EDITORIAL OVERVIEW

On the cutting edge of clinical pulmonary medicine in COPD

This supplement describes the proceedings from a meeting convened in Trevi, Italy, to discuss the cutting edge of clinical pulmonary medicine in chronic obstructive pulmonary disease (COPD). This meeting focused on the management of stable COPD. Clinical approaches to the prevention and treatment of exacerbations is a very important topic, which we would like to address at a subsequent meeting.

COPD represents a serious and growing threat to public health. It is projected that by 2010, deaths arising from COPD will be more common in European countries than from pneumonia, some forms of cancer (colorectal, stomach and breast), cirrhosis of the liver and road traffic accidents. In fact, it is predicted that by 2020, COPD will have become the third most common cause of death worldwide, and the fourth most important disabling condition.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) was established to raise awareness of COPD and stimulate research into this area, as well as to develop evidence-based guidelines for the diagnosis, treatment and management of COPD. The most recent guidelines produced by GOLD were published in 2004 and they define COPD as follows: 'COPD is a disease state characterised by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases'. The American Thoracic Society–European Respiratory Society Statement on COPD, presented in 2004 and updated on-line, represents the largest scientifically supported source of information on this disease and presents the concept that COPD has systemic consequences.

COPD represents an inflammatory response to the inhalation of atmospheric pollution, most commonly cigarette smoke, although a number of poorly defined genetic risk factors also play a role. The pathophysiology underlying COPD arises from varying degrees of airway narrowing, smooth-muscle hypertrophy and fibrosis in the bronchioles, intraluminal secretions, and the loss of elastic recoil pressure that is associated with emphysema. The hyperinflation associated with COPD—which is often increased during exercise—is an important factor associated with dyspnoea. In addition to this symptom, protease–anti-protease imbalance and increased oxidative stress probably contribute to the development of COPD.

Patients with COPD suffer exacerbations—an acute worsening of their condition that requires increased medication—and this is often a result of viral or bacterial infections. Clearly complex in nature, COPD exerts profound systemic effects, including elevated levels of inflammatory markers, muscular metabolic abnormalities, and in some cases, cachexia. As a consequence of the respiratory and systemic derangements, patients experience dyspnoea, fatigue, exercise intolerance, muscular weakness, limitation of daily activities, reduced quality of life (QoL) and, ultimately, increased mortality.

A number of treatments are available for COPD, including bronchodilators (short-acting and long-acting \( \beta_2 \)-agonists and anti-cholinergics), inhaled corticosteroids, combinations involving inhaled corticosteroids and long-acting \( \beta_2 \)-agonists, oxygen therapy and lung-volume-reduction surgery. Bronchodilators reduce the airflow limitation and hyperinflation associated with COPD, helping to alleviate the dyspnoea associated with this disease. To date, however, only smoking cessation has been convincingly demonstrated to modify the progression of this disease, and only oxygen therapy has been shown to favourably affect survival. This
thinking may change in the next few years when data from two, very large, randomised, long-term trials—TORCH and UPLIFT—become available. TORCH (TOwards a Revolution in COPD Health) will examine the long-term effects (including survival) of the inhaled steroid, fluticasone propionate, and the long-acting β2-agonist bronchodilator, salmeterol, alone or in combination. UPLIFT (Understanding Potential Long-term Impacts on Function with Tiotropium) will assess the effect of the long-acting anticholinergic bronchodilator, tiotropium, on the long-term decline in forced expiratory volume in 1 s (FEV1) that occurs in COPD. While these two trials are investigating the long-term efficacy of currently available agents, a number of new pharmacotherapeutic agents are in development for the treatment of this disease. Many of these agents target elements of the inflammatory pathways because systemic inflammation is seen as key to the pathophysiology of COPD. Such agents include inhibitors of phosphodiesterase-4 and leukotriene B4.

Pulmonary rehabilitation complements pharmacotherapy and is now considered central to the management of symptomatic COPD. This form of management has negligible effects on pulmonary function, yet commonly provides substantial relief from dyspnoea, increased exercise tolerance and improved health-related QoL. Pulmonary rehabilitation appears to work via several mechanisms, including reducing some of the comorbidity associated with chronic respiratory disease (such as the physical deconditioning associated with sedentarism) and providing patients with self-management strategies (through disease-related education). Rehabilitation would also seem to reduce subsequent health care utilisation, with the valuable cost reductions that this would imply.

The logical concept of optimising the pharmacologic management of COPD patients prior to, and during pulmonary rehabilitation to achieve greater benefit, is becoming more widely recognised. Despite a growing body of research evidence, further work is needed to determine which patients will benefit most from pulmonary rehabilitation, how this form of management is best prescribed, and how to identify the most suitable practice setting, which is dependent on the stage/phase of this disease.

Improved diagnostic and assessment methods are also important in our management of COPD. Spirometry, and the measurement of the forced vital capacity (FVC) and FEV1, are still our mainstay in establishing a diagnosis of this disease. Nevertheless, other measurements, including the level of dyspnoea, the degree of COPD-associated weight loss, and impairments in functional status and health status, also provide important information for assessing morbidity and predicting mortality. For instance, the recently developed BODE index, which incorporates body-mass index (B), airflow obstruction (O), dyspnoea (D) and exercise capacity (E) into one score, is a better predictor of survival in COPD than any of its individual components.

Extensive research into the genetic basis of COPD is also ongoing. Findings from such investigations may assist with the identification of patients at risk for developing COPD. Novel methods of characterising the anatomical and mechanistic changes associated with COPD may also provide greater phenotypic discrimination and therefore, may be useful in more precisely directing therapy. Less reliance would accordingly be placed upon spirometry as the main means of assessing response to therapy.

Such exciting developments deepen our understanding and widen the scope for managing COPD. Improved diagnosis and evaluation, coupled with better treatment and management regimens for COPD, should improve the efficiency of our treatment, enhancing symptomatic relief, increasing patient participation in daily activities, and perhaps, favourably modifying the course of this disease.

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