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Impact Of Moxifloxacin On Exacerbation Frequency And Potential Pathogenic Microorganisms In Chronic Bronchitis

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Abstract

Chronic bronchitis is a typical respsiratory disorder that is typified by continuous cough, sputum, and inflammation of the airways, which may develop repetitive attacks in most cases. The period between these exacerbations which are usually caused by the bacterial pathogens may lead to frequent hospitalization and lung functioning deterioration. The aim of the study was to compare the effects of moxifloxacin, a fluoroquinolone antibiotic and placebo in exacerbation management and maintenance of potential pathogenic microorganisms (PPM) in the sputum of patients with chronic bronchitis. One hundred and sixty patients were randomly allocated to two groups, 80 patients received moxifloxacin and 80 patients received placebo. The main outcome was the rate of exacerbations and secondary ones were the results of the sputum culture, PCR to identify PPMs, and the presence of these microorganisms after 2 weeks, 8 weeks and 5 months of follow-up. The 2-week follow-up showed that the percent of patients with persistent PPMs in sputum was significantly lower with moxifloxacin than with placebo (25% vs. 70% p=0.01). Nevertheless, there was no major difference between the acquisition of new PPMs or long-term exacerbation. The logistic regression analysis demonstrated that when the follow-up was characterized by the acquisition of a new PPM, the risk of exacerbation was significantly high (OR 9.63, 95% CI: 1.0191.64). These results indicate that moxifloxacin might decrease the persistence of microbes in the short-term, but it is not clear how this drug will affect the preventive of new infections and exacerbation in the long term. Continuous monitoring of the new PPMs will be necessary in treating the chronic bronchitis attacks.

Keywords: Chronic bronchitis, moxifloxacin, exacerbations, potential pathogenic microorganisms (PPMs), sputum culture

Introduction

Chronic bronchitis is a symptomatic disease affecting the respiratory system, especially in former smokers, and is manifested by permanent cough and sputum, airways inflammation(1). It is frequently linked with the frequent exacerbations that may result in the higher number of hospitalizations, worsening of the lung functioning, and a decline of the quality of life (2). Chronic bronchitis is normally treated by use of bronchodilators, inhaled corticosteroids and antibiotics in instances of bacterial infection. Bacterial pathogens are often identified to cause exacerbations, and are found in the sputum of an affected patient. Haemophilus influenzae, Haemophilus parainfluenzae, Moraxella catarrhalis, and other possible pathogenic microorganisms (PPMs) are usually isolated among them (3,4). The fact that these pathogens persist in the follow-up may be connected with the risk of additional exacerbations, which can result in additional interventions occurring. Moxifloxacin is a broad-spectrum fluoroquinolone antibiotic that has demonstrated activity in a range of respiratory pathogens, and those that are currently of concern in the attack of chronic bronchitis. Nevertheless, the value of moxifloxacin in exacerbation prevention, especially its impact on the continuation of PPMs in sputum, is still under research (5,6). Although antibiotics are commonly employed in acute exacerbations, the effects of antibiotic therapy on long-term outcomes, including the decreased microbial persistence and the risk of occurrence of further exacerbations, are not well comprehended. The current study will be used to compare the effect of moxifloxacin versus placebo on chronic bronchitis patients, and the variables to be assessed will be exacerbation cases and persistence of PPMs in the follow up. In a five-month trial, it was moxifloxacin that was tested in relation to its possible usage in managing chronic bronchitis (7-9). Moreover, the paper investigated the acquisition of microorganisms that were new in relation to exacerbations in the process of follow-up. The patients with chronic bronchitis were divided into two groups of 160 patients randomly divided into moxifloxacin treatment and placebo treatment. The main outcome was the rate of exacerbations, whereas as the secondary outcomes were the frequency of PPM in the sputum, PCR results of PPM, and the persistence of PPM at the 2 week, 8 week, and 5 months follow-up. The follow-up data analyzable by us had a logistic regression model with the adjustment of pulmonary function and age.

Methodology

The purpose of the study was to examine the impact of moxifloxacin versus placebo in patients with chronic bronchitis with regard to exacerbations and the presence of the possible pathogenic microorganisms (PPM) in sputum. One hundred and sixty patients were recruited and 80 in the placebo and 80 in the moxifloxacin group. The patients were matched using the baseline parameters such as age, gender, smoking status, and parameters of pulmonary function such as post-bronchodilator FVC and FEV1.
Inclusion Criteria: The patients having a clinical diagnosis of chronic bronchitis and having frequent exacerbations were included. The mean age of both of the groups was 69 years old and 95 percent of the participants were males. Only those who had history of chronic bronchitis were subject to the study with a large proportion of those who were in the placebo group (95%), and those in the moxifloxacin group (100%) fulfilling this requirement.

Exclusion Criteria: Patients with other comorbidities like severe cardiovascular diseases and active cancer were excluded and those whose conditions would affect the treatment regimen. Patients that were already taking other antibiotics or treatments that would confound the results were also excluded.

The treatment plan involved oral moxifloxacin (400mg/day) in the group with moxifloxacin and a similar placebo in the placebo group. Both treatments were run over the 2 weeks and were followed up at after 2 weeks, 8 weeks and 5 months. The most important outcome was the event of exacerbations, which is an increase in the intensity of symptoms that necessitated medical care. The secondary outcomes were the results of the sputum culture, PCR of PPMs and persistence of their presence during the follow-up. Sputum samples were also taken at every follow-up to be analyzed by microbiologists and PCR to detect PPMs.

Statistical Analysis:

Baseline characteristics were summarized with the use of a descriptive statistical analysis. A Chi-square test was conducted on categorical variables and t-test on continuous variables that compared the groups. Logistic regression model adjusting the age and post-bronchodilator FEV1% predicted was applied to determine factors related to exacerbation in the follow-up. This was a way to compare moxifloxacin and placebo since the presence and strength of bacteria was objective.

Result

Table 1 indicates that the average age of patients in both groups was approximately the same with 69 years as the average of the patients in the placebo group and the moxifloxacin group. There were 95% males per 5% females in both groups where 95% of the participants were males. Current smokers were only found in 5% in both groups and the moxifloxacin group smoked the most tobacco (49±24 pack-years) as compared to the placebo group (43±21 pack-years). Moxifloxacin and placebo treated patients with chronic bronchitis reported 95% and 100% of cases respectively. The patients who were treated with moxifloxacin (30 percent) were more prone to cardiovascular comorbidities compared to those who were treated with placebo (40 percent). Regarding past exacerbation, 60 percent of the persons taking moxifloxacin had more than two in the past year to 30 percent taking placebos. The rate of hospitalization was also greater in a placebo group as compared to that of a control group (20% vs. 15%). There was an improvement of forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) in the placebo group (78 24 and 53 16) compared to the moxifloxacin group (70 18 and 47 15). The use of inhaled corticosteroids was very high in both groups as placebo patients used it 80 and moxifloxacin patients used it 75 percent of the times. There were also some significant differences between patients in the placebo group and those in moxifloxacin group in terms of sputum characteristics with Haemophilus influenzae being present in 55 percent of placebo patients and 40 percent of moxifloxacin patients. Moxifloxacin was also linked to a higher prevalence (55% vs. 30% of Haemophilus parainfluenzae) when compared to placebo group. The results of the follow-ups at two weeks, eight weeks and five months follow-up are depicted in the table below. Two weeks later, sputum PPMs in the moxifloxacin arm had reduced by 25% (p=0.01) in comparison with the placebo arm (70%). The two groups had positive sputum samples, but the difference was not significant (p= 0.19). The placebo group gained more PPMs (35% vs 10%) as compared to the moxifloxacin group (p=0.013). The difference though was not statistically significant. Moxifloxacin had no statistically significant difference (p=0.18) in PPM persistence 8 weeks in placebo and moxifloxacin groups. The two groups were not different insofar as the acquisition of new PPMs (70% versus 60% in the moxifloxacin group versus the placebo group, p>0.25) is concerned. Table 3 showed that there were significant correlations between exacerbation and follow-up variables. The persistence of PPM that occurred at randomisation did not seem to be connected to exacerbation (OR 0.45, 95% confidence interval 0.04-4.51). Moxifloxacin had a small, but not significant, increase in the rate of exacerbation (OR 1.38, 95% CI: 0.33-0.76). The factor of other infections as major causes of

exacerbation was related to the higher risk of exacerbations (OR 9.63, 95% CI: 1.01-91.64) at a follow-up compared to the past PPMs. Due to these findings, it appears relevant to observe new PPMs in the process of follow-up because it can be one of the risk factors of exacerbations.

Table 1: Symptoms of patients receiving placebo and doxifloxacin at baseline

Characteristics	Placebo (n=80)	Moxifloxacin (n=80)
Age (years)	69±10	69±7
Gender		
Males	76 (95%)	76 (95%)
Those who smoke currently	4 (5%)	4 (5%)
Smoking (pack-years)	43±21	49±24
Inflammation of the bronchi	76 (95%)	80 (100%)
Heart disease and comorbidities	32 (40%)	24 (30%)
An exacerbation within the past year	24 (30%)	48 (60%)
Hospitalizations in the past year	16 (20%)	12 (15%)
FVC % following bronchodilator	78±24	70±18
FEV1 percentage postbronchodilator	53±16	47±15
Corticosteroid treatment with inhalation	64 (80%)	60 (75%)
Aspects of sputum		
Washington-Murray ≥3	56 (70%)	56 (70%)
The influenza virus		
Themes	44 (55%)	32 (40%)
106 CFU per mL, divided by 1	30 (0.5–60)	30 (1–50)
Parainfluenza virus		
Themes	24 (30%)	44 (55%)
(1 x 106×CFU·mL−1)	0.7 (0.4–188)	0.6 (0.1–4.2)
Catarrhal microorganisms	4 (5%)	4 (5%)
Pneumococcus streptococcal	2 (5%)	4 (10%)
Species of enterobacteria	2 (5%)	0
Antimicrobial	4 (5%)	12 (15%)

Table 2: Follow-up Outcomes and Sputum Characteristics at 2-week, 8-week, and 5-month Follow-ups in Placebo and Moxifloxacin Groups

Characteristics	Placebo (n=80)	Moxifloxacin (n=80)	p-value
At 2-week Follow-up			
Smoke PPMs	56 (70%)	20 (25%)	0.01
Positivity of sputum culture	40 (50%)	20 (25%)	0.19
Test for PPM positive by PCR	16 (20%)	0	0.09
Maintaining PPM	28 (35%)	12 (15%)	>0.25
Purchase of new PPMs	28 (35%)	8 (10%)	0.13
Eight-week follow-up			
Sputum cultures that are positive	64 (80%)	60 (75%)	>0.25
Maintaining PPM	20 (25%)	4 (5%)	0.18
Purchase of new PPMs	48 (60%)	56 (70%)	>0.25
Eight-week follow-up PPMs			
The influenza virus	40 (50%)	16 (20%)	0.10
Parainfluenza virus	28 (35%)	36 (45%)	>0.25
Aspergillus niger	0	4 (5%)	>0.25
Catarrhal microorganisms	4 (5%)	4 (5%)	>0.25
Antimicrobial	8 (10%)	0	>0.25
A follow-up of 5 months			
Those with exacerbations	20 (25%)	24 (30%)	>0.25
(Days between exacerbations)	60±32	74±39	>0.25

Table 3: Logistic Regression Model Results for Variables Associated with Exacerbation During Follow-up

Variables	OR (95% CI)
Persistence of PPM isolated at randomisation	0.45 (0.04–4.51)
Treatment with Moxifloxacin	1.38 (0.33–5.76)
Acquisition of a new PPM during follow-up	9.63 (1.01–91.64)

Discussion

This paper was aimed at evaluating the effects of moxifloxacin relative to placebo on chronic bronchitis patients in terms of the rate of exacerbations and persistence of potential pathogenic microorganisms (PPMs) in sputum during a 5-month follow-up period (10-13). The findings show that although the two groups differed to some extent, the clinical and microbiological outcomes differed significantly depending on the presence and persistence of PPMs, which explains the need to monitor cases of microbial infections among patients of chronic bronchitis. The demographic variables, including age, gender, and smoking status, demonstrated the baseline characteristics of the two groups showed that the placebo and moxifloxacin groups were identical in terms of demographic characteristics. Most of the patients in the two groups had previous chronic bronchitis and there was an equal number of patients in the two groups receiving inhaled corticosteroids. Yet, the moxifloxacin group consumed a bit more tobacco that may affect the level of chronic bronchitis and the frequency of attacks. In spite of these base similarities, there were variations in clinical history of exacerbations whereby a higher number of patients in the moxifloxacin group (60%) had more than two exacerbations in the last year than in the placebo group (30%). This implies that the moxifloxacin group experienced a greater burden of disease at the time of onset of the study and this could affect the results. The follow-up data showed certain impressive trends. The moxifloxacin group had a significant decrease in the percentage of patients with persistent PPMs in the sputum as compared to the placebo group at the 2-week follow-up (25% vs. 70%, p=0.01). This implies that so far it can be proposed that moxifloxacin can be used to decrease the number of microbes in the airways in the short run. The positive sputum cultures were not however significantly different between the two groups (p=0.19), neither was the acquisition of new PPMs significantly different (p=0.13). It means that moxifloxacin might decrease the survival of PPMs, but has no significant effect on the occurrence of new infections in the short-term perspective. At 8 weeks follow-up, although there was a tendency towards less PPM persistence in the moxifloxacin group (5percent vs. 25 percent), this was not statistically significant (p=0.18). This may indicate that the usefulness of moxifloxacin in the PPM persistence reduction process is more evident at the beginning of treatment but it does not always promote the microbiological results in the long-term. On the same note, there was no significant difference between the groups at 8 weeks in the acquisition of new PPMs (p>0.25). According to the logistic regression analysis (Table 3) it became evident that the risk of exacerbation was more likely with the acquisition of a new PPM during follow-up (OR 9.63, 95% CI: 1.0191.64), which means that new infections are significant contributory factors to exacerbation. Though there was no statistically significant relationship with exacerbations between treatment with moxifloxacin (OR 1.38, 95% CI: 0.33576), it demonstrated a tendency of the slight increase in exacerbations, which may be because of the greater burden of disease at the baseline of this group. The exacerbation risk was not significantly linked with the persistence of PPMs isolated at randomization (OR 0.45, 95% CI: 0.044.51) which could potentially be attributed to the observation that chronic bronchitis exacerbations depends on a number of factors including but not confined to microbial infections. This implies that PPM persistence might be a contributing factor in disease progression but other things like environmental exposures and comorbidities in the patient, would most probably have a significant role in exacerbations (14,15). The results of the present research highlight chronic bronchitis management as a complex issue. Although moxifloxacin seems to produce a temporary beneficial effect on the persistence of the PPMs, its effect on the exacerbation prevention is less evident in the long-term. Acquisition of new PPMs in the course of follow up was closely related to exacerbations and that showed that continuous monitoring of microbial infections is paramount in the management of such patients. This should be followed by future research on the long-term impacts of moxifloxacin and other antibiotics on new infections and exacerbations prevention and on the establishment of different with regard to therapeutic methods to reduce the disease burden in chronic bronchitis patients.

Conclusion

This research is quite informative about the moxifloxacin utility in chronic bronchitis treatment particularly in terms of exacerbation decrease and persistence of the possible pathogenic microorganisms (PPMs) in sputum. Though the outcomes indicate that moxifloxacin could have a positive change in the short-term reducing the persistence of PPMs, it did not have a significant effect on the acquisition of new PPMs and long-term exacerbation. The huge decrease in PPM persistence at the 2-week follow-up (25 vs. 70, p=0.01) indicates that moxifloxacin may be used to successfully decrease the airways load of microbes at the initial treatment phases. Nonetheless, the absence of any meaningful differences in the outcome of sputum cultures was also shown, as well as the attainment of fresh PPMs in the two groups, which points to the fact that moxifloxacin can be not so effective in preventing new infections or microbiological relapses in the long-

term. The logistic regression analysis showed that the risk of acquiring a new PPM in follow-up was significantly related with a higher risk of exacerbation (OR 9.63, 95% CI: 1.0191.64) and the role of microbial infections in exacerbation pathogenesis is important. Even though there was no significant difference in the presence of exacerbation in the presence of moxifloxacin and placebo (or OR 1.38, 95% CI: 0.33576), the outcomes indicate that the continuous monitoring of new infections is necessary to manage the chronic bronchitis and prevent exacerbations. The PPMs persistence at randomization were not also significantly associated with exacerbations, which means that additional causes might be comorbidities, environmental exposures, and the severity of the disease, among others, are the factors contributing to the risk. These results highlight the multifacetedness of the treatment of chronic bronchitis and its attacks. Although moxifloxacin might have some short-term effects concerning the decrease of microbial persistence, the long-term effects of this agent regarding the prevention of exacerbations are less evident. It is important to consider the prospective research on the prophylaxis of new infections, asthma attacks, and microbiological relapses with moxifloxacin and other antibiotics. Also, other therapeutic interventions and approaches that can be used to treat the multifactorial aspect of chronic bronchitis and eventually enhance patient outcomes and quality of life in the long term should be investigated in future studies.

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