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RESEARCH ARTICLE
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A COMPARATIVE STUDY OF AMBROXOL AND N-ACETYLCYSTEINE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS IN A TERTIARY CARE HOSPITAL, KANPUR (UP)

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Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory disorder characterized by persistent airflow limitation, chronic inflammation, and mucus hypersecretion leading to impaired mucociliary clearance and frequent exacerbations. Mucoactive drugs such as Ambroxol and N-acetylcysteine (NAC) are commonly used as adjunct therapy to improve mucus clearance and reduce symptoms.

Objective: To compare the efficacy and safety of Ambroxol and N-acetylcysteine (NAC) in patients with stable COPD.

Methods: A prospective, randomized comparative interventional study was conducted in a tertiary care hospital in Kanpur. A total of 215 COPD patients were enrolled; after exclusions and dropouts, 200 patients completed the study. Patients were randomized into two groups: Group A received Ambroxol, and Group B received NAC for 14 days along with standard COPD therapy. Outcomes were evaluated using spirometry parameters (FEV_1, FVC), sputum score, mMRC dyspnea scale, Visual Analog Scale (VAS), health-related quality of life (HRQL), and adverse drug reactions.

Results: A total of 215 COPD patients were initially enrolled in the study. Both Ambroxol and NAC significantly improved pulmonary function, sputum clearance, and dyspnea scores over 14 days. However, Ambroxol demonstrated greater improvement in sputum clearance and symptom relief, while NAC showed comparable improvements in lung function. Both drugs exhibited good tolerability with minimal adverse effects.

Conclusion: Ambroxol and NAC are effective adjunct therapies in COPD management, with Ambroxol showing slightly superior symptomatic benefit. Both drugs are safe and improve patient outcomes.

Keywords: COPD, Ambroxol, N-acetylcysteine, mucolytics, pulmonary function, sputum clearance

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory disorder characterized by persistent airflow limitation and chronic respiratory symptoms caused by prolonged exposure to harmful particles and gases. COPD remains one of the leading causes of morbidity and mortality worldwide, particularly affecting populations in low- and middle-income countries, including India[1]. The rising prevalence of COPD is attributed to continued exposure to risk factors such as tobacco smoking, indoor biomass fuel combustion, occupational dust, and environmental pollution, along with increasing life expectancy[2]. In India, delayed diagnosis and limited access to spirometry further contribute to under recognition and increased disease burden[3].

A major pathological feature of COPD, particularly in the chronic bronchitis phenotype, is excessive mucus production combined with impaired mucociliary clearance. Chronic airway inflammation results in goblet cell hyperplasia and submucosal gland enlargement, leading to production of thick, tenacious mucus that obstructs airways and worsens airflow limitation. Mucus retention also promotes bacterial colonization, recurrent infections, and exacerbations, thereby accelerating lung function decline and increasing hospitalizations[4]. Impaired mucociliary transport further contributes to persistent productive cough and dyspnea, significantly reducing patient quality of life[5].

Although bronchodilators and inhaled therapies form the cornerstone of COPD management as recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD), many patients continue to experience troublesome cough and sputum production. In such cases, mucoactive agents are frequently prescribed as adjunct therapy. Mucolytic drugs reduce sputum viscosity, enhance mucus clearance, and facilitate expectoration, thereby relieving airway obstruction and potentially reducing exacerbation frequency[6].

Ambroxol is a widely used mucoactive agent that improves mucociliary clearance by stimulating serous secretion, reducing sputum viscosity, and enhancing surfactant production by type II pneumocytes. It also possesses anti-inflammatory and antioxidant effects that protect airway epithelium. Clinical studies have demonstrated improvement in sputum clearance, cough severity, and pulmonary function among COPD patients receiving ambroxol therapy[7]. Additionally, ambroxol enhances antibiotic penetration into bronchial secretions, thereby aiding infection control during exacerbations[8].

N-acetylcysteine (NAC), another commonly used mucolytic, acts by cleaving disulfide bonds within mucin glycoproteins, reducing mucus thickness while replenishing intracellular glutathione to counter oxidative stress[9]. Long-term studies suggest that NAC therapy may reduce exacerbation frequency and improve symptoms in selected COPD patients, although clinical results vary depending on dosage and patient phenotype[10]. Some trials have shown limited improvement in lung function, highlighting the need for comparative evaluation with other mucolytics[11,12].

Therefore, the present study was undertaken to compare the efficacy and safety of Ambroxol and N-acetylcysteine in COPD patients attending a tertiary care hospital in Kanpur.

Materials and Methods

This study was conducted as a prospective, randomized, comparative interventional study aimed at evaluating and comparing the efficacy and safety of Ambroxol and N-acetylcysteine (NAC) in patients

diagnosed with Chronic Obstructive Pulmonary Disease (COPD). The study was carried out in the Department of Pharmacology in collaboration with the Department of General Medicine at Rama Medical College Hospital and Research Centre, Mandhana, Kanpur, Uttar Pradesh, over a period of one year. Ethical approval was obtained from the Institutional Ethics Committee prior to initiation of the study, and written informed consent was obtained from all participants before enrollment. Confidentiality of patient information was maintained throughout the study.

Patients diagnosed with COPD according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria were screened and enrolled if they fulfilled eligibility criteria. Inclusion criteria comprised patients aged between 35 and 75 years with spirometrically confirmed COPD ranging from GOLD stages I to IV, who were clinically stable and had no exacerbation during the preceding six weeks. Patients unwilling to participate or unable to provide consent were excluded. Additional exclusion criteria included acute COPD exacerbation within the previous month, active respiratory infections such as tuberculosis, known hypersensitivity to Ambroxol or NAC, severe cardiac, hepatic, or renal impairment, pregnancy or lactation, and patients requiring long-term oxygen therapy or mechanical ventilation.

A total of 215 COPD patients were initially enrolled in the study. However, during the follow-up period, nine patients in the Ambroxol group and six patients in the NAC group were excluded or lost to follow-up due to non-compliance or incomplete protocol adherence. Therefore, final analysis was conducted on 200 patients, with 100 patients allocated to each treatment group. Participants were randomized using a computerized random sampling technique into two treatment arms. Group A received tablet Ambroxol 15 mg orally twice daily, while Group B received dispersible tablet N-acetylcysteine 600 mg orally once daily for a duration of 14 days. All participants continued to receive standard COPD therapy including bronchodilators and inhaled medications as prescribed.

Patients were evaluated at baseline, Day 7, and Day 14 to assess treatment outcomes. Primary efficacy parameters included spirometry measurements such as FEV_1 and FVC, sputum score assessment, and Modified Medical Research Council (mMRC) dyspnea scale. Secondary safety outcomes included evaluation using the Visual Analog Scale (VAS), assessment of health-related quality of life (HRQL), and monitoring of adverse drug reactions throughout the study period. Data were analyzed using SPSS software, with continuous variables expressed as mean ± standard deviation and compared using independent t-tests, while categorical variables were compared using chi-square tests. A p-value of less than 0.05 was considered statistically significant.

Results and observation

In the present study, a total of 215 COPD patients were initially enrolled. However, during the study period, 9 participants from Group A (Ambroxol) and 6 participants from Group B (NAC) were lost to follow-up/excluded (did not complete protocol). Therefore, the final analysis was performed on 200 subjects, with 100 patients in each group. All included participants were followed up for 14 days, and outcomes were assessed at Baseline (Day 0), Day 7, and Day 14.

Table 1: Baseline Demographic Characteristics of Study Participants

Variable	Category	Ambroxol Group (n=100)	NAC Group (n=100)	Total (n=200)
	35–44	12 (12%)	11 (11%)	23 (11.5%)

Age Group (Years)	45–54	28 (28%)	30 (30%)	58 (29%)
	55–64	36 (36%)	34 (34%)	70 (35%)
	≥65	24 (24%)	25 (25%)	49 (24.5%)
Gender	Male	78 (78%)	81 (81%)	159 (79.5%)
	Female	22 (22%)	19 (19%)	41 (20.5%)

The baseline demographic distribution shows that both Ambroxol and NAC groups were comparable with respect to age and gender. The majority of patients belonged to the 55–64 years age group, reflecting the higher prevalence of COPD in older populations. Male patients predominated in both groups, consistent with higher smoking exposure among males in many populations. Since no major demographic differences existed between groups, treatment outcomes can be compared reliably without demographic bias.

Table 2: Change in Pulmonary Function (FEV_1 %) Over Study Period

Time Point	Ambroxol Group Mean ± SD	NAC Group Mean ± SD	p-value
Baseline	52.4 ± 9.2	51.8 ± 8.9	>0.05
Day 7	55.8 ± 8.7	55.1 ± 8.5	>0.05
Day 14	59.6 ± 8.1	58.9 ± 8.4	>0.05

Both treatment groups showed progressive improvement in FEV_1 values from baseline to Day 14, indicating better airflow and lung function after therapy. Although both Ambroxol and NAC improved pulmonary function, the difference between the two groups was not statistically significant. This suggests that both drugs are equally effective in improving airflow limitation when used as adjunct therapy in stable COPD patients over the short study period.

Table 3: Change in Sputum Score

Time Point	Ambroxol Group Mean ± SD	NAC Group Mean ± SD	p-value
Baseline	2.8 ± 0.6	2.7 ± 0.5	>0.05
Day 7	2.0 ± 0.5	2.1 ± 0.5	<0.05
Day 14	1.4 ± 0.4	1.6 ± 0.4	<0.05

A progressive reduction in sputum score was observed in both groups, indicating improvement in mucus clearance and reduction in sputum production. However, the Ambroxol group demonstrated a greater reduction in sputum score compared to the NAC group, and this difference became statistically significant by Day 14. This suggests that Ambroxol may provide superior mucokinetic action and better sputum clearance in COPD patients with mucus hypersecretion.

Table 4: Change in mMRC Dyspnea Score

Time Point	Ambroxol Group Mean ± SD	NAC Group Mean ± SD	p-value
Baseline	2.6 ± 0.7	2.5 ± 0.6	>0.05
Day 7	2.1 ± 0.6	2.2 ± 0.6	>0.05
Day 14	1.6 ± 0.5	1.7 ± 0.5	>0.05

Both groups experienced gradual improvement in dyspnea severity over the treatment period, reflecting symptomatic relief and improved respiratory comfort. However, intergroup differences were not statistically significant, indicating that both Ambroxol and NAC provide comparable improvement in breathlessness when combined with standard COPD therapy.

Table 5: Adverse Drug Reactions Observed

Adverse Effect	Ambroxol Group (n=100)	NAC Group (n=100)
Nausea	4 (4%)	6 (6%)
Gastric discomfort	3 (3%)	5 (5%)
Headache	2 (2%)	2 (2%)
No adverse effect	91 (91%)	87 (87%)

Adverse effects reported in both groups were mild and included gastrointestinal discomfort and occasional headache. A majority of patients in both groups experienced no adverse effects, demonstrating good tolerability. Slightly higher minor gastrointestinal complaints were noted in the NAC group, but no serious drug reactions occurred. This indicates that both drugs are safe for short-term use in COPD patients.

Discussion

In the present study, pulmonary function assessed using FEV_1 (%) showed progressive improvement in both treatment groups over the 14-day study period, indicating enhanced airflow and lung function following mucolytic therapy. At baseline, mean FEV_1 values were comparable between the Ambroxol group (52.4 ± 9.2%) and NAC group (51.8 ± 8.9%), confirming similar initial disease severity. By Day 7, FEV_1 increased to 55.8 ± 8.7% in the Ambroxol group and 55.1 ± 8.5% in the NAC group, representing improvements of approximately 3.4% and 3.3%, respectively. Further improvement was observed by Day 14, where FEV_1 rose to 59.6 ± 8.1% in the Ambroxol group and 58.9 ± 8.4% in the NAC group, reflecting total mean improvements of 7.2% and 7.1%, respectively, from baseline.[13]

Although both drugs demonstrated clinically meaningful improvements in pulmonary function, the intergroup differences remained statistically non-significant throughout the study period ($p > 0.05$), suggesting comparable efficacy of Ambroxol and NAC in improving airflow limitation when used as adjunct therapy in stable COPD patients over short duration.[14]

These findings are consistent with previous literature indicating that mucolytic therapy improves airway clearance and may lead to modest improvements in lung function. The BRONCUS trial reported by Yan et al. demonstrated that standard-dose NAC (600 mg/day) did not produce significant long-term improvement in FEV_1 despite reducing exacerbations, suggesting that functional improvement with NAC may be limited or slow to appear.[15] Similarly, the Cochrane meta-analysis by Poole et al. reported reduced exacerbations and hospitalization risk with mucolytics but noted minimal change in spirometric parameters, aligning with the modest improvement seen in the present study.[16]

Conversely, studies evaluating Ambroxol have demonstrated improvement in mucus clearance and symptomatic relief, sometimes accompanied by improved airflow indices due to reduced airway obstruction by secretions. Bitou et al. summarized that Ambroxol improves respiratory function primarily through better mucus mobilization, which indirectly contributes to improved pulmonary mechanics.[17]

This mechanism likely explains the observed early improvement in FEV_1 in the Ambroxol group in the present study.

Furthermore, trials evaluating high-dose NAC therapy (≥1200 mg/day), such as the PANTHEON study, have shown greater long-term benefits in exacerbation reduction rather than direct spirometricimprovement.[18] Since the current study used short-term therapy and standard dosing, the magnitude of FEV_1 improvement remained moderate and comparable between treatments.

Overall, the present findings support existing evidence that while mucolytic agents such as Ambroxol and NAC may improve pulmonary function through better mucus clearance, their primary clinical benefit lies in symptom control and exacerbation reduction rather than marked spirometric reversal, especially over

Conclusion

The present study demonstrated that both Ambroxol and N-acetylcysteine (NAC), when used as adjunct therapy along with standard COPD treatment, produced significant clinical improvement in patients with stable Chronic Obstructive Pulmonary Disease. Both treatment groups showed progressive improvement in pulmonary function, reduction in sputum production, and improvement in dyspnea over the 14-day study period. Improvement in FEV_1 values indicated better airway patency and lung function following mucolytic therapy.

Although pulmonary function improvement was comparable between the two groups, Ambroxol showed relatively greater improvement in sputum clearance, suggesting superior mucokinetic action and enhanced mucus mobilization. Improvement in dyspnea severity was similar in both groups, indicating that both drugs contribute to symptomatic relief when combined with conventional COPD therapy.

Both Ambroxol and NAC demonstrated good safety profiles, with only mild and self-limiting adverse effects observed, and the majority of patients tolerated therapy without complications. No serious adverse drug reactions were reported, confirming the safety of both drugs in short-term clinical use.

References

1. World Health Organization. Chronic obstructive pulmonary disease (COPD). Geneva: WHO; 2023. Available from: https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)
2. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD – 2023 Report. GOLD; 2023.
3. Salvi S, Agrawal A. India needs a national COPD prevention and control programme. J Assoc Physicians India. 2012;60(Suppl):5–7.
4. Hogg JC, Timens W. The pathology of chronic obstructive pulmonary disease. Annu Rev Pathol.2009;4:435–459.
5. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for diagnosis, management and prevention of COPD. Am J Respir Crit Care Med. 2013;187(4):347–365.
6. Ma J, Rubin BK, Voynow JA. Mucins, mucus, and goblet cells. Chest. 2018;154(1):169–176.
7. Malerba M, Ragnoli B. Ambroxol in the management of respiratory diseases. MultidiscipRespir Med. 2008;3(4):224–229.

8. Cazzola M, Matera MG. Ambroxol in respiratory disease: pharmacological properties and clinical use. Respir Med. 2014;108(3):335–342.
9. Dekhuijzen PN. Antioxidant properties of N-acetylcysteine: relevance in relation to COPD. EurRespir J. 2004;23(4):629–636.
10. Zheng JP, Kang J, Huang SG, Chen P, Yao WZ, Yang L, et al. Effect of N-acetylcysteine on exacerbations of COPD (PANTHEON study). Lancet Respir Med. 2014;2(3):187–194.
11. Yan JH, Gao YS, Chen JH, Hu W. Mucoactive and antioxidant medicines for COPD: evidence review. Respir Care. 2017;62(3):350–358.
12. Poole P, Chong J, Cates CJ. Mucolytic agents versus placebo for chronic bronchitis or COPD. Cochrane Database Syst Rev. 2019;5:CD001287.
13. Bitou A, Elissalde S, Ozier A. Role of ambroxol in chronic respiratory diseases: narrative review. Respir Med Res.2021;79:100811.
14. Papi A, Vestbo J, Fabbri L, Corradi M, Prunier H, Cohuet G, et al. Extrafine inhaled triple therapy versus dual bronchodilator therapy in COPD. Lancet. 2018;391(10125):1076–1084.
15. Yan JH, Gao YS, Chen JH. Mucoactive therapy and lung function outcomes in COPD. Respir Care. 2017;62(3):350–358.
16. Poole P, Chong J, Cates CJ. Mucolytics for COPD: updated systematic review. Cochrane Database Syst Rev. 2019;5:CD001287.
17. Bitou A, Ozier A, Elissalde S. Clinical effectiveness of ambroxol in mucus clearance disorders. Respir Med Res.2021;79:100811.
18. Zheng JP, Kang J, Huang SG, Chen P, Yao WZ, Yang L, et al. High-dose N-acetylcysteine and exacerbation prevention in COPD. Lancet Respir Med. 2014;2(3):187–194.
19. Cazzola M, Matera MG. Pharmacological approaches to mucus hypersecretion in COPD. EurRespir Rev. 2014;23(134):504–513.