Withdrawal of inhaled corticosteroids in COPD

To the Editor:

The recently published European Respiratory Society guideline on withdrawal of inhaled corticosteroids (ICS) in COPD makes a "conditional recommendation for the withdrawal of ICS in patients with COPD without a history of frequent exacerbations" [1]. The authors appropriately specify that a "conditional recommendation" indicates that there is "uncertainty about the balance of desirable and undesirable consequences of the intervention, and that well-informed patients may make different choices regarding whether to have or not have the specific intervention" [1]. In order to inform patients correctly, however, physicians must have a clear idea of what to recommend in different individual circumstances. It is therefore important to know how to exclude that the absence of exacerbations in a given COPD patient treated with ICS (on top of one or two bronchodilators, as recommended by the Global Initiative for Chronic Obstructive Lung Disease [2]) may not be due, precisely, to ICS treatment itself [3]. If this was the case, withdrawal of ICS in this patient may not be a wise and safe decision. I would be very interested in knowing the view of the panel on this specific scenario. Thanks very much and congratulations for the work done.

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Withdrawal of inhaled steroid treatment in COPD patients is challenging. The history of the patient needs to be carefully assessed to exclude that they are not being effective and/or safe; and a stepwise approach with careful monitoring seems advisable. https://bit.ly/2y3Tt2k

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References

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From the authors:

We thank A. Agusti for his interest in the European Respiratory Society (ERS) guideline on withdrawal of inhaled corticosteroids (ICS) in COPD [1]. He raises an important concern, that we might be recommending discontinuing a potentially effective treatment. This was carefully considered by the panel and there are important reasons to be sure that this is not the case.

We absolutely agree that if ICS was the reason for an individual patient not to have exacerbations, it would not be wise to discontinue it. However, how can we assess whether ICS was the cause for an individual patient not to have exacerbations?

It is very difficult to know the reason why a patient had exacerbations, but it is even more difficult to understand why a patient did not have exacerbations. Was it because of the ICS, because of the bronchodilators, because of a milder winter season, because of the anti-influenza vaccination, a change in their lifestyle or just because of chance?

This is a good example of the *Post hoc ergo propter hoc* fallacy (after this, therefore because of this), which impacts much of clinical medicine and, in particular for ICS withdrawal, it is critical to challenge this fallacy. The evidence shows that ICS are modestly (if at all) effective in preventing exacerbations in COPD patients with low blood eosinophil counts [2]. There is therefore no reason to think that if a patient with low eosinophils is not having exacerbations, this is because of the ICS therapy. Similarly, when and if a patient has an exacerbation following ICS withdrawal it does not necessarily mean that this is the result of withdrawal. Randomised trials and the natural history of COPD tell us that exacerbations, in the vast majority of cases, would have happened anyway.

The only way to evaluate whether discontinuation of a drug is safe is to design randomised clinical trials specifically for this purpose and the only way to deliver informed recommendations about clinical practice is by unbiased evaluation of the evidence generated in these clinical trials. Fortunately, for the particular question of "Should ICS be withdrawn in patients with COPD?", there were several well-designed randomised clinical trials of ICS withdrawal that informed the panel recommendation [1]. The evaluation of the evidence produced the conditional recommendation for the withdrawal of ICS in patients with COPD without a history of frequent exacerbations [1]. However, A. Agusti does not mention another of our recommendations: "strong recommendation not to withdraw ICS in patients who have a blood eosinophil count ⩾300 eosinophils per µL, with or without a history of frequent exacerbations" [1]. It is well known that ICS are more effective in preventing exacerbations in patients with high blood eosinophil counts [2, 3], and this may be the reason why withdrawal studies consistently show that discontinuation of ICS in patients with high blood eosinophil counts may result in increased risk of exacerbations and therefore should not be discontinued in these patients.

It is reassuring that a recent American Thoracic Society (ATS) guideline using a strict methodology reached a similar conclusion and published a similar recommendation: "a conditional recommendation for ICS withdrawal for patients with COPD receiving triple therapy (ICS/long-acting β-agonist/long-acting muscarinic antagonist) if the patient has had no exacerbations in the past year" [4]. The key difference between the two recommendations is the focus on the use of blood eosinophil counts in the ERS guideline, which provides a means of identifying those patients where discontinuation of ICS may put patients at risk.

In conclusion, both the ERS and the ATS have made a conditional recommendation to withdraw ICS in patients with COPD without history of exacerbations, and the ERS extends this recommendation with a strong recommendation not to withdraw ICS in patients who have a blood eosinophil count ⩾300 eosinophils per µL. These recommendations are not based on personal opinions of the panellists, or on hypothesis, but on a standardised evaluation of the evidence generated in randomised clinical trials.

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ICS can be withdrawn in COPD patients without history of exacerbations https://bit.ly/2TorQZd

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