±SD and range. Independent sample t-test was applied for comparison of mean duration of hospital stay between the two groups.
2. Categorical Variable i.e gender and history of diabetes were presented as frequency and percentage.
3. Data was stratified for age, gender and history of diabetes. Post stratification independent sample t-test was applied taking p value of ≤0.05 as statistically significant.

RESULTS

A total 122 patients presenting with acute exacerbation of COPD were selected to conduct this study.

Patients were randomly divided into two groups, In group A patients were given azithromycin prophylaxis and in group C patients were not given azithromycin prophylaxis.

Group 'A' included 61 subjects of which 38 patients (31.1%) were male while 23(18.9%) were female, with mean age of 40.9016+10.833 years, while group 'C' also included 61 patients of which 39 patients (32%) were male while 22(18%) were female, with mean age 45.4590+10.394 years,(as shown in table:1 and Table-2). The overall mean age came out to be 43.1830+10.8170 years (as shown in table-1) The frequency distribution of age is shown in Graph-1.

In Group A the history of diabetes was present in 12 patients (9.8%), while in Group C the history of diabetes was seen in 19 patients (15.6%), as shown in table-3.

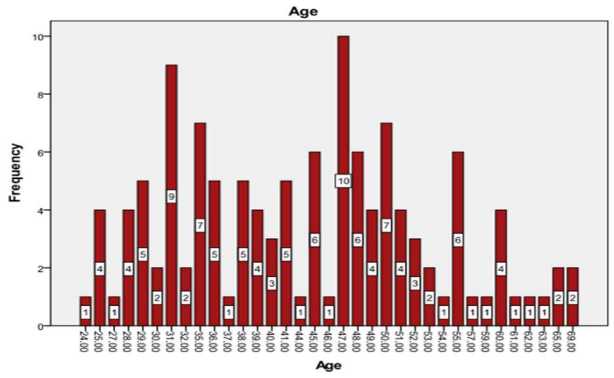
The mean duration of hospital stay in group A was 4.2787+1.880 days while in group C it was 9.4262+2.224 days with overall mean duration of hospital stay of 6.8264+3.300 days (as shown in table:4). The frequency distribution of duration of hospital stay is shown in Graph-II.

There is significant difference of mean duration of hospital stay between the group A and group C was noted with p-value of 0.001 (as shown in table- 5).

The frequencies of age, gender & history of diabetes groups were calculated according to mean duration of hospital stay. The results are presented in Table-6, Table-7 and Table-8 respectively.

In our study there was no significance difference in the mean duration of hospital stay was noted with age, gender, & history of diabetes between the two groups.

Graph-1: Frequency Distribution of Age



Graph-11: Frequency Distribution of Duration of Hospital Stay (Days)

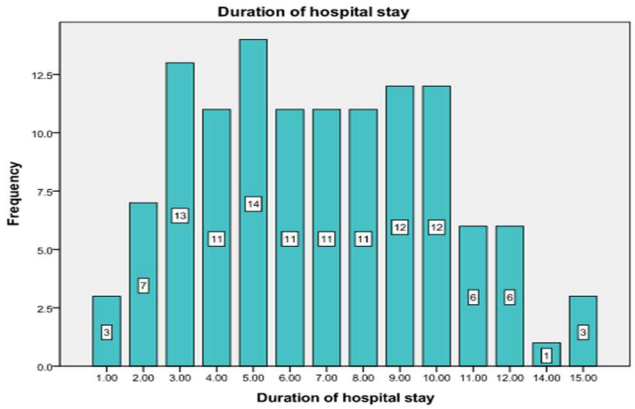


Table 1: Age Distribution with respect to groups

Age groups	G-A	G-C	Overall
18-44 years	36(29.50%)	24(19.68%)	60(49.18%)
45-70 years	25(20.5%)	37(30.32%)	62(50.82%)
Total	61(50%)	61(50%)	122(100%)
Mean+SD	40.9016+10.833	45.4590+10.394	43.1830+10.8170

Table 2: Gender distribution with respect to groups

Distribution of gender :(n=122)				
Gender	G-A	G-C	Total	P-value
Male Female	38(31.1%) 23(18.9%)	39(32%) 22(18%)	77(63.1%) 45(36.9%)	0.698
Total	61(50%)	61(50%)	122(100%)	

Table 3: History of diabetes distribution with respect to groups

Distribution of history of diabetes:(n=122)				
History of diabetes	G-A	G-C	Total	P-value
Yes No	12(9.8%) 49(40.2%)	19(15.6%) 42(34.4%)	31(25.4%) 91(76.6%)	0.608
Total	61(50%)	61(50%)	122(100%)	

Table 4: Duration of hospital stay distribution with respect to groups

Duration of hospital stay groups	G-A	G-C	Overall
1-7	47(39%)	12(10%)	59(49%)
8-15	14(11%)	49(40%)	63(20.6%)
Total	61(50%)	61(50%)	122(100%)
Mean+SD	4.2787+1.880	9.4262+2.224	6.8264+3.300

Table 5: Comparison of mean duration of hospital stay (days) between two groups :(n=122)

(Comparison of mean duration of hospital stay (days) between two groups:(n=122)				
Groups	G-A	G-C	Over all mean duration of hospital stay	P-value
Mean duration of hospital stay (days)	4.2787 +1.880	9.4262+2 .224	6.8264+3.300	0.001

Table 6: Stratification of mean duration of hospital stay between two groups with respect to age: (n=122)

Age groups (years)	Groups	Mean duration of hospital stay	P-value
18-44	A C	4.333+1.788 9.173+1.527	0.788
45-70	A C	4.200+2.041 9.578+ 2.564	0.495

Table 7: Stratification of mean duration of hospital stay between two groups with respect to gender: (n=122)

Gender	Groups	Mean duration of hospital stay (days)	P-value
Male	A C	4.342+1.878 9.0769+2.005	0.738
Female	A C	4.173+1.922 10.0455+ 2.4971	0.103

Table 8: Stratification of mean duration of hospital stay between two groups with respect to history of diabetes: (n=122)

History of diabetes	Groups	Mean duration of hospital stay (days)	P-value
Yes	A C	4.666+2.534 9.052+1.899	0.430
No	A C	4.183+1.703 9.595+ 2.358	0.382

DISCUSSION

Macrolides are a class of antibiotics characterized by the presence of a macrocyclic lactone ring.[17] They have great bioavailability, extensive tissue penetration, and broad-spectrum antibacterial activity, making them effective for treating infectious respiratory diseases.[18],[19] In recent years, studies have shown that macrolides also possess immune-modulatory and physiological properties, including anti-inflammatory and antiviral effects, reduction of mucus secretion, and inhibition of bacterial virulence and biofilm formation.[20] Previous studies have demonstrated that long-term macrolide therapy is effective in controlling diffuse panbronchiolitis and cystic fibrosis.[21],[22] Considering that the occurrence of acute exacerbations of COPD (AECOPDs) is associated with increased airway inflammation and infection, prophylactic macrolide therapy could be beneficial for patients with COPD.[20]

By both unweighted and weighted approaches, the pooled evidence of our meta-analysis confirmed that prophylactic macrolide therapy significantly reduces the frequency of exacerbations in patients with COPD.

Our study compares the mean duration of hospital stay in patients with chronic obstructive pulmonary disease presenting with acute exacerbations treated with and without prophylactic azithromycin.

In our study, the mean duration of hospital stay in Group A (azithromycin prophylaxis) was 4.28 ± 1.88 days, while in Group C (without azithromycin prophylaxis) it was 9.43 ± 2.22 days. These findings are comparable to those of Naderi et al.,[23] who in 2018 reported a mean hospital stay of 6.5 ± 4.7 days versus 10.4 ± 9.8 days, respectively.

In our study, we used 250 mg of azithromycin once per day on alternate days of the week for at least 12 weeks. The optimal regimen for macrolide treatment has not yet been well established. Different durations and dosages were used among studies included in this meta-analysis. For azithromycin, three studies using 1500–1750 mg/week for 6–12 months observed a significantly lower frequency of exacerbations in treatment groups,[24] while two other studies using 750 or 1750 mg/week for three months found no reduction in exacerbations.[25],[26] Moreover, the most appropriate timing to commence prophylactic therapy requires further investigation. Gómez et al. reported that patients with COPD receiving azithromycin for three days every 21 days during winter experienced fewer exacerbations.[27] Considering that AECOPDs occur more frequently during colder seasons such as winter and spring,[28] prophylactic therapy should ideally cover these periods.

In summary, our study confirms that prophylactic azithromycin therapy significantly reduces the duration of hospital stay in patients with acute exacerbations of COPD. However, long-term use may increase adverse events and contribute to macrolide resistance. Therefore, recommendations for prophylactic macrolide therapy should be made on a case-by-case basis after carefully weighing clinical benefits against potential risks.

The limitations of our study include its single-center design and small sample size. Further multicenter studies with larger sample sizes are required.

CONCLUSION

Azithromycin prophylaxis therapy could effectively reduce the duration of hospital stay among patients with AECOPDs. However, it may bring increased adverse events and the emergence of resistance. A recommendation for its prophylactic use should weigh both the advantages and disadvantages.

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