INHALED THERAPIES FOR COUGH RESOLUTION IN ACUTE BRONCHITIS: SINGLE CENTER CROSS-SECTIONAL STUDY FROM PAKISTAN

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ABSTRACT

Background: Acute bronchitis is a common clinical problem, usually caused by a viral infection. It presents with troublesome cough as its main symptom, which takes days to a few weeks to resolve. Different therapies have been studied to hasten cough resolution, including inhaled and oral corticosteroids, inhaled bronchodilators, antibiotics, and over-the-counter cough syrups, but no effective treatment has been found to date. The objectives of our study were to assess the time to cough resolution and quality of life (QoL) measures when comparing different inhaled therapies in patients with acute bronchitis.

Methods: A prospective cross-sectional study was performed from March 2023 to March 2024 at an outpatient clinic at a tertiary care center in Pakistan. Patients with acute viral bronchitis were given treatment options of inhaled corticosteroid plus long-acting beta-agonists combination (ICS-LABA), and/or short-acting anti-muscarinic antagonists and/or intranasal steroids. Patients were followed for a period of 3 weeks and the subsequent information about the number of days to cough resolution and the patient satisfaction scores were taken.

Results: Thirty-seven patients were studied. Majority of the participants were female (70.3%), and the mean age of patients was 43.6 ± 17.24 years. The mean duration of cough was 2.35 ± 0.89 weeks. The treatment most prescribed for acute bronchitis was inhaled corticosteroids/long-acting beta2-agonists (ICS-LABA) (73.7%), followed by antihistamines (60.5%), inhaled short-acting muscarinic-antagonist (SAMA) (44.7%), and intranasal steroids (34.2%). The mean duration of cough resolution among patients was 9.09 ± 5.04 days following the start of treatment. The mean satisfaction and improvement in quality of life (QoL) among patients was ranked at 8.14 ± 2.02 on a scale 1-10.

Conclusion: In conclusion, acute viral bronchitis requires an average of 9 days of inhaled therapies to provide cough resolution. Most patients improved significantly in their QoL due to the cough, with the inhaled medications.

Keywords: Bronchitis; Cough; Bronchodilators; Corticosteroid; Quality of Life

INTRODUCTION

Acute bronchitis is the most common cause of ambulatory care visits in the United States, accounting for 2.7 million outpatient visits annually.[1] It is a clinical entity characterized by inflammation of the trachea and larger airways, presenting with cough as the primary symptom, which persists for approximately 3 weeks.[2, 3]

Viruses are implicated in most cases of acute bronchitis with bacteria accounting for less than 10% of the cases[4]; hence, antibiotics are not proven to be effective despite being widely prescribed.[5]

Although no clear mechanism has been identified, experiments show that many factors may be involved to cause prolonged cough after acute bronchitis: increased production of leukotrienes and neuropeptides, altered expression of neural receptors, mucus hypersecretion, and probably, overactivity of cholinergic pathways.[6, 7]

The diagnosis of acute bronchitis must be made after exclusion of a chronic lung disease such as asthma, chronic obstructive pulmonary disease or interstitial lung disease, and in the absence of clinical and radiological evidence of pneumonia .[8, 9] Even though chest radiographs

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are typically normal, temporary abnormal pulmonary function testing with obstruction may be found in some cases.[10] This transient reduction in lung function has led to off-label use of various inhaled bronchodilators and corticosteroids. Often patients self-medicate or with traditional home remedies, antitussives, and antihistamines.[11]

There is a lack of consensus towards the effective treatment of acute bronchitis, particularly to reduce the duration of cough which remains the most troublesome and long-lasting symptom of this illness. Antibiotics have no proven role in uncomplicated acute bronchitis.[5, 12] Multiple trials have been done to gauge the efficacy of inhaled corticosteroids, beta-agonists, and muscarinic antagonists with conflicting data.[13, 14] Some studies show improvement in the cough symptoms, whereas some show no significant change.

Through this research, we aimed to assess the time to cough resolution with a combination of inhaled steroids and bronchodilators. Our secondary objectives were to assess comfort and improvement in the quality of life (QoL) with the treatment offered and to assess the difference between the inhaled therapies on the duration of cough resolution.

MATERIALS AND METHODS

This is a cross-sectional study performed at an outpatient clinic at a tertiary care center in Pakistan. The study period was from March 2023 to March 2024. Informed consent was taken from all patients prior to enrolment in the study. This study was approved by the Institutional Review Board of the institution (ERC # 2023-8859-25982).

Patients of age more than 18 years with an acute cough, lasting for less than four weeks' duration, and diagnosed by the treating physician as uncomplicated acute bronchitis were included in the study. Exclusion criteria comprised presence of an underlying lung disease, active or previous smoking history, evidence of peripheral eosinophilia or an abnormal chest radiograph at the clinic visit. A chest x-ray was obtained in all cases. If after initial inclusion, the patient was lost to follow-up, then also they were excluded from the study. Patients needing antibiotics or systemic corticosteroids were also excluded from the study.

The treating physicians were pulmonologists, and the treatment options were inhaled corticosteroid plus long-acting beta-agonists combination (ICS-LABA), and/or short-acting muscarinic antagonists and/or intranasal steroids. Data was collected using a questionnaire. Details including patients' demographics, co-morbidities, and duration of cough were obtained at the first clinic visit. Patients were followed for 3 weeks and the subsequent information about the number of days to cough resolution and the patient satisfaction scores were taken later, either at the follow-up visit or through telephone calls. Quality of Life (QoL) indicators were assessed on a scale of 1-10, with 1 showing disturbed quality of life due to cough severity, and 10 being significantly improved quality of life due to cough improvement. Patients were asked to compare the QoL with the inhaled therapies compared to what the QoL was prior to intervention.

Data entry and analysis were performed using the Statistical Package of Social Sciences (SPSS) for Windows (IBM Corp., Armonk, N.Y., USA) version 19.0. Quantitative variables were expressed as mean ± standard deviation (SD) and qualitative variables were shown as frequency and percentages. One-way analysis of variance (ANOVA) was used to compare the difference in the mean duration of cough resolution with different therapies and mean satisfaction and improvement in quality of life scores for different types of treatments. *P* value <0.05 was considered statistically significant.

RESULTS

A total of 51 patients were enrolled in the study at the first clinic encounter. However, 14 patients were either lost to follow-up or did not respond to telephone calls, and hence were excluded from the study. Finally, 37 patients were included in the study. The majority of the participants were female (70.3%), and the mean age of patients was 43.6 ± 17.24 years. Almost half of the patients (49.8%) had no co-morbidities. Among those who had co-morbid conditions, hypertension was the most common (29.7%).

Table 1 describes details of patient demographics.

Table 1: Demographic and Clinical Characteristics of Acute Bronchitis Patients

Characteristics	Total (*n*=37)
Age, Mean ± SD (years)	43.62 ± 17.24
Gender, No. (%)	
Male	11 (29.7%)
Female	26 (70.3%)
Comorbidities, No. (%)	
Diabetes Mellitus	5 (13.5%)
Hypertension	11 (29.7%)
Ischemic Heart Disease	1 (2.7%)
Congestive heart failure	2 (5.4%)
Hypothyroidism	2 (5.4%)
Cough duration prior to presentation, Mean ± SD (Weeks)	2.35 ± 0.89

The mean duration of cough with which the patients presented was 2.35 ± 0.89 weeks.
The treatment most prescribed for acute bronchitis was ICS-LABA (73.7%), followed by antihistamines (60.5%), inhaled SAMA (44.7%), and intranasal steroids (34.2%). The mean duration of cough resolution among patients was 9.09 ± 5.04 days following the start of treatment. Compared to ICS-LABA, inhaled treatment with SAMA led to earlier resolution of cough (on average, 3 - 5 days). Further details are listed in **Table 2**.

The mean increase/change in satisfaction and improvement in quality of life (QoL) among patients was ranked at 8.14 ± 2.02 on a scale 1-10. The sub-group analysis among the patients did not reveal any statistically significant results in the sub-groups of inhaled ICS-LABA, inhaled SAMA or nasal steroids treatment arms.

Table 2: Comparison of Mean Increase/Change in Cough Resolution (Days) and QoL in Acute Bronchitis Patients for Inhaled Therapies

		N	Mean ± SD	P-value
Cough Resolution (Days)	ICS-LABA	11	11.09 ± 5.79	0.488
	ICS-LABA and SAMA	10	9.60 ± 4.74	
	SAMA Only	6	6.67 ± 2.88	
	ICS-LABA and Nasal Steroid	7	10.57 ± 9.57	
	Nasal Steroid	3	15.33 ± 14.05	
QoL Score	ICS-LABA	11	9.00 ± 1.34	0.236
	ICS-LABA and SAMA	10	8.00 ± 1.49	
	SAMA Only	6	8.17 ± 1.47	
	ICS-LABA and Nasal Steroid	7	7.86 ± 2.85	
	Nasal Steroid	3	6.00 ± 3.61	

QoL: Quality of Life; SD: Standard Deviation; ICS: Inhaled Corticosteroid

DISCUSSION

Our study shows that patients presenting with acute bronchitis and cough, on average need 9 days for resolution of their cough with inhaled therapies. This shows that with adequate treatment, the viral bronchitis cough still would take more than a week to resolve, and patients should be counseled accordingly for needing time to resolve. Our study showed that in 95% of the patients, the cough took 4 to 14 days to resolve. This can be compared to the data shown by Ebell M.et al. He studied 713 outpatients with acute cough and found that mean duration of cough in acute bronchitis was 14.7 days with viruses, 17.3 with bacteria, and 16.9 with mixed infection.[15]

Acute viral bronchitis cough often causes significant disturbance to patients' functioning and sleep. Our patients compared their QoL with the cough prior to intervention and after treatment with inhaled therapies. With the intervention, most patients were satisfied with their QoL improving to an average of 8 (on a 1-10 scale). This gives us some guidance that with inhaled therapies, most patients would have significant improvement in their daily functioning from the cough.

Our study compared different modalities of inhaled therapies which were, ICS-LABA combination, inhaled SAMA, and intranasal steroids. There was no difference found between any of the treatments in terms of earlier cough resolution or better QoL improvement (details are shown in table 2). However, the inhaled SAMA trended towards improved cough resolution, 3-5 days earlier than patients receiving ICS/LABA or ICS/LABA in combination with SAMA. Patients on inhaled SAMA had cough resolution at an average of 6.6 days compared to 11.1 days in patients who were receiving ICS/LABA alone. However, it is likely that our study was underpowered to detect a significant difference. Prior data suggest that muscarinic antagonists may suppress the cough reflex and improve the cough in viral bronchitis.[14, 16]

A randomized controlled trial with upper respiratory tract infection (URTI) symptoms, found that inhaled tiotropium reduced cough reflex sensitivity (measured in response compared to capsaicin).[16] Another study demonstrated significant improvement in cough symptoms with ipratropium bromide in patients with persistent post-viral cough, compared to a placebo.[17]. A Cochrane meta-analysis, which included seven randomized controlled trials, found that most trials did not show statistically significant benefits of oral or inhaled beta-2 agonists in terms of quicker cough resolution in acute bronchitis.[13] This aligns with our study's results, which showed that inhaled LABA therapy did not lead to earlier cough resolution.

Our study also highlights that for patients with normal chest imaging and relatively normal examination findings, excess testing such as pulmonary function testing or CT imaging can be avoided by continuing the treatment for approximately 14 days. As this would be the natural resolution of the cough on treatment. If symptoms persist beyond 2 weeks on inhaled therapies, then further testing should be pursued.

Our study has many limitations. Firstly, our sample size is small, likely leading to our study being under-powered and not being able to detect a difference between the therapies. This was due to resource limitations and low recruitment. Secondly, patients were not blinded to the treatments, which can result in biases. Thirdly, we did not have a control arm with no inhaled treatments, therefore we cannot confirm that these treatments are more effective than placebo.

CONCLUSION

Our study shows that acute viral bronchitis needs an average of 9 days for cough resolution. Most patients had improvement in their QoL with the inhaled medications. Further controlled randomized studies are needed to study the improvement in cough duration and QoL for patients with viral bronchitis.

DECLARATIONS

Authors' contributions:

- MS: Study design, data collection, data analysis, manuscript writing, manuscript editing, final approval of the manuscript
- UA: Study design, data collection, data analysis, manuscript writing
- MI: study design, manuscript editing, manuscript review, final approval of the manuscript

Conflict of Interests:

There are no conflicts of interest to declare on behalf of any author.

Funding:

No sponsors, funding or grant was received for this study.

Acknowledgements:

We acknowledge the contribution of our statistician and analyst Akbar Shoukat Ali for his services and Dr. Ali Bin Sarwar Zubairi for the support throughout the study.

Declaration:

- The manuscript has been read and approved by all the authors, that the requirements for authorship as stated below in this document have been met, and that each author agrees to be accountable for all aspects of the work. Moiz Salahuddin takes responsibility for the integrity of the work, from inception to published article and should be designated as 'guarantor'.
- This study has not been submitted or presented elsewhere.

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