International Primary Care IPCRG Respiratory Group

DESKTOP HELPER

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Appropriate use and withdrawal of inhaled corticosteroids (ICS) in patients with chronic obstructive pulmonary disease (COPD)

The purpose of this desktop helper for the appropriate use and withdrawal of inhaled corticosteroids (ICS) is to:

1. Help primary care clinicians identify patients with chronic obstructive pulmonary disease (COPD) who would benefit from ICS treatment compared to those in whom it may not be appropriate, and
2. Provide guidance on how to withdraw ICS in patients with COPD in whom it is not needed.

THE ROLE OF ICS IN THE TREATMENT OF PATIENTS WITH COPD

In COPD, evidence supports the use of an inhaled corticosteroid (ICS) in combination with a long acting beta-agonist (LABA) or as part of a triple therapy regimen with the addition of a long acting muscarinic-antagonist (LAMA) to reduce the risk of symptomatic exacerbations.[1] The effect of these regimens (ICS/LAMA/LABA and ICS/LABA vs LABA/LAMA) is greater in patients with high exacerbation risk (≥2 exacerbations and/or 1 hospitalization in the previous year).[2–4] However, until recently there has been no consistent evidence on the long-term effects of ICS on mortality or the group of patients who would benefit most.[1]

Recent studies have shown that blood eosinophil counts predict the effect of ICS in preventing future exacerbations in COPD[3,5] and they can be used as a biomarker to estimate the benefits of adding ICS to regular bronchodilator treatment for individual patients.[1]

ADVERSE EFFECTS ASSOCIATED WITH ICS THERAPY

There is high quality evidence from randomized controlled trials (RCTs) that ICS use is associated with many adverse effects including oral candidiasis, hoarse voice, skin bruising and pneumonia and results of observational studies suggest that ICS treatment could also be associated with increased risk of diabetes/poor control of diabetes, cataracts, osteoporosis, fracture and mycobacterial infection including tuberculosis.[1]

CURRENT RECOMMENDATIONS ON ICS USE FOR PATIENTS WITH COPD

For all patients with COPD, LABDs are recommended as first-line treatment. For patients whose disease is classified as GOLD 'D' (i.e. symptomatic with exacerbations) with a history of asthma or with blood eosinophil counts ≥300 cells/μL, initial therapy with LABA/ICS combination may be the first choice.[1] Patients with concomitant asthma should be treated with ICS combined with a LABA.[6] After initial therapy, clinical response should be reviewed and adjustments made to pharmacological treatment, increasing or decreasing therapy, to obtain optimal symptom control. When patients with COPD are experiencing increased breathlessness and other symptoms, adjustment of therapy to ensure maximal bronchodilation is warranted. Current guidelines do not recommend ICS therapy if deterioration is driven by symptoms.[1]

In COPD patients who continue to experience frequent exacerbations despite appropriate bronchodilator therapy and have blood eosinophils <100 μL^{-1}, ICS are not recommended unless the individual patient has a history of asthma; alternative treatments such as roflumilast and azithromycin can be considered.

In patients with blood eosinophils >300 μL^{-1}, the addition of ICS to LABA therapy is recommended. For patients with blood eosinophils of 100–300 μL^{-1}, careful consideration of the potential benefits and risks of ICS therapy should be undertaken.[7]

IPCRG GUIDANCE ON WHEN TO BEGIN ICS IN PATIENTS WITH COPD

1. Consider ICS combined with broncho-dilators as initial treatment in a recently diagnosed patient and/or a patient who is pharmacological treatment "naïve" based on the history of asthma, risk of exacerbation, and eosinophils as shown in Table 1.
2. Consider ICS after reassessment of patients with COPD not previously treated with ICS based on risk of exacerbations and eosinophils as shown in Table 1.

In both cases, optimal bronchodilation is critical.

CURRENT USE OF ICS FOR PATIENTS WITH COPD

Despite recent recommendations that ICS use should be reserved for a small proportion of patients with COPD, there is evidence of continued inappropriate use of ICS in these patients. Guidelines implementation has been inconsistent as evidenced by numerous studies showing inappropriate prescription or over-prescription of ICS by up to 50%, a situation that has also been shown in the IPCRG UNLOCK study.[8]

EVIDENCE FOR ICS WITHDRAWAL IN PATIENTS WITH COPD

Updated COPD guidelines support ICS withdrawal[1] and recent studies indicate ICS can be withdrawn in both low- and high-risk patients, provided adequate bronchodilator therapy is in place.[9-17]

A detailed review of these studies is in preparation. If you have a specific query in the meantime, please contact IPCRG businessmanager@theipcrg.org.

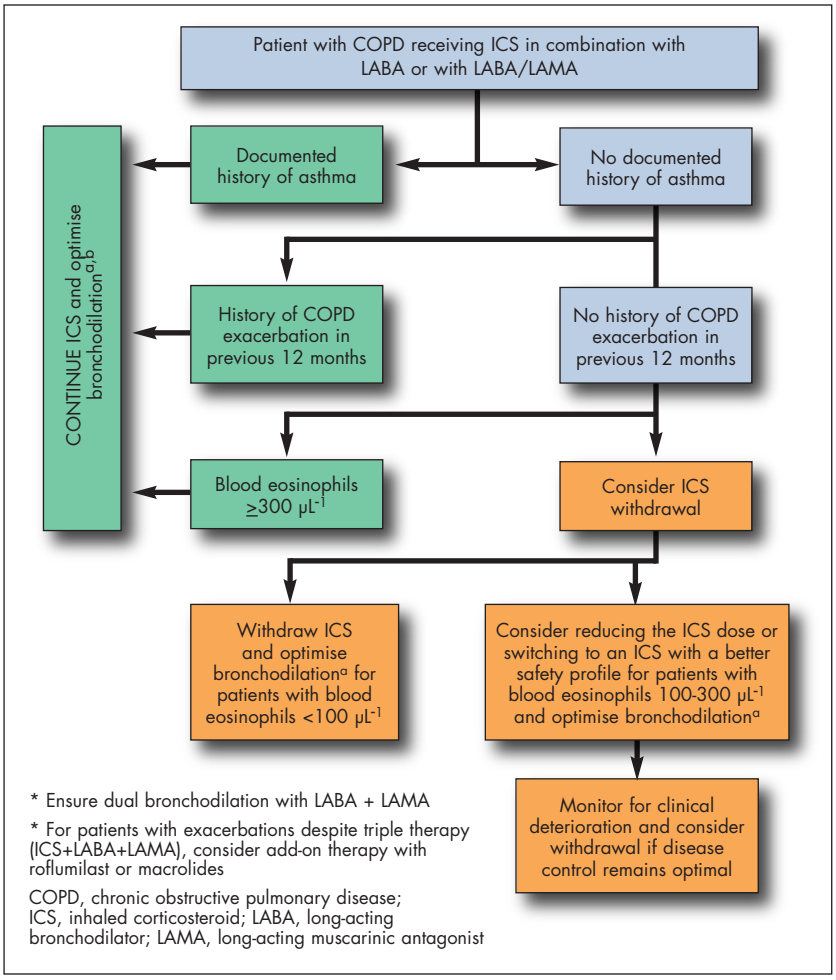
IPCRG GUIDANCE ON WHEN AND HOW TO WITHDRAW ICS IN PATIENTS WITH COPD

An internationally agreed algorithm to guide the management of patients with COPD in primary care clarifying for whom, when and how ICS withdrawal should be performed is currently lacking. The first edition of this desktop helper provided some guidance based on a limited evidence base. With the availability of new evidence, the IPCRG has updated their guidance as detailed in the algorithm below.

TABLE 1. IPCRG GUIDANCE ON WHEN TO BEGIN ICS IN PATIENTS WITH COPD. FIRST OPTIMISE BRONCHODILATION.

1. Initial treatment	a. Well documented previous history of asthma, especially if diagnosis under 40 years' old b. ≥2 moderate exacerbations or 1 hospitalization in the previous year and >300 eosinophils μL^{-1}
2. Reassessment†	a. ≥2 moderate exacerbations or 1 hospitalization in the previous year* and >300 eosinophils μL^{-1}* b. ≥2 moderate exacerbations or 1 hospitalization in the previous year* and eosinophils μL^{-1} >100 but <300 after carefully balanced risk-benefit considering: o Recent pneumonia o Confirmed bacterial colonization o Bronchiectasis o Comorbidities, especially diabetes and osteoporosis or those at risk for these conditions

† Patient not previously on ICS
* Or since previous assessment if less than 12 months



* Ensure dual bronchodilation with LABA + LAMA

* For patients with exacerbations despite triple therapy (ICS+LABA+LAMA), consider add-on therapy with roflumilast or macrolides

COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; LABA, long-acting bronchodilator; LAMA, long-acting muscarinic antagonist

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