International Journal of COPD

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GUEST EDITORIAL

ICS and COPD: Time to clear the air

This article was published in the following Dove Press journal:
International Journal of COPD
29 July 2009
Number of times this article has been viewed

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The debate about what constitutes the correct treatment for COPD has recently intensified.[1] This discussion has grumbled on ever since the first multicenter trials using inhaled corticosteroids (ICS) in chronic obstructive pulmonary disease (COPD) such as the European Respiratory Society study on chronic obstructive pulmonary disease (EUROSCOP) and Inhaled Steroids in Obstructive Lung Disease (ISOLDE) were published in the late 1990's and the results of trials such as TORCH (TOwards a Revolution in COPD Health) using combination products has only added to the confusion.

Complex debate predominantly pertaining to statistical methodology has muddied the waters. Concepts such as immortal time bias and selection bias introducing regression to the mean are often too difficult to grasp for the average reader.

However, some of the methodological flaws identified by Suissa and colleagues[2] are much easier to understand and solutions to these are potentially at hand. Firstly, it is clear trials investigating the effects of ICS on COPD may in fact be trials predominantly examining the effects of ICS withdrawal. It is not sufficient to state a treatment works simply because patients deteriorate when that treatment is withdrawn. Re-analysis of all data such that treatment effects are stratified according to pre-use of ICS is easy to do as all the data is there, as Suissa eloquently showed in his re-working of the OPTIMAL trial data.[3] Even though most of the ICS/COPD trials have approximately 50% of subjects on ICS at randomization, some have a much lower rate, such as in Szfranski and colleagues[4] (26%) and this may not necessarily skew the overall conclusions of the trial(s). Secondly, when assessing the impact of combination treatments it is imperative to present the correct 2×2 factorial analysis such that the impact of each individual component can be assessed as Suissa performed for TORCH.[2] Thus it becomes clear the effect on mortality may be entirely long-acting β-agonists (LABA) dependant. The issue of systemic side effects and pneumonia in COPD patients treated with high doses of ICS over long periods also needs further careful evaluation.

It would be disingenuous of us to suggest ICS have no place in the management of COPD. We know a proportion of patients benefit from their bronchoprotective effect and that this subset of patients with COPD has a higher mortality risk.[5] ICS are also indicated in the patients with more reversible COPD who probably suffer from concomitant asthma. It is time that some fundamental issues are addressed. We strongly urge the pharmaceutical industry to re-analyze the underlying data and demystify at least some of the methodological smog.

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