

Chronic Unexplained Cough And Gastroesophageal Reflux Disease: A Quick Clinical Review

R Makkar, G Sachdev

Citation

R Makkar, G Sachdev. *Chronic Unexplained Cough And Gastroesophageal Reflux Disease: A Quick Clinical Review*. The Internet Journal of Internal Medicine. 2002 Volume 4 Number 1.

Abstract

Chronic cough may be caused or triggered by gastroesophageal reflux disease (GERD), which is the third most common cause of chronic unexplained cough after bronchial asthma and postnasal drip. Many patients with unexplained cough have underlying GERD without the classic reflux symptoms making clinicians unaware that GERD may be playing a crucial role in these patients. Aggressive therapy of GERD results in resolution of cough in almost 80 to 95% of patients with GERD associated cough. This short review attempts to describe the underlying mechanisms, diagnostic evaluation and the current management of GERD related cough in the general practice.

INTRODUCTION

'Chronic persistent cough' has been defined as the presence of cough for at least three weeks, while 'chronic unexplained cough' is defined as cough which lasts for at least three weeks, when cough is the only presenting symptom, there is no associated hemoptysis, no prior history of chronic respiratory disease to account for the cough and current chest X ray does not contribute to the diagnosis ¹. Chronic cough may be caused or triggered by gastroesophageal reflux disease (GERD), which is the third most common cause of chronic unexplained cough after bronchial asthma and postnasal drip ^{1, 2}. Many patients with cough aggravated by GERD do not have classic reflux symptoms making clinicians unaware that GERD may be playing a crucial role in these patients.

PREVALENCE

The prevalence of GERD associated cough ranges between 10 to 40% depending on the patient population, type of diagnostic test used and whether more than one etiology of cough is ascertained. GERD is found to be the cause of chronic cough in up to 10% of patients when the diagnosis of reflux is made by history, endoscopy or barium esophagogram ¹. Adding 24 hour esophageal pH testing in the diagnostic armamentarium, GERD can account for chronic cough in up to 40% of patients ³.

In children the prevalence of GERD as a cause of chronic cough is reported to be 4 to 15% ^{4, 5}.

Pathogenesis Of Cough Associated With GERD

There are two proposed mechanisms of GERD associated cough:

1. Acid in the distal esophagus stimulating a vagally mediated esophagealtracheobronchial cough reflex ^{6, 7}.
2. Micro or macroaspiration of esophageal contents into the larynx and tracheobronchial tree ^{8, 9}.

Ing et al⁶ proposed that gastroesophageal reflux causes cough through an esophagotracheobronchial reflex. Using dual probe 24 hour esophageal pH monitoring, they found that reflux occurred simultaneously in 78% and within 5 minutes in 90% of cough episodes. They found no evidence of aspiration of the esophageal contents into the larynx or trachea. The afferent pathway of the arc comprising signals from the peripheral cough receptors in the laryngotracheobronchial tree to the cough center in the medulla was inhibited by esophageal instillation of local anesthetic (4% topical lignocaine) whereas the efferent pathway carrying signals from the cough center to the effector musculature responsible for cough was inhibited by nebulized ipratropium bromide. They proposed that this reflex arc is the likely mechanism by which gastroesophageal reflux disease leads to cough in these patients; although intraesophageal pH may not be the sole mediator ⁷.

Microaspiration of the contents from the proximal esophageal refluxate can also result in GERD related cough and can account for up to 10 to 15% of cases unexplained chronic cough^{8,9}. It results from smaller volume refluxate and produces laryngeal inflammation with or without bronchial inflammation. The resulting inflammation due to the mucosa damage leads to cough and hoarseness in such patients, without producing the classical symptoms of GERD.

THE COUGH REFLUX SELF PERPETUATING CYCLE

According to this mechanism, cough from any cause may precipitate further reflux^{10,11}. It has been speculated that chronic cough from any cause may trigger swallow related lower esophageal sphincter (LES) relaxation or transient LES relaxation which on a background of raised trans diaphragmatic pressure may lead to reflux^{10,12}. The clinical significance of the cough reflux cycle is that management of both cough and reflux needs to be directed at breaking this cycle.

SYMPTOMS IN PATIENTS OF GERD RELATED COUGH

Since GERD related cough is most commonly due to a vagally mediated distal esophagotracheobronchial reflex mechanism, the classical reflux symptoms like heartburn, acid regurgitation, water brash etc. are unusual in such patients. Instead, cough may be the sole presenting manifestation of GERD and it can be clinically silent in up to 50 to 75% of the patients¹³. Cough that gets worsened after heavy meals or with foods that decrease LES pressure (chocolates, caffeine, peppermint, alcohol, high fat foods) can be due to underlying GERD. Other clues that can point towards underlying GERD as the cause of chronic unexplained cough are hoarseness especially in the morning, nocturnal cough, or cough which gets aggravated after lying down or exercise.

In patients with microaspiration, gastrointestinal symptoms of GERD are more prominent and may predate the onset of cough. Patients with pulmonary macroaspiration syndromes may present with cough in association with other symptoms such as purulent sputum, wheeze, dyspnoea, hemoptysis, chest pain, nocturnal fever, night sweats, and dysphagia with prominent GERD symptoms such as heartburn, waterbrash and oral regurgitation¹⁴.

DIAGNOSTIC EVALUATION

Patients with chronic cough should have a history and physical examination targeted at the most common causes of cough (asthma, sinusitis, GERD, angiotensin converting enzyme inhibitors use) as well as a chest radiograph. GERD should be considered if there are typical gastrointestinal symptoms or if cough remains unexplained after standard investigations. If heartburn and/or acid regurgitation are present, no further testing is required before starting medical antireflux therapy. The diagnosis of GERD as the cause of cough can only be made with certainty when cough goes away with specific antireflux therapy. Empirical medical therapy targeted towards reducing reflux is justified in such patients and is more cost effective than testing followed by treatment¹⁵. The diagnostic evaluation of patients with GERD related cough may include a barium study, esophageal endoscopy and esophageal manometry but the initial investigation of choice to assess GERD is 24 hour ambulatory dual probe esophageal pH monitoring, which has a sensitivity and specificity approaching 95%¹⁶. Infact, intraesophageal pH monitoring may be the only method of diagnosing GERD in up to 32% patients with cough¹⁷. 24 hour esophageal pH testing should be performed in patients in whom cough is still yet unexplained even after a detailed history and physical examination, chest X ray, pre and post bronchodilation spirometry, upper airway examination, laryngoscopy and paranasal imaging¹⁸.

MANAGEMENT OF GERD RELATED COUGH

Aggressive therapy of GERD results in resolution of cough in almost 80 to 95% of patients with GERD associated cough, although an optimal therapeutic regimen has not been investigated. Irwin¹⁷ recommends that all patients be placed on high protein, low fat diet, avoid large meals, omit acidity / spicy foods and beverages, avoid foods that decrease LES pressure (chocolates, caffeine, alcohol), limit eating or drinking between meals and sleep with raised head end of the bed.

Medical therapy should be targeted towards reducing the reflux and should include prokinetic agents such as metoclopramide or cisapride and gastric acid inhibitors such as an H₂ antagonist or a proton pump inhibitor (PPI). Proton pump inhibitors (omeprazole 40 mg or lansoprazole 30 mg daily) have shown better results than H₂ blockers or prokinetic agents^{14,19,20}. It is unlikely that the newer proton pump inhibitors (rabeprazole, esomeprazole) will be more efficacious than omeprazole or lansoprazole in reducing GERD related cough²¹. Dosages should be individualized.

Therapy should continue for an additional 3 months after cough resolution, then gradually should be discontinued. Any obvious cause of reflux such as drugs (agonists, calcium channel blockers, benzodiazepines, barbiturates etc.) or precipitation factors such as obesity etc. should be taken care of at the same time.

Antireflux surgery including Nissen Fundoplication (open or laparoscopic) for patients of GERD related cough is generally reserved for those with proven GERD and who have failed to respond to medical treatment including high dose proton pump inhibitors, or who have recurrence of symptoms after stopping treatment^{22, 23}. It may also be indicated in patients with continuing micro or gross aspiration (including those with recurrent aspiration pneumonias) who fail to respond to appropriate dietary measures, prokinetic agents and PPI. Clinical symptomatic improvements in patients with cough and aspiration following fundoplication surgery is 45 to 80% with follow up periods of 3 to 18 months.

CORRESPONDENCE TO

Ravinder PS Makkar, MD D-40, Preet Vihar, New Delhi-110092, India Tel: (0091) (11) 22545183 E mail: makkar_r@yahoo.com

References

1. Irwin RS, Corrao WM, Pratter MR. Chronic persistent cough in the adult: the spectrum and frequency of causes and successful outcome of specific therapy. *Am Rev Respir Dis* 1981; 123(4 Pt 1):413-7.
2. Alonso Munoz J, Gallego Carrion B, Carrizo Sierra SJ, Vicente Gonzalez E, Marin Trigo JM. Management of chronic cough in high volume medical offices: efficacy of a sequential protocol. *Rev Clin Esp* 2001; 201(5):239-44.
3. Mello CJ, Irwin RS, Curley FJ. Predictive values of the character, timing, and complications of chronic cough in diagnosing its cause. *Arch Intern Med* 1996; 156(9):997-1003.
4. Holinger LD, Sanders AD. Chronic cough in infants and children: an update. *Laryngoscope* 1991; 101(6 Pt 1):596-605.
5. Juchet A, Bremont F, Dutau G, Olives JP. Chronic cough and gastroesophageal reflux in children. *Arch Pediatr* 2001; 8 (Suppl 3):629-34.
6. Ing AJ, Ngu MC, Breslin AB. Chronic persistent cough and gastroesophageal reflux. *Thorax* 1991; 46(7):479-83.
7. Irwin RS, Madison JM, Fraire AE. The cough reflex and its relation to gastroesophageal reflux. *Am J Med* 2000; 108 (Suppl 4a):73S-78S.
8. Ruth M, Carlsson S, Mansson I, Bengtsson U, Sandberg N. Scintigraphic detection of gastropulmonary aspiration in patients with respiratory disorders. *Clin Physiol* 1993; 13(1):19-33.
9. Hogan WJ, Shaker R. Supraesophageal complications of gastroesophageal reflux. *Dis Mon* 2000; 46(3):193-232.
10. Laukka MA, Cameron AJ, Schei AJ. Gastroesophageal reflux and chronic cough: which comes first? *J Clin Gastroenterol* 1994; 19(2):100-4.
11. Davis MV. Relationship between pulmonary disease, hiatal hernia, and gastroesophageal reflux. *N Y State J Med* 1972; 72(8):935-8.
12. Ing AJ, Ngu MC, Breslin AB. Pathogenesis of chronic persistent cough associated with gastroesophageal reflux. *Am J Respir Crit Care Med* 1994; 149(1):160-7.
13. Irwin RS, French CL, Curley FJ, Zawacki JK, Bennett FM. Chronic cough due to gastroesophageal reflux. Clinical, diagnostic, and pathogenetic aspects. *Chest* 1993; 104(5):1511-7.
14. Pellegrini CA, DeMeester TR, Johnson LF, Skinner DB. Gastroesophageal reflux and pulmonary aspiration: incidence, functional abnormality, and results of surgical therapy. *Surgery* 1979; 86(1):110-9.
15. Lin L, Poh KL, Lim TK. Empirical treatment of chronic cough : a cost effectiveness analysis. *Proc AMIA Symp* 2001:383-7.
16. Irwin RS, Mark Madison J. Diagnosis and Treatment of Chronic Cough due to Gastroesophageal Reflux Disease and Postnasal Drip Syndrome. *Pulm Pharmacol Ther* 2002; 15(3):261-6.
17. Irwin RS. Management of chronic cough. In: George R (ed.) *Pulmonary and critical care update*, Vol.9, Northbrook III ACCP, 1994; 9:1-8.
18. Pratter MR, Bartter T, Akers S, DuBois J. An algorithmic approach to chronic cough. *Ann Intern Med* 1993; 119(10):977-83.
19. Kiljander TO, Salomaa ER, Hietanen EK, Terho EO. Chronic cough and gastroesophageal reflux: a double blind placebo controlled study with omeprazole. *Eur Respir J* 2000; 16(4):633-8.
20. Beck IT, Champion MC, Lemire S, et al. The Second Canadian Consensus Conference on the Management of Patients with Gastroesophageal Reflux Disease. *Can J Gastroenterol* 1997; 11 (Suppl B): 7B-20B.
21. Vanderhoff BT, Tahboub RM. Proton pump inhibitors: an update. *Am Fam Physician* 2002; 66(2):273-80.
22. Thoman DS, Hui TT, Spyrou M, Phillips EH. Laparoscopic antireflux surgery and its effect on cough in patients with gastroesophageal reflux disease. *J Gastrointest Surg* 2002; 6(1):17-21.
23. Novitsky YW, Zawacki JK, Irwin RS, French CT, Hussey VM, Callery MP. Chronic cough due to gastroesophageal reflux disease: efficacy of antireflux surgery. *Surg Endosc* 2002; 16(4):567-71.

Author Information

Ravinder PS Makkar, MD

Attending Physician, Department of Medicine, Sitaram Bhartia Institute of Science and Research

Gopal KR Sachdev, DM (Gastroenterology), FRCP

Professor of Medicine, Department of Medicine, Maulana Azad Medical College