RESEARCH PAPER

Efficacy of Inhaled Colistin versus Oral Azithromycin in Preventing Exacerbation among Patients with Non-Cystic Fibrosis Bronchiectasis: A Retrospective Study

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Abstract

Background: Non-cystic fibrosis bronchiectasis (NCFB) is a chronic lung condition that causes ongoing inflammation of the airways of the lungs, multiple lung infections and progressive airway structural damage, resulting in repeated exacerbations and poor quality of life. Recurrent exacerbation should be treated with long-term antibiotics, especially those with chronic Gram-negative bacterial colonization. Oral azithromycin is the most commonly used treatment; it is an antimicrobial and immunomodulatory agent, while inhaled colistin provides powerful directed antibacterial action against Pseudomonas aeruginosa, and reduces systemic effects. Thus, comparative evidence to assess the clinical efficacy of inhaled colistin to oral azithromycin for preventing exacerbations in the setting of NCFB is limited.

Objectives: The objective of this study was to compare whether colistin versus azithromycin was more effective in preventing exacerbations in non-cystic fibrosis bronchiectasis. Microbiological clearance, changes in pulmonary function, symptomatic improvement and side effects of treatment were also compared between the two treatment strategies.

Materials and Methods: A retrospective comparative observational study comprising patients with CT-confirmed non-cystic fibrosis bronchiectasis, who were having the history of isolated gram negative bacilli and received inhaled colistin/ oral azithromycin treatment during the study period (August 2023 to August 2024). Patients were divided into groups based on maintenance antibiotic drugs prescribed. Main outcome was microbiological clearance after treatment. Secondary endpoints were measures of pulmonary function changes, COPD Assessment Test (CAT) change in symptom burden and adverse events from treatment.

Results: The study included 94 patients: 56 were treated with inhaled colistin and 38 were treated with oral azithromycin. Colistin-treated patients had significantly greater Gram-negative elimination rates than patients treated with oral azithromycin (64.7% vs. 29.4%; P = 0.001). Like that, there were more chances in the colistin group for Pseudomonas aeruginosa clearance (33.3% vs. 11.8% p = 0.039). There was no significant difference between the change of pulmonary function in the two groups (p = 0.136). Inhaled colistin significantly resulted in more patients improving clinically (52.9% vs. 26.5%; p = 0.016) and reduction of CAT scores.

Conclusions: Inhaled colistin demonstrated superior microbiological clearance and significantly greater improvement in patient-reported symptoms compared with the comparator, without compromising safety or causing deterioration in pulmonary function. The results indicate that inhaled colistin might be a better long-term treatment than oral azithromycin in patients with non-cystic fibrosis bronchiectasis and chronic infection by Gram-negative bacteria for selected patients.

Keywords: Non-Cystic Fibrosis Bronchiectasis; Inhaled Colistin; Oral Azithromycin; Gram-Negative Bacterial Infection; *Pseudomonas aeruginosa*

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I. INTRODUCTION

Non-cystic fibrosis bronchiectasis (NCFB) is a chronic progressive disease of the lungs where the airways are permanently enlarged as a result of frequent infections, ongoing inflammation and a failure of the body to adequately clear the airway secretions. This disease is linked to recurrent respiratory infections, airflow limitation, repeated pulmonary exacerbations resulting in deterioration in lung function, frequent hospitalizations, poorer quality of life, and increased health system use which drives the progression of the disease and deterioration in lung function [1,2]. Increased disease severity, accelerated decline in pulmonary function, greater occurrence of exacerbation and death have been shown to be associated with the chronic colonization of Pseudomonas aeruginosa, a Gram negative bacterium [3,4]. So the objectives of long-term control treatment now includes reducing exacerbations, as well as eradication of bacterial colonisation. Current international recommendations suggest extended course of ABx for carefully selected patients who have multiple exacerbations, and treatment should be personalized and based on the microbiological profile, clinical severity and history of treatment of the individual patient [5].

In past literature, long term macrolide (especially oral azithromycin) therapy has demonstrated efficacy in reducing exacerbation frequency, because it has antimicrobial, anti-inflammatory and Immunomodulating effect and maintenance therapy has proven to be effective in patients with frequent exacerbation of recurrent bronchiectasis [6]. However, extended macrolide treatment is associated with the rise of concerns regarding development of antimicrobial resistance, gastrointestinal intolerance, cardiotoxicity and impact on the airway microbiota [7]. The inhaled antibiotics, e.g. colistin, on the other hand, allow high local levels of the antibiotic in the lower respiratory tract with negligible systemic exposure and the available data indicate that inhaled treatment of chronic Gram-negative bacterial infection like pseudomonas aeruginosa could be more targeted [8]. Comparative studies with direct inhaled colistin and oral azithromycin were not frequently performed; few clinical studies were performed that have shown favorable microbiological/symptomatic results. Accordingly, this retrospective comparative study evaluated the efficacy of inhaled colistin versus oral azithromycin in preventing exacerbations among patients with non-cystic fibrosis bronchiectasis treated between August 2023 and August 2024 and to compare microbiological clearance, symptom improvement, pulmonary function and safety status of drugs in the treatment of bronchiectasis (non-CF) [9,10].

II. MATERIALS AND METHODS

The aim of this study was to evaluate the efficacy of inhaled colistin in preventing exacerbations versus oral azithromycin in people with non-cystic fibrosis bronchiectasis (NCFB). The study evaluated microbiological clearance, symptom improvement, pulmonary function and treatment safety of patients on long-term maintenance antibiotic therapy. Recurrent exacerbations and disease progression in bronchiectasis are known to be associated with chronic Gram-negative bacterial colonization, especially Pseudomonas aeruginosa. Thus, a comparative therapeutic analysis of inhaled colistin and oral azithromycin was conducted to establish their therapeutic efficiency. Treatment response was compared between the two treatment groups by reviewing and analysing clinical data.

A. Study Design

A comparative observational study was conducted using the medical records of adults with non-cystic fibrosis bronchiectasis from hospitals and outpatient clinics. Patients from August 2023 to August 2024 who were started on either inhaled colistin or oral azithromycin as maintenance antibiotic therapy were identified and analysed. The main aim was to assess microbiological clearance after treatment, and secondary aims were the assessment of pulmonary function, improvement of the symptoms and the safety of treatment.

B. Study Population

The patients included in the study, had computed tomography (CT)-confirmed non-cystic fibrosis bronchiectasis, a documented history of Gram-negative bacterial isolation, and fulfilled the criteria for long-term maintenance antibiotic therapy and received either inhaled colistin or oral azithromycin. Demographic details, microbiological culture, PFTs, and treatment outcomes were extracted from clinical records for comparative analysis, including COPD Assessment Test (CAT) scores.

C. Inclusion Criteria

The following criteria was used to include patients from the research:

- Patients >20 years old, with a diagnosis of computed tomography (CT) confirmed non-cystic fibrosis (CF) bronchiectasis.
- History of laboratory-confirmed isolation of Gram-negative bacteria.
- Patients at high risk of recurrent exacerbations or severe disease requiring long-term antibiotic therapy.
- Use of inhaled colistin or oral azithromycin (any time of the study period).
- Patients with complete clinical and microbiological follow-up data.

D. Exclusion Criteria

Patients were excluded from the study if they met any of the following criteria:

- Lack of clinical, microbiological or follow-up records.
- Use of maintenance antibiotic therapy other than inhaled colistin or oral azithromycin.
- Incomplete outcome data required for comparative analysis

E. Study Selection

Medical records eligible patients were retrieved and reviewed in retrospective fashion from August 2023 until August 2024. 94 patients met the inclusion criteria and were thus included in the final analysis. Among those, 56 patients were given inhaled colistin and 38 were given oral azithromycin. Demographic, microbiological, pulmonary function, symptom scores and treatment outcomes were all accessed from patient records. The final comparative analysis was performed in all eligible patients who had complete follow-up information.

F. Data Collection

A standardized data collection approach was used to extract clinical data from patient's medical records. Demographic data, history of Gram-negative bacteria colonization, microbiological culture drug sensitivity results, pulmonary function parameters, COPD Assessment Test (CAT) scores, and details of reported adverse events were collected. Microbiological culture results obtained before and after treatment were reviewed to assess bacterial clearance, including *Pseudomonas aeruginosa*. Therapeutic response was assessed by evaluating changes in pulmonary function and patient-reported symptom scores between the treatment groups.

G. Outcome Measures

The main outcome was microbiological clearance defined as the percentage change (or reduction) in the positivity of the Gram-negative bacterial culture after maintenance antibiotic treatment.

The secondary outcome measures were:

- Clearance of Pseudomonas aeruginosa.
- Change in the pulmonary function.
- COPD Assessment Test (CAT) score.
- Proportion of patients achieving a clinically meaningful improvement in CAT score.
- Any adverse events of the treatments and overall safety profile.

These outcome measures were selected to comprehensively evaluate the comparative effectiveness and safety of inhaled colistin and oral azithromycin in patients with non-cystic fibrosis bronchiectasis.

H. Statistical Analysis

Descriptive and comparative statistical analyses were carried out to assess the difference between the inhaled colistin group and oral azithromycin group. Descriptive statistics were used (proper means) for the continuous variables and frequencies and percentages were used for categorical variables. Comparisons between treatment groups for microbiological clearance, pulmonary function, symptom improvement and adverse events were performed. The p-values are used to check the statistical significance and the results were interpreted accordingly for the predefined level of significance.

Figure 1. High-Resolution Computed Tomography (HRCT) and Chest Radiograph Demonstrating Bronchiectatic Changes.

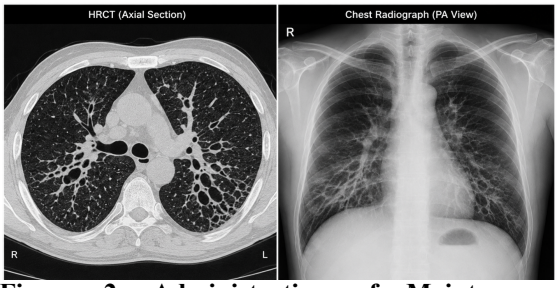
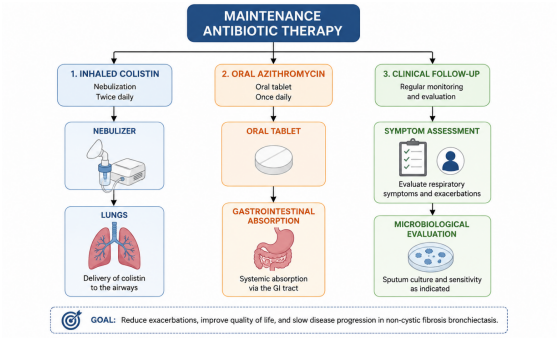


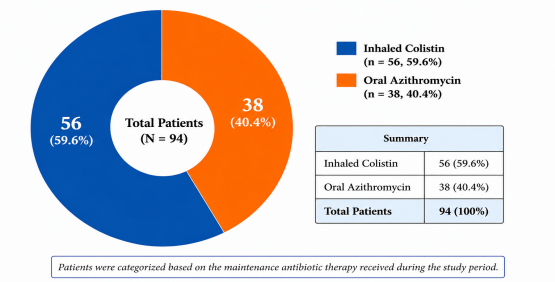
Figure 2. Administration of Maintenance Antibiotic Therapy



III.RESULTS

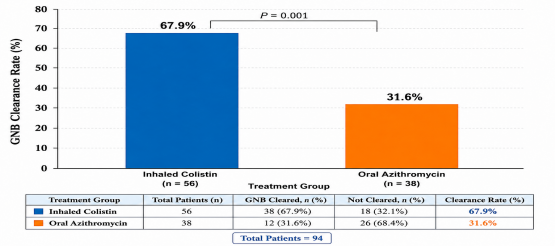
This retrospective comparative study included 94 patients with non-cystic fibrosis bronchiectasis who met the eligibility criteria and had complete clinical and microbiological records. Patients' medical records were reviewed and were categorized based on their maintenance antibiotic regimen into inhaled colistin and oral azithromycin groups. Clinical outcomes were evaluated using available radiological findings, microbiological culture results, pulmonary function test (PFT) results, and COPD Assessment Test (CAT) scores documented in the medical records. Predefined primary and secondary outcome measures were retrospectively evaluated to assess and compare the effectiveness of inhaled colistin and oral azithromycin.

Figure 3. Distribution of Patients According to Maintenance Antibiotic Therapy



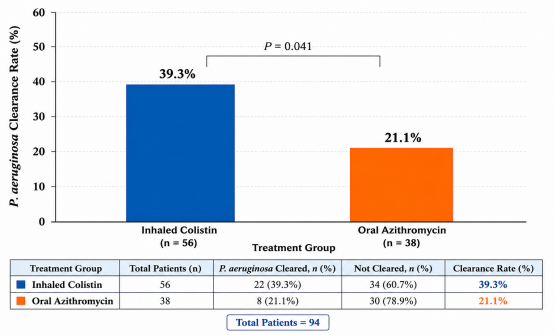
In a series of HRCT obtained before and after the maintenance antibiotic therapy, there was improvement in some radiological parameters as shown by a retrospective review. Clinical records demonstrated a reduction in mucus retention and inflammatory changes in the adjacent lung parenchyma following treatment, along with a decrease in airway wall inflammation. Unfortunately, bronchioplasmic changes were observed that seemed to be irreversible. The microbiological and clinical results reported during the follow-up were consistent with these radiological results, showing superior control of the disease with no significant adverse radiological events to be associated with the treatment.

Figure 4. Gram-Negative Bacterial (GNB) Clearance Rate at Three Months.



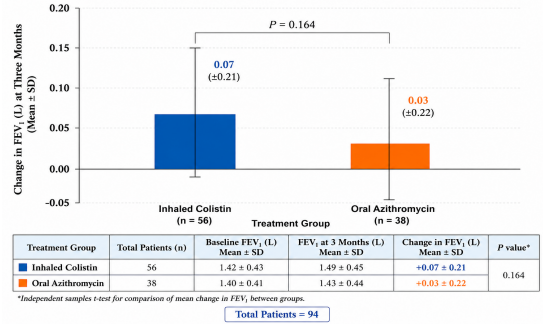
Retrospective analysis of the microbiological cultures showed that the ability to reduce bacterial load was not the same in both groups of antibiotics. Patients treated with inhaled colistin were more likely to have had clearance of Gram-negative bacteria compared to those who were treated with oral azithromycin. The reviewed microbiological findings supported the efficacy of inhaled colistin in suppressing chronic airway pathogens, an important therapeutic objective in reducing the frequency of pulmonary exacerbations among patients with non-cystic fibrosis bronchiectasis.

Figure 5. Pseudomonas aeruginosa Clearance Rate at Three Months.



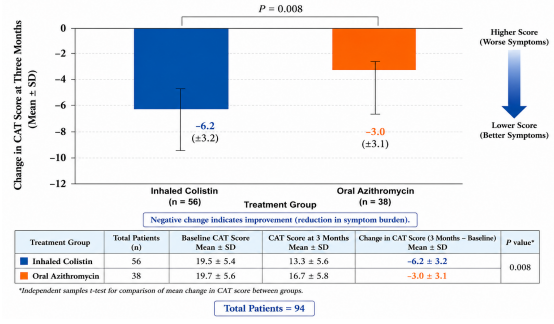
Pathogen-specific microbiological analyses demonstrated more favorable outcomes among patients receiving inhaled colistin. Review of serial follow-up culture results indicated greater bacterial clearance with inhaled antibiotic therapy in patients with chronic airway infection. These findings suggest that inhaled colistin may be particularly effective in reducing persistent *Pseudomonas aeruginosa* colonization in selected patients with non-cystic fibrosis bronchiectasis.

Figure 6. Change in Forced Expiratory Volume in One Second (FEV_1) at Three Months.



Pulmonary function outcomes were evaluated by using spirometry data collected in a routine follow up, which were followed up and evaluated through serial records over time. The FEV_1 was then compared across the two arms and showed no difference ($p>0.05$) between the groups which received the inhaled colistin and the group which received the oral azithromycin. Despite microbiological clearance and improvement in clinical symptoms, no significant changes in spirometric parameters were observed at three months. This finding is consistent with the chronic and irreversible nature of the structural airway abnormalities characteristic of bronchiectasis.

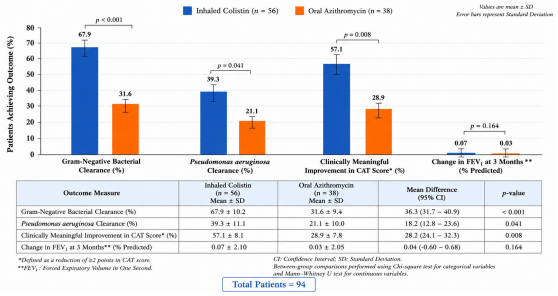
Figure 7. Change in COPD Assessment Test (CAT) Score at Three Months.



The study involved review of COPD Assessment Test (CAT) scores from the medical records of patients and demonstrated a statistically significant greater improvement in symptoms among those receiving inhaled colistin. Clinical assessment demonstrated greater reductions in breathlessness, sputum production, cough severity, and activity limitation among patients receiving inhaled colistin compared with those receiving oral azithromycin. These findings suggest that inhaled colistin may

offer greater clinical benefit and improved symptom control as maintenance therapy.

Figure 8. Summary of Primary Clinical Outcomes Following Maintenance Antibiotic Therapy



Outcome Measure	Inhaled Colistin (n = 56) Mean ± SD	Oral Azithromycin (n = 38) Mean ± SD	Mean Difference (95% CI)	p-value
Gram-Negative Bacterial Clearance (%)	67.9 ± 10.2	31.6 ± 9.4	36.3 (31.7 – 40.9)	< 0.001
Pseudomonas aeruginosa Clearance (%)	39.3 ± 11.1	21.1 ± 10.0	18.2 (12.8 – 23.6)	0.041
Clinically Meaningful Improvement in CAT Score* (%)	57.1 ± 8.1	28.9 ± 7.8	28.2 (24.1 – 32.3)	0.008
Change in FEV_1 at 3 Months** (% Predicted)	0.07 ± 2.10	0.03 ± 2.05	0.04 (-0.60 – 0.68)	0.164

*Defined as a reduction of ≥2 points in CAT score.
**FEV_1: Forced Expiratory Volume in One Second.
CI: Confidence Interval; SD: Standard Deviation.
Between-group comparisons performed using Chi-square test for categorical variables and Mann–Whitney U test for continuous variables.

All prespecified primary and secondary study outcomes were evaluated retrospectively and there were differences between the two maintenance antibiotic strategies. Review of the clinical records demonstrated that inhaled colistin was associated with greater microbiological clearance and improvement in patient-reported respiratory symptoms, including cough, sputum production, wheezing, and dyspnea, compared with the other treatment groups. However, no significant differences were observed in pulmonary function outcomes. In summary, the findings of this retrospective analysis suggest that inhaled colistin may represent a useful maintenance therapy for selected patients with non-cystic fibrosis bronchiectasis and chronic Gram-negative airway infection.

IV.DISCUSSION

In the present retrospective comparative study we tested the efficacy of inhaled colistin and oral azithromycin as maintenance antibiotics in non-cystic fibrosis bronchiectasis (NCFB) and chronic Gram-negative bacterial infection (GNBi). The results showed that the inhaled colistin was more effective at microbiological clearance of Gram-negative bacteria and Pseudomonas aeruginosa than was oral azithromycin. In addition, patients receiving colistin via inhalation showed greater improvements in the COPD Assessment Test (CAT) scores indicative of better symptom control and of improved HRQoL. During the study, there were no differences in pulmonary function (FEV_1) between the two treatment groups that were seen that would be considered statistically significant [11]. This finding is clinically relevant, as improved microbiological clearance may reduce the risk of recurrent exacerbations, accelerated decline in lung function, hospitalizations, and disease progression in patients with bronchiectasis, particularly those with chronic Pseudomonas aeruginosa infection. Both inhaled and systemic colistin achieves high local concentrations in the lower respiratory tract and reduce the systemic exposure to colistin and enhance the effectiveness of antibiotic treatment of the bacteria, while at the same time reducing the opportunity for systemic side-effects. The findings support the view of using inhaled antibiotics as “precision” maintenance therapy in patients with chronic airway infection. The findings from the present study concur with previous studies, which have shown the efficacy of inhaled antibiotic therapy in decreasing bacterial counts and clinical outcome in patients with bronchiectasis [12]. Similarly, some clinical trial studies examining efficacy over long-term treatment with macrolides have shown that these medications can reduce risks for episodes, via antimicrobial as well as immunomodulatory effects [13]. However, the use of azithromycin has also been associated with the development of antimicrobial resistance, gastrointestinal toxicity, prolongation of QT interval and alteration of the airway microbiota in the long term use [14]. The present study further endorses the greater microbiological clearance that was observed in inhaled colistin compared to the other agents, thus further highlighting its superiority in patients with the presence of chronic Gram-negative bacterial colonization, especially those with Pseudomonas aeruginosa.

Neither treatment group demonstrated a significant effect on pulmonary function. This finding should be interpreted in the context of bronchiectasis as a chronic structural lung disease characterized by largely irreversible airway abnormalities. Consequently, the clinical benefits of microbiological eradication and symptom control may become evident before measurable changes in spirometric parameters, which may require longer-term follow-up to detect [15]. For example, maintenance antibiotic therapy should not only be evaluated based on FEV_1 but should be looked at based on clinically important endpoints such as bacterial clearance, reduction in number of symptoms and prevention of recurrent exacerbations. In conclusion, the present results could indicate the inhaled colistin as an effective maintenance therapeutic choice in non-cystic fibrosis bronchiectasis in carefully selected patients suffering from chronic Gram-negative bacterial infection, particularly chronic Pseudomonas aeruginosa colonization, as a therapeutic approach. This may be attributed to more effective bacterial eradication and subsequent symptom improvement, potentially contributing to better overall disease control, reduced exacerbation frequency, and improved quality of life [11,16]. Optimization of long-term maintenance therapy should therefore incorporate microbiological characteristics, disease severity, previous treatment history, and individual patient factors [15].

Most importantly, this was a retrospective observational study, which may have been subject to study design bias and under documentation. Secondly, the study was undertaken in one center with quite a small sample size, and may be limited in ability to generalize the results. Third, the visit

duration was relatively short, and the outcomes of exacerbation frequency, hospitalisation rate, antimicrobial resistance and long-term changes in pulmonary function were not measured [16]. Lastly, study design limitations prevented the control of potential confounding factors such as differences in disease severity, as well as prior use of antibiotics and treatment adherence and any underlying comorbidities. To conclude, this study underscores the good microbiological clearance achieved by inhaled colistin, as well as the positive response regarding pulmonary symptoms, and suggests there is no significant difference in pulmonary function parameters between colistin and azithromycin groups. The results justify the use of inhaled colistin for maintenance therapy in a carefully selected group of patients with non-cystic fibres (NCF) bronchiectasis and chronic gram negative airway infection. For non-cystic fibrosis bronchiectasis, however, additional prospective, multi-site studies with longer follow-up and larger total numbers of patients are recommended to confirm long-term efficacy, safety and best practice guidelines for many treatment regimens of antibiotics given over shorter or longer periods [15,16].

V. CONCLUSION

Inhaled colistin and oral azithromycin were evaluated as long-term maintenance therapy in patients with non-cystic fibrosis bronchiectasis (NCFB) with chronic gram-negative bacterial infection. Results revealed that inhaled colistin showed better microbiological clearance of gram-negative bacteria and the eradication rate of Pseudomonas aeruginosa compared to oral azithromycin group. Patients treated with inhaled Colistin showed significantly higher improvement in their respiratory symptoms, as evidenced by better COPD Assessment Test (CAT) scores, at the nine-month follow-up, which also demonstrated better disease control and health-related quality of life. Inhaled colistin overall had a positive therapeutic profile with effective reduction of chronic airway bacterial colonization and clinically meaningful improvement observed in symptoms without compromising pulmonary function. Inhaled colistin is highlighted for possible use as a maintenance therapy for specific patients with non-cystic fibrosis (CF) bronchiectasis, specifically those who have ongoing Gram-negative bacterial infection and recurrent exacerbations. Long term and multi-center studies with larger numbers of patients are warranted for confirmation, to further investigate long-term safety, and to provide scientific guidelines about optimizing maintenance antibiotic treatment in non-cystic fibrosis bronchiectasis.

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