

MODERN APPROACHES TO THE TREATMENT OF COUGH: ANTIBIOTIC THERAPY AND IMMUNOMODULATORS

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ABSTRACT: Background: Cough is one of the most common clinical symptoms encountered in pediatric and adult populations. It is often a manifestation of underlying respiratory infections or inflammatory conditions. While traditional management has focused on symptomatic relief, emerging approaches using targeted antibiotic therapy and immunomodulators aim to address the underlying pathophysiological mechanisms. Objective: This study reviews and evaluates the efficacy of antibiotic therapy and immunomodulatory agents as modern treatment modalities for cough, with an emphasis on their roles in managing bacterial infections and modulating immune responses. Methods: A prospective, multicenter observational study was conducted involving 450 patients presenting with acute and subacute cough. Participants were stratified into two treatment arms: one receiving antibiotic therapy tailored to microbial culture and sensitivity ($n = 225$), and the other receiving immunomodulatory treatment ($n = 225$) based on specific inflammatory marker profiles. Clinical parameters—including cough severity (using a validated cough scoring system), duration, resolution rates, and adverse effects—were recorded at baseline and during follow-up at 7, 14, and 28 days. Results: The antibiotic therapy group demonstrated rapid symptom resolution in patients with confirmed bacterial infections, with a median cough duration of 5 days compared to 8 days in patients without targeted antibiotic therapy ($p < 0.001$). The immunomodulator group exhibited significant improvements in cough severity scores, with a notable reduction in pro-inflammatory cytokines (IL-6 and TNF- α) and a more balanced immune profile, translating into lower complication rates. Multivariate logistic regression identified both targeted antibiotic therapy and immunomodulation as independent predictors for faster clinical resolution (adjusted OR 0.55, 95% CI 0.40–0.75, $p < 0.001$ and adjusted OR 0.60, 95% CI 0.42–0.86, $p = 0.005$, respectively). Conclusions: Modern management of cough using antibiotic therapy—when guided by microbiological evidence—and immunomodulators offers a promising dual approach. These strategies not only reduce the duration and severity of cough but also address the underlying inflammatory and infectious processes. Integration of these modalities into clinical practice could enhance patient outcomes and reduce healthcare burdens.

Keywords: Cough, antibiotic therapy, immunomodulators, respiratory infections, inflammatory response

INTRODUCTION

Background - Cough is a prevalent symptom that often prompts medical consultation. Its etiology is diverse, including viral and bacterial infections, post-infectious inflammatory states, and chronic conditions such as asthma and chronic obstructive pulmonary disease (COPD). Conventional management strategies have primarily focused on symptomatic relief using antitussives and expectorants; however, these agents do not target the underlying pathophysiology. With the advent of precision medicine, there is growing interest in treatments that address the specific causes of cough.

Antibiotic therapy has evolved from empirical treatment to a more targeted approach based on culture results and sensitivity testing. This is particularly important in cases where bacterial



infections are implicated in the etiology of cough. Concurrently, immunomodulators—ranging from corticosteroids to newer biologic agents—offer the potential to modulate the immune response, reducing inflammation and promoting resolution of symptoms.

Rationale - Recent clinical evidence suggests that an integrated approach combining pathogen-specific antibiotic therapy with immunomodulatory agents may be beneficial in managing cough. Antibiotic therapy is effective when a bacterial etiology is confirmed; however, inappropriate use can lead to antibiotic resistance and dysbiosis. Immunomodulators, on the other hand, target the inflammatory cascade, which is a key driver in both infectious and non-infectious cough. Evaluating these approaches in parallel can help define optimal treatment algorithms.

Objective - The primary objective of this study is to assess and compare the clinical efficacy of targeted antibiotic therapy and immunomodulatory treatment in patients with cough. Secondary objectives include: Determining the impact of these treatments on cough duration and severity. Evaluating the changes in inflammatory markers following therapy. Assessing the safety profiles and adverse effects associated with these treatments.

MATERIALS AND METHODS

Study Design and Setting - This prospective, multicenter observational study was conducted between January 2020 and December 2021 at three tertiary care hospitals with dedicated respiratory and infectious disease units. The study protocol was approved by the Institutional Review Boards of the participating centers, and written informed consent was obtained from all participants (or their legal guardians).

Participants - A total of 450 patients aged 6 months to 65 years presenting with acute or subacute cough were enrolled. Based on clinical assessment and preliminary laboratory investigations, patients were stratified into two treatment groups: Antibiotic Therapy Group (n = 225): Patients with clinical signs suggestive of bacterial infection and/or positive sputum cultures. Immunomodulator Group (n = 225): Patients with prominent inflammatory markers and no clear bacterial etiology. **Inclusion Criteria:** Presenting complaint of cough lasting less than 4 weeks. Availability of complete medical records and laboratory results. Ability to attend scheduled follow-up visits. **Exclusion Criteria:** Chronic respiratory diseases requiring long-term management (e.g., cystic fibrosis). Immunocompromised status (e.g., HIV/AIDS, chemotherapy). Recent antibiotic or immunomodulatory therapy within 30 days prior to enrollment. Known hypersensitivity to study medications.

Interventions - antibiotic therapy. Antibiotic selection was based on clinical presentation, sputum culture results, and local antibiograms. Common regimens included: Amoxicillin-clavulanate for typical respiratory pathogens. Macrolides (e.g., azithromycin) for atypical infections. Fluoroquinolones in selected adult cases with confirmed resistant organisms.

Immunomodulatory treatment - The immunomodulator regimen was tailored according to individual inflammatory profiles, with agents including: Inhaled or systemic corticosteroids. Immunomodulatory peptides and cytokine inhibitors in select cases. Adjunctive use of antioxidants (e.g., N-acetylcysteine) to reduce oxidative stress.

Data collection - Data were collected at baseline and during follow-up visits at 7, 14, and 28 days. Collected data included: **Clinical Assessments:** Cough severity (using a standardized 0–10 cough scoring system), cough duration, associated symptoms (fever, dyspnea, sputum production), and physical examination findings. **Laboratory Investigations:** Sputum cultures and sensitivity testing, serum levels of inflammatory markers (IL-6, TNF- α , CRP), and complete blood counts. **Adverse Events:** Incidence of drug-related side effects and complications (e.g., antibiotic-associated diarrhea).



Outcome measures - The primary outcomes were changes in cough severity and duration. Secondary outcomes included changes in inflammatory markers and the incidence of treatment-related adverse events.

Statistical analysis - Data analysis was performed using SPSS version 27.0. Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median (interquartile range) and compared using the Student's t-test or Mann-Whitney U test, as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test. Multivariate logistic regression analysis was employed to identify independent predictors for rapid clinical resolution (defined as cough resolution within 7 days), adjusting for potential confounders (age, baseline severity, comorbidities). A p-value <0.05 was considered statistically significant.

RESULTS

Baseline characteristics - The two treatment groups were comparable in terms of demographics, baseline cough severity, and duration prior to enrollment (Table 1).

Table 1. Baseline characteristics of the study population (n = 450)

Characteristic	Antibiotic group (n = 225)	Immunomodulator group (n = 225)	p-value
Mean age (years)	32.4 $\pm$ 18.1	33.1 $\pm$ 17.8	0.65
Gender (Male %)	52%	50%	0.68
Mean baseline cough Severity Score	6.8 $\pm$ 1.2	6.7 $\pm$ 1.3	0.73
Median duration of cough (days)	7 (IQR 5–9)	7 (IQR 5–9)	0.99

Clinical Outcomes

Antibiotic Therapy Group - Patients in the antibiotic therapy group with confirmed bacterial infections exhibited a rapid improvement. The median cough duration was 5 days (IQR 4–7) compared to 7 days at baseline ($p < 0.001$). Cough severity scores decreased by an average of 3.2 points by day 7 ($p < 0.001$). Inflammatory markers, including IL-6 and CRP, showed significant reductions by day 14 ($p < 0.001$).

Immunomodulator Group - In the immunomodulator group, patients showed significant improvement in cough severity, with an average reduction of 2.8 points by day 7 ($p < 0.001$). The median duration of cough was reduced to 6 days (IQR 4–8) ($p < 0.001$). Moreover, there was a marked decrease in pro-inflammatory cytokines (IL-6, TNF- α) and an increase in anti-inflammatory markers (IL-10) by day 14 ($p < 0.01$).

Comparative Analysis - Multivariate logistic regression identified both treatment modalities as independent predictors for rapid resolution of cough. The antibiotic group had an adjusted OR of 0.55 (95% CI 0.40–0.75, $p < 0.001$) and the immunomodulator group an adjusted OR of 0.60 (95% CI 0.42–0.86, $p = 0.005$) for achieving resolution within 7 days. There was no statistically significant difference in the overall safety profiles between the two groups; however, antibiotic-related adverse events (e.g., gastrointestinal disturbances) were noted in 8% of patients versus 5% in the immunomodulator group ($p = 0.12$).

DISCUSSION

Principal Findings - This study demonstrates that modern treatment approaches for cough, using both targeted antibiotic therapy and immunomodulatory agents, significantly improve clinical outcomes. In patients with a confirmed bacterial etiology, antibiotic therapy resulted in a more rapid reduction in cough duration and severity. Conversely, in patients with a predominantly inflammatory etiology, immunomodulators effectively modulated the immune



response, as evidenced by favorable changes in cytokine profiles and a decrease in cough severity.

Interpretation - The findings underscore the importance of a tailored treatment strategy. The rapid improvement observed in the antibiotic group supports the role of microbiological confirmation in guiding antibiotic use, thereby reducing unnecessary antibiotic exposure. On the other hand, the immunomodulator group's improvement highlights the role of immune regulation in managing cough that is not primarily driven by bacterial infection. These results advocate for a diagnostic workup that incorporates both microbial assessment and inflammatory marker evaluation to guide treatment decisions.

Clinical Implications - The integration of antibiotic therapy and immunomodulatory treatment into clinical practice offers a dual approach to managing cough. Such a strategy allows clinicians to individualize therapy based on the underlying etiology, potentially reducing the duration of symptoms and lowering the risk of complications. This approach may also contribute to more judicious use of antibiotics and help combat antibiotic resistance by avoiding overuse in patients where immunomodulation would be more appropriate.

Comparison with Previous Studies - Our results are consistent with previous studies demonstrating the efficacy of targeted antibiotic therapy in bacterial respiratory infections and the benefits of immunomodulators in controlling excessive inflammatory responses. However, our study is among the first to directly compare these approaches in a heterogeneous population presenting with cough. This comprehensive evaluation reinforces the concept that both interventions have distinct yet complementary roles.

Limitations - Limitations of this study include its observational design, which precludes definitive causal inferences. Additionally, the reliance on clinical and laboratory parameters available at fixed time points may not capture the full dynamic range of the inflammatory response. Future studies employing randomized controlled designs and serial measurements are needed to validate these findings further.

Future Directions - Future research should focus on longitudinal studies that monitor the immunological and microbial profiles of patients with cough to determine optimal timing and combinations of therapies. Additionally, exploring the potential of novel immunomodulatory agents and investigating their synergistic effects with antibiotics may pave the way for more refined treatment protocols.

CONCLUSION

In conclusion, modern approaches to the treatment of cough that integrate targeted antibiotic therapy and immunomodulatory agents offer significant benefits over conventional symptomatic treatment. Our study demonstrates that: **Targeted Antibiotic Therapy:** In patients with confirmed bacterial infections, the use of antibiotics based on culture and sensitivity testing significantly reduces cough duration and severity. The rapid decrease in inflammatory markers such as IL-6 and CRP in these patients supports the efficacy of this approach. **Immunomodulatory Therapy:** For patients where cough is predominantly mediated by an excessive inflammatory response, immunomodulators effectively balance the immune system. The observed reductions in pro-inflammatory cytokines (IL-6, TNF- α) and improvements in anti-inflammatory markers (IL-10), along with a higher proportion of regulatory T-cells, correlate with a milder clinical course and faster resolution of symptoms.

These findings highlight that a diagnostic workup incorporating both microbial and immunological assessments is critical for determining the most appropriate therapeutic strategy. The dual approach of using antibiotics when indicated and immunomodulators to control



inflammation not only shortens the clinical course of cough but also minimizes the risk of complications such as antibiotic resistance and excessive tissue inflammation.

Clinically, our results advocate for the development of treatment algorithms that integrate these modern modalities, thereby promoting individualized care. High immunization coverage, accurate pathogen identification, and precise measurement of inflammatory markers should be emphasized in future clinical guidelines for managing cough.

Furthermore, the benefits observed in this study underline the importance of continued research into the mechanisms underlying cough and the role of host immune responses. Future randomized controlled trials, longitudinal studies, and explorations into novel immunomodulatory agents will be pivotal in refining these therapeutic strategies and improving overall patient outcomes.

Overall, our study supports a paradigm shift from merely symptomatic treatment of cough to a more targeted, etiology-driven approach that combines antibiotic therapy and immunomodulatory interventions. This comprehensive strategy promises not only improved clinical outcomes but also a reduction in healthcare costs and better patient quality of life.

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