Comparative study on short-term treatment with Levofloxacin and azithromycin in Bronchiectasis patients for respiratory attacks prevention

Nezarali Moulaei[1]*, Farzaneh Peik Falak[2]

1. **Nezarali Moulaei [1]***
Assistant Professor of Pulmonary Diseases, Department of Internal Medicine, School of Medicine, Infectious Diseases and Tropical Medicine Research Center, Zahedan University of Medical Sciences, Zahedan, Iran.
2. **Farzaneh Peik Falak [2]**
Resident of Internal Medicine, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran.

Abstract

Introduction:

Bronchiectasis is an abnormal and permanent dilation of the bronchi. Bronchiectasis may be a local, in which only the airways of a limited area of the lung parenchyma are involved. However, bronchiectasis may be diffused, in which the wider airways areas of the lung are affected. Given that no study has ever compared the effect of levofloxacin with routine therapies, this study was conducted to compare the prophylactic effect of short-term treatment with levofloxacin and azithromycin in patients hospitalized in Zahedan, Iran.

Materials and methods:

This was a clinical trial study. After entering the study, 90 patients were randomly divided into two equal groups. In one group, levofloxacin patients received 5 days a month, and in the other group, azithromycin patients received a dose of 250 mg per day throughout the study. Patients were followed for one year, during which they were evaluated for the number of hospitalizations and the number of exacerbation cases. It was also explained to the patients that due to the use of blinding techniques, the type of administrated drug and the group in which they are placed will not be informed and if they are not satisfied, they will not enter the study. Initial patient information such as age and sex were recorded for each individual. At the end of the study, the data were entered into SPSS statistical software version 19 and examined based on descriptive statistics and independent t-test. The significance level was considered 0.05.

Findings:

According to the findings, the average number of exacerbations of bronchiectasis symptoms per year in azithromycin group was 4.42 ± 2.00 and in levofloxacin group, was 2.44 ± 1.34 and the average number of hospitalization cases per year in azithromycin group was 0.75 ± 1.40 and in the levofloxacin group was 0.88 ± 0.60 ($p < 0.001$).

Conclusion:

The results of the present study showed a significant difference between the number of exacerbations and hospitalizations per year in levofloxacin and azithromycin groups, and the levofloxacin group indicates favorable results in this case. However, it is essential to conduct further studies on the effect of azithromycin and levofloxacin on the rate of exacerbation and hospitalization in patients with bronchiectasis.

Keywords: Levofloxacin, Prevention, Bronchiectasis.

Introduction

Bronchiectasis is a word of Greek origin meaning dilation of the bronchi. A more suitable definition for bronchiectasis is "abnormal and persistent dilation of sub-segmental bronchi" [1]. Clinically, this abnormal dilation of the bronchi may involve a lobe or segment of the lung or multiple lobes and the whole lung. Pathologically, the destruction of elastic and muscular parts of the bronchial walls is visible [2-4] considering three pathological types for bronchiectasis [5]. Form the clinical point of view, bronchiectasis usually shows a certain sign as chronic and recurrent respiratory infections with high sputum productions [6 & 7]. In terms of etiology, bronchiectasis is divided into two major congenital and acquired types. However, in both types, infection leads to inflammation and the destruction of the bronchial wall. The most important factors that directly cause bronchiectasis include congenital disorders of the mucociliary system of the bronchial epithelium, immune globulin disorders, cystic fibrosis. A1-antitrypsin disorders, Cartagener syndrome, congenital disorders of the bronchial cartilages, sequestrations, acquired infection diseases especially measles and pertussis, bronchial obstruction due to foreign bodies and tumors, pressure on the bronchi due to abnormal lymph nodes, middle lobe syndrome, and bronchial constriction due to tuberculosis. Now, the diagnosis of bronchiectasis is based on the case history and CT scan (particularly HRCT). Treatment of bronchiectasis is now a medical therapy. The basis of this therapy is control and prevention of infection and includes antibiotic therapy, postural drainage of the bronchi, strengthening the immune system, use of bronchodilators, and removal of foreign bodies or tumors that cause bronchial obstruction. In the past, surgery was the common treatment of bronchiectasis while this method is rarely used because of the available suitable antibiotics and other supportive therapies [8 & 9]. However, in cases where a segment of the lung is involved and medical treatment does not effectively control the symptoms, resection of the affected segment is the best treatment for the patient. Surgery in bronchiectasis includes the anatomic removal of the affected area (segmental or lobar). Before surgery, CT-scan should be performed to detect the site pf lesion accurately without excising the normal lung tissue [10-14]. About 64% of patients with chronic bronchiectasis have been infected with pathogenic bacteria that Pseudomonas Aeruginosa and Homophiles Influenza are the most common pathogens. These infections affect the immune system and respiratory epithelium system of the host. They also cause a vicious infection-inflammation cycle with persistent symptoms, intermittent acute exacerbations, and disease progression. Control of chronic bacterial infection leads to reduced inflammation and evidence indicates that long-term antibiotic treatment can improve the clinical consequence of patients [15]. There has not been any comparative study on the impact of levofloxacin and routine treatments. Accordingly, this comparative study was conducted on the prophylactic effect of short-term treatment with levofloxacin and azithromycin on the bronchiectasis patients who liv in Zahedan, Iran.

Materials and Methods

This was a randomized, double-blind clinical study performed in Ali Ibn Abitaleb Hospital in Zahedan, Iran 2019. The studied population comprised all of the patients with generalized bronchiectasis along with purulent sputum secretions that suffer from more than 3 times of exacerbation per year. Inclusion criteria included having informed consent, having generalized bronchiectasis with purulent sputum and more than 3 exacerbations per year, and patients who needed antibiotic prophylaxis. Exclusion criteria

included dissatisfaction with participation, side effects of drugs, pregnant and breastfeeding women, and sensitivity to drugs. According to the average number of exacerbations in the study [15] and the following equation, the sample size was calculated (n=82) then 90 subjects were entered into the study considering the loss of samples.

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2 (\delta_1^2 + \delta_2^2)}{(\mu_1 - \mu_2)^2} = 82$$

$$Z_{1-\frac{\alpha}{2}} = 1.96$$

$$Z_{1-\beta} = 0.85$$

$$\mu_1 + \delta_1 = 3.1 \pm 2.8$$

$$\mu_2 + \delta_2 = 2.1 \pm 1.6$$

The sampling method of simple convenience was used at the first step then block randomization with a block size of 4 was done. Data collecting was done by information gathering. The objective of this study was to compare the effects of levofloxacin and azithromycin in preventing exacerbation attacks in patients with bronchiectasis. To this end, the author entered 90 subjects with inclusion criteria to the plan approved in the Research Department of Medical University. All of the subjects were explained about the terms and objectives of the study then they participated with informed consent. After entry to the study, subjects were randomly assigned to two equal groups based on the randomized blocks. In one group, patients received 5-day treatment with levofloxacin per month, and azithromycin group received a 250mg dose per day during the study. Patients were followed for one year, during which they were evaluated for the number of hospitalizations and the number of exacerbation cases. The study terms were explained then patients were entered into the study based on their informed consent and inclusion criteria. It was also explained to the patients that due to the use of blinding techniques, the type of administrated drug and the group in which they are placed will not be informed and if they are not satisfied, they will not enter the study. Initial patient information such as age and sex were recorded for each individual.

The randomized assignment was performed based on the block randomization with a block size of 4. In this case, of the calculated sample size with 90 subjects (45 subjects in the first group and 45 subjects in the second group), 10 blocks (including 9 subjects) were determined then equal cards of levofloxacin and azithromycin groups were assigned to each block. Then, a card was selected from the first block and another card was chosen for the next patient from the same block. Therefore, eight patients were assigned to each group equally by taking the measure for each block. Finally, the data were entered into SPSS statistical software version 19 and examined based on descriptive statistics (Mean, Standard Deviation, Frequency, and Percent). Data analysis was done using an independent t-test at the significance level of 0.05.

Results

In this research, 90 subjects were assigned to two levofloxacin and azithromycin groups. According to the obtained findings, the mean age of azithromycin and levofloxacin groups was 35.60 ± 11.04 and 39.37 ± 14.82, respectively. The independent t-test indicated no significant difference between the mean ages of both groups (P=0.17). According to the results, 50 women and 40 men were entered into the study; of them, 25 women and 20 men were assigned to each levofloxacin and azithromycin group. Fisher's exact test showed no significant difference in sex distribution in two groups (P=1). According

to the findings, the average number of exacerbations of bronchiectasis symptoms per year in the azithromycin group was 4.42±2.00 and in the levofloxacin group, was 2.44±1.34. According to an independent t-test and the significance level less than 0.05, there is a significant difference between exacerbations of bronchiectasis symptoms per year in levofloxacin and azithromycin groups (See Table 1 and Fig.1).

Table 1. Comparative means of exacerbations of bronchiectasis per year in levofloxacin and azithromycin groups

| Variable	Group	Mean	SD	P.Value
Number of exacerbations	Azithromycin	4.42	2.00	<0.001
	Levofloxacin	2.44	1.34	
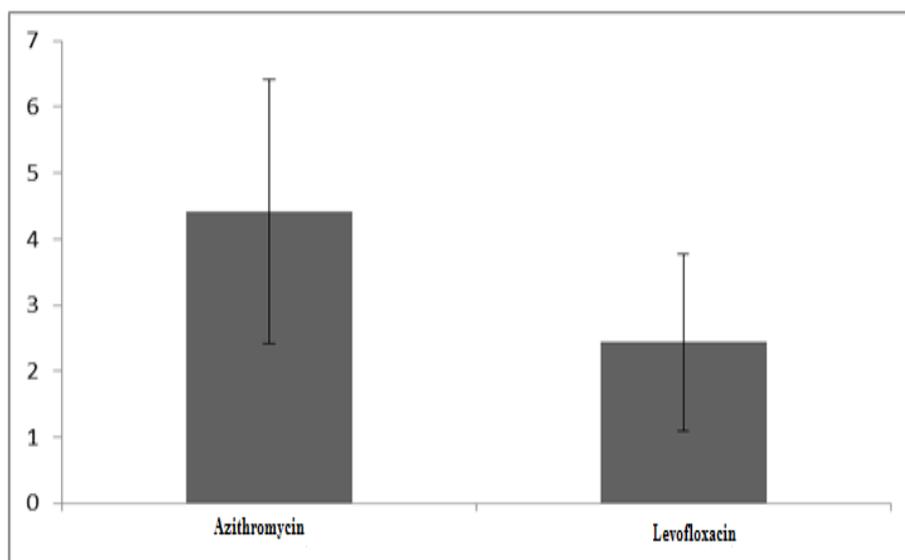
Fig 1. The mean and standard deviation of exacerbations of bronchiectasis per year in levofloxacin and azithromycin groups

According to the obtained findings, the average number of hospitalization cases per year in the azithromycin group was 1.40±0.75 and in the levofloxacin group was 0.60±0.88. According to an independent t-test and the significance level less than 0.05, there is a significant difference between the number of hospitalizations per year in levofloxacin and azithromycin groups (See Table 2 and Fig.2).

Table 2. Comparative means of hospitalizations per year in levofloxacin and azithromycin groups

Variable	Group	Mean	SD	P.Value
Number of hospitalizations	Azithromycin	1.40	0.75	<0.001
	Levofloxacin	0.60	0.38	
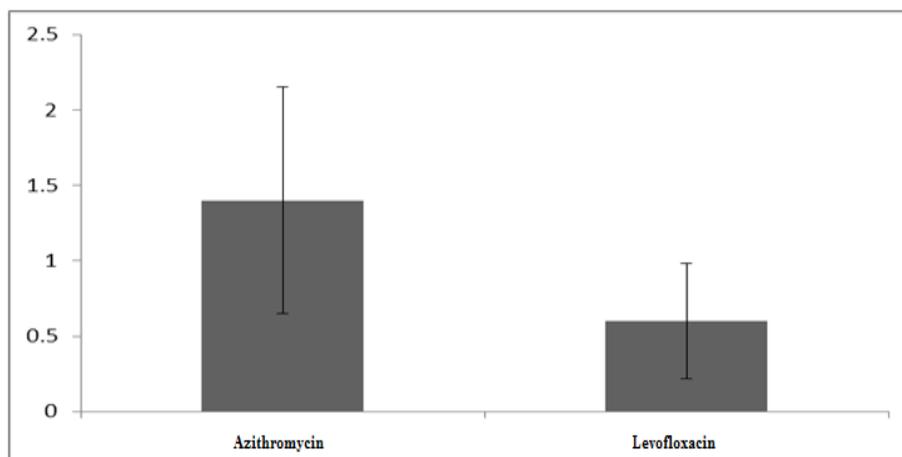
Fig 2. The mean and standard deviation of hospitalizations per year in levofloxacin and azithromycin groups

Discussion and Conclusion

As mentioned, about 64% of patients with chronic bronchiectasis have been infected with pathogenic bacteria that Pseudomonas Aeruginosa and Homophiles Influenzae are the most common pathogens. These infections affect the immune system and respiratory epithelium system of the host. They also cause a vicious infection-inflammation cycle with persistent symptoms, intermittent acute exacerbations, and disease progression. Control of chronic bacterial infection leads to reduced inflammation and evidence indicates that long-term antibiotic treatment can improve the clinical consequence of patients. There has not been any comparative study on the impact of levofloxacin and routine treatments. Accordingly, this comparative study was conducted on the prophylactic effect of short-term treatment with levofloxacin and azithromycin on the bronchiectasis patients who liv in Zahedan, Iran.

According to the findings, the average number of exacerbations of bronchiectasis symptoms per year in the azithromycin group was 4.42±2.00 and in the levofloxacin group, was 2.44±1.34. According to an independent t-test, there was a significant difference between exacerbations of bronchiectasis symptoms per year in levofloxacin and azithromycin groups.

According to the obtained findings, the average number of hospitalization cases per year in the azithromycin group was 1.40±0.75 and in the levofloxacin group was 0.60±0.88. According to the independent t-test and the significance level, there is a significant difference between the number of hospitalizations per year in levofloxacin and azithromycin groups.

K.W.T. Tsang and colleagues carried out a comparative study on the efficacy of levofloxacin and ceftazidime in acute exacerbation of bronchiectasis. They divided patients into two groups of oral levofloxacin (300mg b..d.) and ceftazidime (1g I .v.t.d) and reported a significant improvement in 24-h sputum volume, cough score, and dyspnea score in both group but there was not any significant difference between these two groups. However, the administration duration of levofloxacin was lower and this made it the better choice [15].

Conroy Wong and colleagues (2012) conducted a study in New Zealand to examine the effect of azithromycin in the prevention of exacerbation in bronchiectasis. They evaluated 71 patients in azithromycin (300mg daily 3 times a week for 6 months) and 70 patients in the placebo group and reported exacerbation rates of 0.59 and 1.57 per patient in azithromycin and placebo groups, respectively. There was not any significant difference between these two groups [16]. In the present

paper, exacerbation in the azithromycin group was higher that was not matched with the findings of the abovementioned study. Further studies should be done to examine the exacerbation and hospitalization rate in bronchiectasis patients who use azithromycin and levofloxacin.

The results obtained from the present study indicated a significant difference between numbers of exacerbation and hospitalization in levofloxacin and azithromycin groups although the levofloxacin group indicated more optimal results. However, it is essential to conduct more studies on the impact of azithromycin and levofloxacin on the exacerbation and hospitalization rate in patients with bronchiectasis. It is suggested carrying out similar research for a larger population in other cities of Iran. Moreover, it is recommended to consider more accurate control terms to find the effects of these two drugs (regardless of the impact of other factors) on the exacerbation and hospitalization rate in patients with bronchiectasis. Finally, it is required to conduct studies on the advantages and side effects of these drugs within a long-term follow-up.

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