The role of Inhaled corticosteroids: Why, Who and When

Inhaled corticosteroids (ICS) have been examined in a large number of well-powered trials in COPD, either as monotherapy or in combination with a long-acting beta-agonist (LABA). In both settings, they reduce exacerbations and symptoms, and they increase lung function (FEV₁) and health status. This has mainly been shown in patients with severe and very severe COPD and a history of exacerbations, but the effect has also been seen in patients without a history of exacerbations, and lately in the SUMMIT trial in patients with FEV₁ between 50 and 70% of predicted. ICS may reduce rate of FEV₁ decline in moderate to very severe COPD and did so as well in the SUMMIT trial.

However, ICS have side effects; they cause oral candidiasis, hoarse voice and in patients with severe and very severe COPD an 80% increase in risk of pneumonia. ICS have been linked to osteoporosis, diabetes and other conditions but these associations have never been proven.

Because of these adverse effects, ICS are recommended only for prevention of exacerbations in patients at high risk of frequent exacerbations (2 or more per year, or one hospital admission, or FEV₁ < 50% predicted) and their efficacy is better when looking at exacerbations requiring treatment with oral corticosteroids.

It may be time to review these recommendations. First, initial data from a study of limited size in low risk patients indicate that dual long-acting bronchodilators may be at least as effective as combined ICS/LABA in preventing exacerbations and a press release on the larger FLAME study seems to confirm this. In addition, the WISDOM trial – despite methodological shortcomings – showed that some patients on ICS could be managed well on a non-steroid containing regimen. Thus, there is an impetus to further explore if there is a subset of patients getting more benefit from ICS; i.e., a better benefit / risk ratio. Blood eosinophils have been suggested as an indicator of increased efficacy of ICS and post-hoc analyses have confirmed this, mainly using a 2% cut-off for blood eosinophilia. However, the cut-off on 2% has been disputed, not least because the association between blood eosinophils and risk of exacerbations is questionable for a 2% cut-off but decent for an absolute cut-off, with 0.34 x 10⁹/L being suggested as optimal.

In addition, the possible effect on FEV₁ decline needs to be considered. Slowing disease progression has for years been seen as the holy grail of COPD. Again, retrospective analyses of the ISOLDE trial have indicated that ICS may be more effective at slowing decline of FEV₁ in patients with COPD but as the data on ICS and decline are in general somewhat inconsistent, it is currently not timely to use disease modification as an indication for ICS. Closer scrutiny of SUMMIT data may give reason for reconsideration; however, with our growing understanding of the complexity of interpreting FEV₁ decline the question is not an easy one.

So, for whom, why and when? I believe ICS are for exacerbation prevention only. It should be aimed at frequent exacerbators without typical infectious exacerbations and preferably to individuals with a blood eosinophil count of 0.300 x 10⁹/L or higher. In patients with side effects or recurrent pneumonia, ICS should not be used.
References


