

Controversies in Cough Management: An Indian Perspective

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Abstract

Chronic cough is one of the most common symptoms for patients-seeking consultation in an outpatient clinic. It is associated with substantial psychological, physical, and social burdens and impaired quality of life. This review highlights some of the major diagnostic and management challenges confronted in the field of cough with a special focus on the Indian perspective. Heterogeneity in definitions and classifications and challenges associated with over-the-counter drug use and irrational drug use are some of the major controversies. Streamlined diagnostic approach involving a combination of subjective and objective tools, evidence-based amendments in clinical practice, and stringent implementation of regulatory guidelines are mandatory to address controversies in cough management in developing countries.

Keywords: Antitussive, chronic cough, expectorant, over-the-counter, tuberculosis

INTRODUCTION

Chronic cough without identifiable causes, even after basic evaluation, is one of the most common reasons for referral to specialty clinics, and it can be due to respiratory or nonrespiratory causes.^[1] It poses a major challenge to both clinicians and patients due to the complexity in the diagnosis and the physical, social, and psychological burdens. Persistent/high-intensity coughing may cause considerable morbidity such as chest pain, fractured ribs, exhaustion, dizziness, lightheadedness, urinary incontinence, sleep interference, and work absenteeism.^[2]

A cross-sectional European survey involving 1120 participants has noted that only 53% had achieved a diagnosis, of the 70% of the respondents who had \geq three consultations for chronic cough. Most of the respondents judged the treatment as having limited or no effectiveness.^[3] In India, around 70% of the individuals with cough undergo empirical therapy without a definite diagnosis.^[4]

COUGH: HETEROGENEITY IN DEFINITIONS AND CLASSIFICATIONS

Literature evidence reports the CHEST's 2006 Cough Guidelines and management algorithms as useful for classifying, diagnosing, and treating patients with cough worldwide.^[5] The classification proposed by the algorithm is as

follows: acute cough – <3 weeks, subacute cough – 3–8 weeks, and chronic cough – >8 weeks. However, the range reported in diverse studies and by patients presenting to the clinic are of larger duration.^[6] A 2015 systematic review and meta-analysis has highlighted the need for developing an international consensus definition. The researchers considered 19 different definitions for scrutinizing the data from more than 80% of the epidemiological studies. It was noted that most of the studies had adopted 3 months as the cutoff for the duration of chronic cough, whereas the cutoff proposed by the current guidelines is 8 weeks.^[7]

ASSESSMENT CHALLENGES AND THE NEED FOR EXTENSIVE INVESTIGATIONS

Varying success rates of chronic cough management noted in the primary research studies could be attributed to the lack of fidelity to the core principles of diagnostic/therapeutic interventions.^[8] The “anatomic diagnostic protocol” put forth by Irwin *et al.* suggests considering the following diagnostic

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triad in most of the cases: rhinitis, eosinophilic airway inflammation, and gastroesophageal reflux disease.^[9]

However, the practical implementation of this protocol in the clinical practice is associated with several discrepancies. Nearly 12%–42% did not belong to any of the categories, despite extensive investigations. A cough may not be the common presentation in some patients with these conditions; in individuals having cough as prominent symptoms, the prognosis of specific treatment is uncertain. Reported success rates of this protocol have been <58%, and the reasons are still elusive. Moreover, the pathogenetic implications of these conditions in cough are unclear.^[1,2,9]

A 2018 review by Perotin *et al.* has presented an overview of currently available recommendations and has summarized the following steps in chronic cough management [Table 1].^[10]

The current international recommendations on cough diagnosis are customized for specialty care, and they are not compatible to address the diagnostic challenges in developing countries.^[4] Faruqi and Song have reported that the etiology and risk factors for chronic cough in tropical regions can be quite different from those reported from other parts. The risk factors that can be considered in an Indian perspective include bidi smoking, outdoor air pollution, and biofuel.^[11] Affordability, unavailability, and prolonged waiting for definite diagnoses are the other major challenges confronted in the Indian primary settings, as opposed to the international recommendations.^[12] To circumvent these shortcomings, experts from across India have put forth a consensus document to provide a systematic approach for effective cough management. The document advocates aggressive investigations with the presence of red flag signs [Table 2]. These signs have also been recommended by the 2018 American College of Chest Physicians (ACCP), CHEST Expert Cough Panel.^[4]

SUBJECTIVE VERSUS OBJECTIVE MEASUREMENTS

The use of cough diary scores, visual analog scales, subjective quality-of-life questionnaires, and objective ambulatory cough monitoring systems has significantly improved the assessment of chronic cough. The cough-specific quality-of-life questionnaire and the Leicester cough questionnaire and the cough-specific quality-of-life questionnaire are the commonly used validated questionnaires.^[2] Although the need for objective measures of cough severity has been highlighted in the European Respiratory Society guidelines, the optimal assessment strategy is still unknown.^[1]

Several studies have underscored the significance of a combination approach of subjective and objective measurements. However, there are no guidelines recommending the same. Moreover, there are very limited studies comparing subjective and objective cough measures.^[2] The diagnostic importance of cough intensity, rhythm, nature, and frequency has not been clearly explored. Cough frequency may be indicative of the disease prognosis following treatment.

Table 1: Steps in chronic cough management recommended by the international guidelines

| |
|---|
| 1. Initial clinical evaluation |
| Checking for warning signs |
| Drugs intake (ACE inhibitor) |
| Environmental and occupational assessment |
| 2. Assessment and treatment of the most common causes |
| Gastroesophageal reflux disease |
| Upper airway cough syndrome |
| Asthma and cough-variant asthma |
| Nonasthmatic eosinophilic bronchitis |
| 3. Evaluation of other causes in cases with inadequate treatment response |
| Cardiac arrhythmia |
| Somatic cough syndrome |
| Nonasthmatic pulmonary diseases |
| Obstructive sleep apnea |
| 4. Consideration of refractory chronic cough |

Source: Perotin *et al.* ACE: Angiotensin-converting enzyme

Table 2: Red flag signs for aggressive investigations

| Red flag signs | |
|---|-------------------------|
| Hemoptysis | Hoarseness of voice |
| Prominent dyspnea | History of tuberculosis |
| Systemic symptoms (weight loss, fever, and sore throat) | Immunosuppression |
| Smokers' cough (especially in patients >35 years) | Cough syncope |

Source: Guleria *et al.*

However, there is a paucity of data from the clinical trials evaluating the cough frequency or its effects on the quality of life.^[12]

TREATMENT-RELATED CONTROVERSIES

Watchful waiting is generally recommended for managing children having chronic dry cough, without any cough pointers (signs, symptoms, and simple investigations). Distinguishing nonspecific from specific cough might be clinically useful for deciding on watchful waiting. However, the definition of chronic cough in children is controversial. The British Thoracic Society guidelines have defined the duration of chronic cough in children as >8 weeks, as opposed to >4 weeks recommended by the ACCP guidelines. This recommendation is intended to provide a period of the resolution, without any specific treatment, if the cough is associated with a simple head cold persisting for 2–3 weeks. In contrast, ACCP and Australian and ACCP guidelines have defined chronic cough duration as >4 weeks.^[13,14]

CHALLENGES ASSOCIATED WITH OVER-THE-COUNTER DRUG USE

Abuse of over-the-counter (OTC) cough products has been recognized as an international concern. There are limited research and studies quantifying the scale of abuse. The use

of opioids among substance abusers in India is estimated to be around 0.4%–26%. Studies have indicated that abuse in the majority of the cases was initiated as a part of recreational activities through friends, whereas very few had started the consumption as a treatment of chest/cough problems.^[15]

DRUG USE IN SPECIFIC POPULATION

Several studies have raised concerns on the potential benefits of OTC cough medications in children <6 years of age and the direct and indirect associations of their ingredients with pediatric morbidity and mortality.^[16] Several medical governing bodies in Australia, Europe, and the USA and medical experts in international chronic cough guidelines have consistently highlighted the lack of sufficient evidence on the efficacy and safety of codeine-based medications in managing childhood chronic cough. Despite the warnings and policy amendments by the Food and Drug Administration and ACCP, children between 2 and 5 years, followed by children <2 years, have been identified as common users of such medications.^[17] A cross-sectional Indian study has underscored the need to create awareness among pediatricians regarding the cautious prescription of cough and cold medications. The present study has noted that data on the prescription pattern of these medications from India are very limited, and there are medication overuse, regardless of the patient's age, hospital setting, or seniority of the physician.^[18]

The cough reflex in the elderly may be compromised due to aging or illness, and overuse of cough suppressants in such patients may modify the cough response. The medications may decrease the airway clearance due to suppression of the cough center, thereby increasing the risk of aspiration pneumonia.^[19]

IRRATIONAL DRUG USE

A 2011 study has noted 72% increase in the number of cough and cold medications in the Indian drug market from 2011. The number of banned cough and cold medications had increased from 9 in 2001 to 27 in 2007. Many of the preparations had constituents with antagonistic actions and more than one ingredient belonging to the same pharmacological group. Rationality assessment revealed that most of the cough and cold preparations were irrational without any recorded benefits.^[20] Unconventional combinations of formulations (e.g., cough medications with cough suppressant + expectorant two or more antihistamines + decongestant + bronchodilator) increase the risks of adverse events and associated morbidities.^[21]

Availability of a large number of irrational drugs in the Indian drug market is mainly due to the nonrevision of legal provisions and lack of stringent implementation of policy guidelines.^[21] A 2016 literature review has noted that irrational drug use in India is extensive and multifactorial. The present study highlighted the need of addressing the issue at all levels of health systems and has suggested the following:^[22]

- Evaluation of the interplay by the policy-makers at the systemic, provider, dispenser, and consumer levels

- Conducting awareness campaigns for public, pharmacists, and clinicians regarding the risks of inappropriate use
- Further research to identify the effective strategies to tackle social factors associated with irrational use.

CONCLUSION

Amendment of international guidelines and validation of the streamlined diagnostic approach involving a combination of subjective and objective tools through further research are warranted to address the diagnostic challenges in developing countries. Developing consensus and conducting longitudinal studies and clinical trials for evidence-based amendments in clinical practice are necessary to address treatment-related controversies. Harmonization of licensing procedure, stringent enforcement of regulatory guidelines, and good pharmacovigilance are mandatory to prevent irrational use of fixed-dose combination in India.

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Conflicts of interest

There are no conflicts of interest.

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