Perspective

Chronic Obstructive Pulmonary Disease COPD, is currently the fourth leading cause of death in the world, but projected to be the 3rd leading cause by 2020. More than 3 million people died of COPD in 2012, accounting for 6% of all deaths worldwide. COPD represents an important public health challenge that is both preventable and treatable, if not curable [1]. Characteristically, bronchitis and emphysema are both present in most patients. Smoking cessation is by far the most effective intervention in COPD resulting in better health status, less exacerbations and improved survival [2]. Physical exercise, especially when in the shape of multidisciplinary rehabilitation also has significant effects [3].

Inhaled bronchodilators improve airflow and hyper inflation, reduce symptoms and exacerbation frequency and improve health status and quality of life [4]. In patients with frequent exacerbations inhaled steroids are advised, although the actual effects of these ICS in COPD are still under debate [5]. They appear to be less effective when added to adequate doses of two types of long acting bronchodilators [6] and can be stopped without increased of exacerbations in many of these patients [7]. Also, ICS were found to increase the risk of pneumonia [8].

The evidence for the effects of ICS in COPD comes from a number of large randomised trials. Typically, these trials have included huge numbers of patients with a diagnosis of COPD, usually based on spirometry findings that fit with such diagnosis. Attempts are made to exclude patients with asthma. However, there are reasons to believe that successful exclusion of asthma is not always achieved as in many of these studies outcomes vary substantially between study subjects, sometimes even to the extent that lung function appears to have normalised altogether. These patients had better not been included in the trial, by putting more effort into excluding these so-called steroid responders using appropriate history-taking. Unfortunately, in many trials this is not done adequately. “Current asthmatics” may be excluded, or “patients with a history of asthma”, but what may very well point at asthma is often over looked. “Childhood bronchitis”, persistent airflow limitation in never-smokers, atopy, subjects with a family history of asthma or atopy should better be excluded as well when studying effects of ICS in COPD.

Some believe that steroids responders can be identified, e.g. with measuring eosinophils in sputum. However, if this is done in post-hoc analyses of the studies with contaminated cohorts the problem is likely to persist [9].

Another means is to reassess all these landmark studies on ICS in COPD by eliminating real responders after 3-6 months of treatment and studying the effects of ICS in the remaining “non-responders”. One might argue that it would be unfair to study the effects of any given drug in non-responders, but my point is, that many of the early responders may not have had COPD in the first place, or that the diagnosis should be discarded in patients with asthma-like responses or even normalization of the lung function. The latter is likely to have been the case in a substantial number of patients, given the wide range of responses seen in many of these trials.

I challenge the companies that have these data on file to share the outcomes of such additional analyses with us!

References


