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REVIEW ARTICLE

Chronic cough: a multidisciplinary approach

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Abstract

Background and methods: Chronic cough is defined as a cough persisting for more than eight weeks. This condition generates significant healthcare and economic costs. It is associated with a spectrum of disorders across multiple medical specialties and can provide significant challenges for effective evaluation and management. The current literature was reviewed to gain further insight into chronic cough, including its relationship with sinonasal disease.

Results: Within the reviewed literature, there was strong emphasis on post-nasal drip syndrome as a major causative factor.

Conclusion: Cough is the most common complaint for which adult patients seek medical consultation in primary care settings. Chronic cough is associated with a deterioration in the quality of patients' lives. Thorough assessment of a patient with a chronic cough relies on a multidisciplinary approach.

Key words: cough; sino-nasal; asthma; gastric acid reflux; multidisciplinary

Introduction

Chronic cough is defined as a cough persisting for more than eight weeks. It is the most common presenting complaint of adults seeking medical treatment in a primary care setting.[1] Chronic cough occurs in up to 40 per cent of the population, with a female preponderance.[2]

Although the aetiology of chronic cough and its association with conditions spanning various medical specialties are well documented in the current literature, the condition itself remains a diagnostic challenge for clinicians.[3] A multidisciplinary approach, with close cooperation between otolaryngologists, respiratory physicians and gastroenterologists, is recommended. Using such an approach, success rates in the order of 90 per cent have been reported.[4]

Although cough is generally caused by a self-limiting illness, it may persist and generate great anxiety in patients worried about a sinister underlying cause. Furthermore, the cost to the UK economy has been estimated to be at least £979 million.[5] This is a consequence of absenteeism and job productivity reduction, as well as prescription and non-prescription costs.

The purpose of this review is to describe, from an otolaryngologist's viewpoint, the mechanism, diagnosis and treatment of chronic cough.

Mechanism of cough

Cough is defined as a forced expulsive manoeuvre against a closed glottis that is associated with a characteristic sound.[6] It is a physiological protective reflex that clears excessive secretions and contents from the respiratory tract. The trigeminal, glossopharyngeal and vagus nerves supply afferent sensory pathways from the cough receptors located throughout the respiratory tract to the brainstem. These receptors are abundant in the larynx and bronchial bifurcations. Subsequently, efferent pathways leave the medulla and supply the respiratory tract and associated muscles of respiration, to complete the reflex arc.

Aetiology

In up to 85 per cent of patients with chronic cough, the aetiological factors, in order of decreasing frequency, are post-nasal drip syndrome, asthma and related syndromes, and gastroesophageal reflux disease.[7] This figure is increased to up to 100 per cent in immunocompetent, non-smoking patients with chronic cough who have normal chest radiograph findings.[8,9]

A thorough, detailed medical history is important to exclude iatrogenic causes of cough, including use of angiotensin-converting enzyme (ACE) inhibitors.[10] Occupational history is equally important, as studies have demonstrated persistent cough as a presenting feature of occupational sensitisation of airways.[11] Furthermore, an association between anxiety and chronic cough has been described, and a combination of speech and language therapy and psychotherapy has been reported to be effective.[12]

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Post-nasal drip syndrome

Post-nasal drip syndrome is also referred to as upper airway cough syndrome. It includes a number of symptoms, including a sensation of secretions from the nasal passages draining into the nasal pharynx, nasal congestion and discharge, and increased frequency of throat clearing.

It has been reported that between 20 and 40 ml of mucus is secreted from the nasal cavity each day. This mucus is moved, via cilia waveform, from the front of the nose to the nasopharynx, where it is expectorated or swallowed.

In addition to nasal secretions, global airway inflammation may occur, releasing histamine and inducing cough by stimulating the respiratory tract.[4] This process underlies the concept of 'one airway, one disease', in which the upper and lower airway are viewed as a continuum of inflammation with a common underlying pathology.[13]

Post-nasal drip syndrome has been reported in the US literature as the commonest cause of chronic cough.[8] However, this remains controversial and is not universally accepted, as the diagnosis of post-nasal drip syndrome is largely based on the subjective symptoms of patients.[14] Without any objective or discrete pathognomonic findings, the diagnosis of post-nasal drip syndrome lacks the relative precision of a diagnosis of asthma (and related syndromes) or gastro-esophageal reflux disease. Furthermore, patients with observable post-nasal secretions do not cough.[3]

A successful response to treatment directed at the upper airway is a recommended diagnostic approach to establish post-nasal drip syndrome as a cause of cough.[15]

The recent Allergic Rhinitis and its Impact on Asthma guideline recommends first-line treatment with intra-nasal corticosteroids for all stages of rhinitis.[16] The use of antihistamines for nasal obstruction is restricted to reduction of physical symptoms, i.e. sneezing, itchy eyes and clear nasal discharge. Current evidence-based guidelines on treatment of chronic rhinosinusitis, with or without nasal polyposis, recommend initial treatment with intra-nasal corticosteroids.[17]

Despite the lack of randomised, controlled trials evaluating the role of topical corticosteroids in chronic cough, one randomised, placebo-controlled trial reported that intra-nasal corticosteroids given for two weeks were effective in allergic rhinitis related cough.[18] A further prospective study demonstrated that topical intra-nasal steroids given for two to eight weeks to patients with chronic cough and post-nasal drip syndrome were effective.[19]

Asthma and related respiratory disorders

A number of respiratory and cardiac conditions have been associated with a chronic cough.[20] Chronic obstructive pulmonary disease occurs usually as a consequence of smoking, and a persistent cough is a characteristic feature that leads to an impaired quality of life.[21]

Persistent cough has also been reported as a common feature of lung cancer[22,23] and sarcoidosis.[24]

Interestingly, there has been a recent global increase in cases of pertussis (whooping cough). This condition is characterised by persisting coughing episodes that can vary from several weeks to months, and should be considered in the differential diagnosis of chronic cough.[25]

Asthma is characterised by variable airflow obstruction, manifesting as dyspnoea, wheezing and cough. Prospective studies have implicated asthma as the most common cause of chronic cough in non-smoking patients.[5]

However, a subgroup of cough-variant asthma exists in which cough is the only physical symptom and other cardinal signs are absent, in the presence of demonstrable airway hyper-responsiveness.[6]

Importantly, not all patients with cough-variant asthma will demonstrate airway hyper-responsiveness or airflow obstruction when subjected to broncho-provocation methacholine and spirometry studies.[26] A definitive diagnosis of cough-variant asthma is made retrospectively following resolution of symptoms with anti-asthma therapy including inhaled corticosteroids. There is also increasing evidence for the positive effect of leukotriene receptor antagonist in reducing symptoms in cough-variant asthma.[27]

Further complicating the diagnosis of cough-variant asthma is non-asthmatic eosinophilic bronchitis, which is characterised by chronic eosinophilic airway inflammation and cough in the absence of airway hyper-responsiveness or variable airflow obstruction.[28] Cough-variant asthma and non-asthmatic eosinophilic bronchitis share similarities – both involve eosinophilic inflammation and show improvement after a trial of inhaled corticosteroids; however, non-asthmatic eosinophilic bronchitis demonstrates a poor response to inhaled bronchodilators.[29]

Gastroesophageal reflux disease

Gastroesophageal reflux disease has been reported to be the cause of chronic cough in up to 40 per cent of patients.[30] Symptoms of reflux include cough, dyspepsia, dysphagia and globus pharyngeus, but up to 75 per cent may be asymptomatic.[8]

Cough associated with gastroesophageal reflux disease may be a consequence of a tracheobronchial or oesophageal cough reflex generated via the vagus nerve, following acid exposure in the distal oesophagus.[14] Further studies have demonstrated that patients with gastroesophageal reflux disease associated chronic cough have a significant increase in cough frequency following acid infusion into the distal oesophagus, in contrast to lignocaine infusion, which appears to block the cough reflex.[31]

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Another potential mechanism of gastroesophageal reflux disease associated cough is micro-aspiration of oesophageal contents into the laryngopharyngeal regions and the tracheobronchial system.[32] In patients with cough, the use of dual channel oesophageal pH monitoring has demonstrated proximal oesophageal reflux disease in the absence of distal reflux disease.[33]

However, the diagnosis of laryngopharyngeal reflux disease remains controversial. Fibre-optic laryngoscopy findings that have been reported to be associated with laryngopharyngeal reflux include vocal fold erythema, posterior commissure hypertrophy and the presence of laryngeal pseudo-sulcus.

In patients with laryngopharyngeal reflux disease, empirical therapy with proton pump inhibitors (PPIs) and reflux lifestyle advice (including weight reduction and dietary modification) are recommended.[34] However, there are no standardised criteria for diagnosing laryngopharyngeal reflux using a proximal probe and dual channel pH monitoring. Controversies arise over positioning of the probe in relation to the upper oesophageal sphincter, and quantifying the number of episodes of proximal reflux to be considered diagnostic.[35]

Furthermore, surgical intervention (including Nissen fundoplication) has benefited patients with gastroesophageal reflux disease associated cough that has not responded to medical therapy.[36]

Importantly, chronic cough associated with chronic aspiration in relation to meals should be excluded as an aetiological factor, particularly in elderly patients. Fibre-optic endoscopic evaluation of swallowing and videofluoroscopy studies can be effective in diagnosing aspiration, and dietary modification with speech and language therapy has been reported to be effective.[37]

Discussion

A multidisciplinary and systematic approach is recommended for the management of chronic cough. Guidelines have been published by the British Thoracic Society and the American College of Chest Physicians.[5,38]

A detailed history, including occupational history, should be completed. Smoking should be discouraged and ACE inhibitors discontinued.

As post-nasal drip syndrome is considered the most common cause of chronic cough, this should be evaluated first.[8] A thorough ear, nose and throat examination should be performed using fibre-optic laryngoscopy to visualise both the nasal passages and the pharyngolaryngeal structures.

In addition, a respiratory examination should be completed; if a respiratory aetiology is suspected, then a referral to a respiratory physician should be made. A chest radiograph is mandatory. In the presence of fundamental upper airway symptoms, a trial of intranasal corticosteroids is recommended. Further management may include allergy testing or radiological imaging of the sinuses as appropriate.

If the cough persists then the patient should be reviewed by a respiratory physician. Subsequently, patients should undergo spirometry and assessment for bronchial hyper-responsiveness and bronchoscopy, particularly when foreign body inhalation is suspected. High-resolution pulmonary computed tomography may be appropriate.

As reflux-associated cough may exist in the absence of gastrointestinal symptoms, a referral to a gastroenterologist should be considered, particularly after a trial of acid suppression and PPIs that has been ineffective.

Despite these measures, cases of idiopathic chronic cough do exist.[39] In such cases, an upper respiratory tract infection often precedes the cough, which may persist for several years due to a hyper-sensitive cough reflex.

Conclusion

Post-nasal drip syndrome, asthma and related syndromes, and gastroesophageal reflux disease are the most prevalent aetiological factors for chronic cough in immunocompetent, non-smoking patients who do not use cough-inducing medication, including ACE inhibitors.

A multidisciplinary, systematic approach is recommended for managing patients with chronic cough. Further randomised, controlled trials are needed to assess the quality of investigations and success of treatment modalities across different specialties, including the effect on patients' quality of life.

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