Inhaled medication other than antibiotics

Inhaled bronchodilators

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Background

There are two distinct classes of inhaled bronchodilators (IBs): anticholinergic (AC) IBs and beta-2 agonist (BA) IBs. Although they have different mechanisms of action, both induce relaxation of bronchial smooth muscle. Each class includes both short- and long-acting drugs, which can be administered via various methods, including dry powder inhalers, metered-dose inhalers, and nebulizers. In addition to their bronchodilator effects, ACs may reduce mucus secretion, whereas BAs can increase it. BAs also enhance mucociliary clearance and may help protect the bronchial mucosa from bacterial damage.

It is important to note that in severe lung disease, IBs may worsen airway function, leading to paradoxical bronchoconstriction due to the abnormal airway compliance associated with bronchiectasis.

IBs are widely used in obstructive lung diseases other than CF, such as COPD, asthma, and bronchiectasis. In these conditions, the potential benefit of long-acting AC and BA combinations has been proposed (Tashking DP, 2013)

Short-term IB administration is recommended in CF to relieve symptoms associated with bronchospasm and to prevent adverse events during nebulized therapies (Mogayzel PJ, 2013). However, in the absence of documented reversible obstruction, recommendations regarding bronchodilator use in CF remain inconsistent (Levine H, 2016), as there is limited evidence supporting their efficacy in improving lung function (Barry PJ, 2017).

Recently, (Kieninger E, 2022) speculated, based on new diagnostic measures such as multiple-breath washout and MRI, that IBs have a short-term positive effect on FEV?, independent of ventilation inhomogeneity. However, the heterogeneous response among patients suggests that IBs should be tested on an individual basis.

Issues

IB efficacy in CF lung disease (lung function, respiratory symptoms, quality of life, pulmonary exacerbation rates, mortality rates)

IB adverse effects (tremor, increased heart rate, dry mouth, increased wheeze, and shortness of breath)

What is known

One Cochrane Review (Halfhide C, 2011) collected eighteen RCTs with a total of 369 patients, both children and adults. Beneficial effects were observed, above all, in patients with evidence of bronchodilator responsiveness or bronchial hyperreactivity. No relevant adverse event was reported also in case of long-term treatment. The use of BA seemed more supported by evidence than the use of AC.

In 2016 this review has been split into the following Cohrane reviews:'Long-acting inhaled bronchodilators for cystic fibrosis' and 'Short-acting inhaled bronchodilators for cystic fibrosis'.

About the first one, a Cochrane Review updated December 2017 (Smith S, 2017) has been published. On the basis of three trials looked at the effects in both the short term (up to 28 days) and the longer term (up to three months) on 1066 CF patients, the Authors concluded that no significant differences have appeared between intervention and placebo groups, in terms of quality of life, adverse events and spirometric changes. Up to now there is limited evidence of IB long-term effect, also considering the concomitant action on mucus production and mucociliary clearance. It would be important to better study the effect of BA and AC combinations and of IB therapy associated with inhaled corticosteroids and/or other mucoactive agents.

In 2022 (Smith S, 2022) a short-acting inhaled bronchodilators for Cistic Fibrosis Cochrane review has been published. 11 trials with 191 partecipants have been included. All the included trials are small, of a cross-over design and did not measure longer term outcomes. On this basis Authors have concluded that the evidence across all outcomes has been very low.

In november 2017 a study (Furlan LL,2017) highlighted the importance of the rs4073 variant of the interleukin 8 gene, regarding response to inhaled bronchodilators,

Unresolved questions

IB efficacy in CF lung disease (lung function, respiratory symptoms, quality of life, pulmonary exacerbation rates, mortality rates)

IB adverse effects (tremor, increased heart rate, dry mouth, increased wheeze, and shortness of breath)

No RCT are ongoing about this issue.

Keywords

Adrenergic beta-Agonists; Anticholinergic Agents; Bronchodilator Agents; Xanthines;