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Editorial

Nosing Around in Chronic Obstructive Pulmonary Disease

"The greater our knowledge increases the more our ignorance unfolds"

John F Kennedy

Chronic bronchitis and emphysema were recognised almost 200 years back when Laennec in 1819[1] described the anatomical changes that occurred in these entities, and used the terms "bronchodilation and emphysema". In the present era, these potentially grave and disabling conditions, seen predominantly in smokers, are grouped under the rubric "chronic obstructive pulmonary disease" (COPD).[2] However, contrary views have called for discarding the umbrella term COPD and characterising the distinct phenotypes to enable tailored management.[3] Biomass smoke exposure has now emerged as a major cause of COPD in non-smokers.[4] Furthermore, there is now compelling evidence to suggest that COPD is not only a disease of the airways but has emerged as a systemic disorder.[5] Some authors have even proposed addition of the term "chronic systemic inflammatory syndrome" to highlight the growing impact of extrapulmonary involvement.[6] Currently the sixth-leading cause of death worldwide, it has been estimated that COPD would climb to the third spot by 2020.[7]

Although the role of upper airway inflammation in asthma in the form of rhinitis and sinusitis was firmly established[8,9] during the last two decades, awareness regarding upper airway inflammation in COPD is just beginning to develop. Nasal inflammation leading to upper airway symptoms was documented over the past decade, and this, undoubtedly, would add to the morbidity caused by COPD.[10]

Epidemiological data on nasal symptoms in COPD are fast emerging. Various studies[11-15] have reported that concomitant nasal and/or sinus-related symptoms occur in 40% to 88% of patients with COPD. A postal questionnaire survey conducted in southern Sweden on 392 self-reported chronic bronchitis or emphysema patients found that two-fifths had experienced recurrent or permanent nasal complaints.[11] In a follow-up study, in the same group of patients eight years later, the authors found that nasal blockage and nasal symptoms provoked by exposure to damp/cold air could predict an increased incidence of self-reported COPD.[14] A high (75.4%) prevalence of nasal symptoms was documented in 61 patients with moderate-to-severe COPD, from the East London COPD (ELCOPD) study cohort.[12] The two most common nasal symptoms in this group of patients were nasal discharge (52.5%) and sneezing (45.9%). In addition, the median nasal score was significantly higher in those with daily symptom production (but not in those with wheezing dyspnoea or cough). Not surprisingly, postnasal discharge and sneezing attacks were significantly more in COPD patients. Subsequently, another study on 65 patients with moderate-to-severe COPD, recruited from the ELCOPD rolling cohort, demonstrated that 88% patients usually were troubled by one or the other nasal symptom.[13] Once again, rhinorrhoea was the most common symptom experienced. We too evaluated the occurrence of upper airway symptoms in 41 patients with COPD and documented symptoms pertaining to the upper airways in 27 (65%).[15] Nasal discharge, reported by all 27 patients, was the most common symptom and in 85%, nasal symptoms occurred during change of seasons rather than perennially. Furthermore, these patients had a significantly lower forced expiratory volume in one second (FEV_1) as compared to those without it. Nineteen of the 27 patients, had evidence of sinusitis on computed tomography (CT) with maxillary sinuses being the most commonly involved.

Since the upper and lower respiratory tract form a single continuous pathway, it is but natural that triggering agents affect the entire airway right from the nostrils to the alveoli. Cigarette smoke, the chief culprit for COPD, is known to cause upper airway inflammation.[16,17] Smoke inhalation leads to increased goblet cell hypertrophy and submucosal gland hyperplasia resulting in excessive mucus production from the nasal mucosal lining.[18] In addition, tobacco smoke also reduces mucociliary clearance.[19] It has also been demonstrated that smoking greater than 20 cigarettes per day significantly prolonged mucociliary clearance time when compared to non-smokers.[20] Moreover, on anterior rhinomanometry, a significant increase in nasal resistance was noted in heavy smokers as compared to non-smokers.[21] The effects of smoking leading to upper airway pathology are such that tobacco smoke is now an established causal factor for exacerbations of nasal and sinus symptoms.[17,22]

Different studies on increased nasal inflammation in patients with COPD have further strengthened the association of upper airways involvement in COPD. Greater nasal neutrophil activity was seen after histamine challenge in COPD patients with nasal symptoms when compared to those without.[23] A subsequent study[24] demonstrated that the nasal inflammation persisted even after smoking cessation. Nasal endoscopy in patients with COPD visualised nasal mucosal abnormalities.[25] When compared with control subjects, these patients had higher levels of

nasal inflammatory markers, but there was no significant correlation to either airflow obstruction or to the severity of nasal symptoms.[24, 25]

During COPD exacerbations, there occurs a heightened systemic inflammatory response that pans into the upper airway mucosa too. A significant correlation was found between the degree of upper and lower airways inflammation during acute exacerbations.[26] Thick yellow nasal discharge, rhinorrhoea and a blocked nose were found to be the risk factors for developing exacerbations of chronic bronchitis.[11] In the ELCOPD cohort,[27] there was a higher incidence of all nasal symptoms in "frequent exacerbators," who were defined as having an exacerbation frequency greater than the median (2.56 exacerbations per year) for the entire ELCOPD cohort. When 150 patients, from among the ELCOPD cohort, were asked to record daily peak expiratory flow (PEF) along with respiratory and nasal symptoms for a median period of approximately three years, the "frequent exacerbators" experienced significantly increased coryzal symptoms when compared to infrequent exacerbators. Also, a significantly higher exposure to cigarette smoke was noted in those with frequent upper respiratory infections.[27]

A further look into the impact of upper airway symptoms on the quality of life (QOL) in patients with COPD deserves mentioning. The 20-item Sino-Nasal Outcome Test (SNOT-20) questionnaire,[28] a validated disease-specific health-related QOL tool for the assessment of rhinosinusitis, was self-administered to 65 patients with moderate-to-severe COPD randomly selected from the ELCOPD cohort.[13] Simultaneously, these patients were also asked to fill the St. George's Respiratory Questionnaire (SGRQ).[29] The QOL was significantly impaired in those with nasal symptoms, and the mean SNOT-20 score showed a direct correlation with the number of nasal symptoms experienced. Expectedly, the "frequent exacerbators" had a greater impact on their health as evidenced from the SGRQ analysis. The highlighting feature of this study was a lack of correlation between the SNOT-20 and the SGRQ scores, thereby indicating that both upper as well as lower airway symptoms were independently responsible for impairment in the QOL. Another key finding was the absence of any significant correlation between the SNOT-20 score and smoking status. The authors postulated that there could possibly be continuing upper airway inflammation even after quitting smoking. We too assessed the impact of upper airways symptoms on the QOL in our 41 patients with COPD with the help of the SNOT-22[30] and the SGRQ[29] questionnaires, and found that the mean scores of both the questionnaires were significantly higher in those with associated nasal and sinus disease.[15] A study assessing "treatment failure" of COPD exacerbations found that a history of sinusitis correlated significantly with treatment failure.[31]

There is now a mounting body of evidence to suggest that upper airway involvement is fairly common in COPD and this clinical entity could perhaps be considered as a "pan airway disease".[32] It has been argued that the association of nasal symptoms with impaired QOL and that the occurrence of sinusitis correlating with treatment failure of exacerbation of COPD should suggest a "therapeutic nasal intervention" in these patients.[10] It appears likely that upper airway symptoms in COPD, if left untreated, could possibly lead to suboptimal control of the disease.

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REFERENCES

1. Laennec RTH. A *Treatise on the Diseases of the Chest*. New York: Hafner Publishing; 1962.
2. Briscoe WA, Nash ES. The slow space in chronic obstructive pulmonary diseases. *Ann NY Acad Sci* 1965;121:706-22.
3. Beasley R, Weatherall M, Travers J, Shirtcliffe P. Time to define the disorders of the syndrome of COPD. *Lancet* 2009;374:670-2.
4. Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non smokers. *Lancet* 2009;374:733-43.
5. Tran B, Kalhan R. The emerging role of systemic inflammation in chronic obstructive pulmonary disease. *Clin Pulm Med* 2008;15:55-62.
6. Fabbri LM, Rabe KF. From COPD to chronic systemic inflammatory syndrome? *Lancet* 2007;370:797-9.
7. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet* 1997;349:1498-1504.
8. Grossman J. One airway one disease. *Chest* 1997;111:11S-16S.
9. Shah A. Rarely does one hear a wheeze without a sneeze [Editorial]. *Indian J Chest Dis Allied Sci* 2000;42:143-5.
10. Hurst JR. Upper airway. 3: Sinonasal involvement in chronic obstructive pulmonary disease. *Thorax* 2010; 65:85-90.
11. Montnemery P, Svensson C, Adelroth E, Lofdahl CG, Andersson M, Greiff L, *et al*. Prevalence of nasal symptoms and their relation to self-reported asthma and chronic bronchitis/emphysema. *Eur Respir J* 2001; 17:596-603.
12. Roberts NJ, Lloyd-Owen SJ, Rapado F, Patel IS, Wilkinson TM, Donaldson GC, *et al*. Relationship between chronic nasal and respiratory symptoms in patients with COPD. *Respir Med* 2003;97:909-14.
13. Hurst JR, Wilkinson TMA, Donaldson GC, Wedzicha JA. Upper airway symptoms and quality of life in chronic obstructive pulmonary disease (COPD). *Respir Med* 2004; 98:767-70.

14. Nihlen U, Montnemery P, Andersson M, Persson CG, Nyberg P, Lofdahl CG, *et al*. Specific nasal symptoms and symptom-provoking factors may predict increased risk of developing COPD. *Clin Physiol Funct Imaging* 2008;28: 240-50.
15. Kumar A, Shah A. Occurrence of upper airway symptoms and their impact on quality of life (QoL) in patients with chronic obstructive pulmonary disease (COPD). *Respirology* 2008;13 (Suppl. 5):A109.
16. Benninger MS. The impact of cigarette smoking and environmental tobacco smoke on nasal and sinus disease: a review of the literature. *Am J Rhinol* 1999;13:435-8.
17. Phillips DE, Hill L, Weller P, Willett M, Bakewell R. Tobacco smoke and the upper airway. *Clin Otolaryngol Allied Sci* 2003;28:492-6.
18. Auerbach O, Stout AP, Hammond EC, Garfinkell L. Changes in bronchial epithelium in relation to cigarette smoking and in relation to lung cancer. *N Engl J Med* 1961;265:253-67.
19. Bascom R, Kesavanathan J, Fitzgerald TK. Sidestream tobacco smoke exposure acutely alters human nasal mucociliary clearance. *Environ Health Perspect* 1995; 103:1026-30.
20. Mahakit P, Pumhiren P. A preliminary study of nasal mucociliary clearance in smokers, sinusitis and allergic rhinitis patients. *Asian Pacific J Allergy Immunol* 1995; 13:119-21.
21. Dessi P, Sambuc R, Moulin G, Ledoray V, Cannoni M. Effect of heavy smoking on nasal resistance. *Acta Otolaryngol* 1994; 114:305-10.
22. Grieff L, Wollmer P, Andersson M, Persson CG. Human nasal absorption of 51 Cr - EDTA in smokers and control subjects. *Clin Exp Allergy* 1994;24:1036-40.
23. Nihlen U, Andersson M, Lofdahl CG, Persson CG, Montnemery P, Greiff L. Nasal neutrophil activity and mucinous secretory responsiveness in COPD. *Clin Physiol Funct Imaging* 2003;23:138-42.
24. Hurst JR, Wilkinson TM, Perera WR, Donaldson GC, Wedzicha JA. Relationships among bacteria, upper airway, lower airway, and systemic inflammation in COPD. *Chest* 2005; 127:1219-26.
25. Hens G, Vanaudenaerde BM, Bullens DMA, Piessens M, Decramer M, Dupont LJ, *et al*. Sinonasal pathology in nonallergic asthma and COPD: ''united airway disease'' beyond the scope of allergy. *Allergy* 2008;63:261-7.
26. Hurst JR, Perera WR, Wilkinson TM, Donaldson GC, Wedzicha JA. Systemic and upper and lower airway inflammation at exacerbation of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2006; 173:71-8.
27. Hurst JR, Donaldson GC, Wilkinson TMA, Perera WR, Wedzicha JA. Epidemiological relationships between the common cold and exacerbation frequency in COPD. *Eur Respir J* 2005;26:846-52.
28. Piccirillo JF, Merritt MG, Richards ML. Psychometric and clinimetric validity of the 20-item Sino-Nasal Outcome Test (SNOT-20). *Otolaryngol Head Neck Surg* 2002;126:41-7.
29. Jones PW. The St. George's Respiratory Questionnaire. *Thorax* 1991;46:676-82.
30. Buckland Jr, Thomas S, Harries PG. Can the Sino-Nasal Outcome Test (SNOT-22) be used as a reliable outcome measure for successful septal surgery? *Clin Otolaryngol Allied Sci* 2003;28:43-7.
31. Dewan NA, Rafique S, Kanwar B, Satpathy H, Ryschon K, Tillotson GS, *et al*. Acute exacerbation of COPD. Factors associated with poor treatment outcome. *Chest* 2000; 117:662-71.
32. Kim J-S, Rubin BK. Nasal and sinus inflammation in chronic obstructive pulmonary disease. *COPD* 2007; 4:163-6.

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