Anti-inflammatory therapy

Inhaled corticosteroids

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Background

Neutrophil-dominated airway inflammation leads to lung damage in CF patients and finding a suitable anti-inflammatory strategy is a relevant issue. Oral prednisolone on alternate days demonstrated to have a good impact on lung condition, but showed severe side effects. Besides their effectiveness in the management of recurrent wheezing or asthmatic symptoms, Inhaled Corticosteroids (ICS) could also be effective in treating lung inflammation. In lung diseases other than CF, ICS risk-benefit profile as anti-inflammatory therapy remains unclear and it has been affirmed (KellY HW, 2012) that, even at moderate doses, ICS, if given consistently and daily, can suppress growth.

In CF one retrospective analysis of data from 2978 patients collected in a period of 10 years showed that ICS therapy is associated with a significant reduction in the rate of FEV1 decline, a decreased linear growth and an increased hypoglycemic therapy use (Ren CL, 2008). These results are confirmed by a study on Belgium CF Registry data (De Boeck K, 2011). In another study (van Horck M, 2018) ICS therapy resulted as not significantly associated with lung disease evolution in CF children. Concerns about ICS adverse effects have been shown (Erdem E, 2012). A study (Noni M, 2014) demonstrated that the duration of ICS treatment is associated with A. fumigatus first isolation and chronic colonization and this issue has been affirmed again (Hong G, 2018).

In the past, even if they are commonly prescribed also without reversible obstruction (Levine H et al, 2016), an eminent part of the international literature affirms that it cannot be concluded that ICS are bene?cial as anti-inflammatory therapy and that the daily dose of ICS should be adapted to control symptoms, in order to prescribe the smallest possible dose (Fayon M, 2014). Previous clinical practice guidelines from the Cystic Fibrosis Foundation for CF children 2-5 years old (Lahiri T, 2016), agreed upon that ICS are not recommended for management of lung disease, as no clear benefit has been. Several Authors (Preville-Ratelle S, 2018) affirmed again that, because of the adrenal insufficiency possibly associated with corticosteroids use, also with the inhaled ones, ICS therapy has to be limited to patients who demonstrate real benefit from it.

A particular point of view is emerging from the use of CFTR modulators. Prior studies support a role for type 2 (T2) inflammation in many pwCF and CF-asthma overlap syndrome (CFAOS) is considered a separate clinical entity (Marion CR, 2021). Preliminar observations showed a significant reduction (20.10%, $p < 0.001$) in 12-month mean IgE following ETI initiation; this change remained statistically significant in the multivariate model. The longitudinal analysis demonstrated no change in absolute eosinophil count (AEC) following therapy initiation. The authors think that the lack of influence on AEC argues against an impact on previously established T2 inflammation and that the reduction in IgE is likely related to antigen load reduction post ETI. Further studies are warranted to determine the underlying mechanism of ETI impact on T2 inflammation and possible role for asthma immunomodulator therapy post ETI initiation in CFAOS (Mehta A, 2023).

Issues

Effectiveness of ICS on lung disease progression.

Effectiveness of ICS on quality of life and long-term prognosis.

Impact on bronchial hyperreactivity.

Impact on nutritional indices.

Occurrence of any adverse event.

Impact of ICS withdrawal on lung condition

What is known

One Cochrane review (Balfour-LynnIM, 2019) is available. Thirteen RCTs on 506 people aged between 6 and 55 years were included. One trial was a withdrawal study in individuals who were already taking ICS. Significant benefits have not been conclusively demonstrated, because it has not been established whether long-term use is beneficial in reducing lung inflammation and so improving survival. Withdrawal in individuals already taking ICS was shown to be safe. There is some concerns about adverse events associated with long-term therapy, above all those affecting growth.

Unresolved questions

Evidences about ICS efficacy and safety in CF patients are not resolved.

Up to now, no registered RCT on ICS is ongoing.

Keywords

Anti-Inflammatory Agents; Steroids;