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[Intervention Review]

Vilanterol and fluticasone furoate for asthma

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ABSTRACT

Background

Vilanterol (VI) is a long-acting beta$_2$-agonist (LABA) that binds to the beta$_2$-adrenoceptor on the airway smooth muscle, producing bronchodilation. LABA therapy, which is well established in adults as part of the British Thoracic Society (BTS) Guidelines for the Management of Asthma, leads to improvement in symptoms and lung function and reduction in exacerbations. At present, the commonly used LABAs licensed for use in asthma management (formoterol and salmeterol) require twice-daily administration, whereas VI is a once-daily therapy.

Fluticasone furoate (FF) is an inhaled corticosteroid (ICS), and ICS therapy is recommended by the BTS asthma guidelines. ICSs, the mainstay of asthma treatment, lead to a reduction in both airway inflammation and airway hyper-responsiveness. Regular use leads to improvement in symptoms and lung function. ICSs are currently recommended as 'preventer' therapy for patients who use a 'reliever' medication (e.g. short-acting beta$_2$ agonist (SABA), salbutamol) three or more times per week. Most of the commonly used ICS treatments are twice-daily medications, although two once-daily products are currently licensed (ciclesonide and mometasone).

At the present time, only one once-daily ICS/LABA combination (FF/VI) is available, and several other combination inhalers are recommended for twice-daily administration.

Objectives

To compare effects of VI and FF in combination versus placebo, or versus other ICSs and/or LABAs, on acute exacerbations and on health-related quality of life (HRQoL) in adults and children with chronic asthma.

Search methods

We searched the Cochrane Airways Group Register of trials, clinical trial registries, manufacturers' websites and reference lists of included studies up to June 2016.

Selection criteria

We included randomised controlled trials (RCTs) of adults and children with a diagnosis of asthma. Included studies compared VI and FF combined versus placebo, or versus other ICSs and/or LABAs. Our primary outcomes were health-related quality of life, severe asthma exacerbation, as defined by hospital admissions or treatment with a course of oral corticosteroids, and serious adverse events.

Data collection and analysis

Two review authors independently extracted data and analysed outcomes using a fixed-effect model. We used standard Cochrane methods.

Main results

We identified 14 studies that met our inclusion criteria, with a total of 6641 randomised participants, of whom 5638 completed the study. All studies lasted between two and 78 weeks and showed good methodological quality overall.

We included 10 comparisons in this review, seven for which the dose of VI and FF was 100/25 mcg (VI/FF 100/25 mcg vs placebo; VI/FF 100/25 mcg vs same dose of FF; VI/FF 100/25 mcg vs same dose of VI; VI/FF 100/25 mcg vs fluticasone propionate (FP) 500 mcg twice-daily; VI/FF 100/25 mcg vs fluticasone propionate/salmeterol (FP/SAL) 250/50 mcg twice-daily; VI/FF 100/25 mcg vs FP/SAL 250/25 mcg twice-daily; FF/VI 100/25 vs FP/SAL500/50) and three for which the dose of VI and FF was 200/25 mcg (VI/FF 200/25 mcg vs placebo; VI/FF 200/25 mcg vs FP 500 mcg; VI/FF 200/25 mcg vs same dose of FF).

We found very few opportunities to combine results from the 14 included studies in meta-analyses. We tabulated the data for our pre-specified primary outcomes. In particular, we found insufficient information to assess whether once-daily VI/FF was better or worse than twice-daily FP/SAL in terms of efficacy or safety.

Only one of the 14 studies looked at health-related quality of life when comparing VI and FF 100/25 mcg versus placebo and identified a significant advantage of VI/FF 100/25 mcg (mean difference (MD) 0.30, 95% confidence interval (CI) 0.14 to 0.46; 329 participants); we recognised this as moderate-quality evidence. Only two studies compared VI/FF 100/25 mcg versus placebo with respect to exacerbations; both studies reported no exacerbations in either treatment arm. Five studies (VI/FF 100/25 mcg vs placebo) sought information on serious adverse events; all five studies reported no serious adverse events in the VI/FF 100/25 mcg or placebo arms. We found no comparison relevant to our primary outcomes for VI/FF at a higher dose (200/25 mcg) versus placebo.

The small number of studies contributing to each comparison precludes the opportunity to draw robust conclusions for clinical practice. These studies were not of sufficient duration to allow conclusions about long-term side effects.

Authors' conclusions

Some evidence suggests clear advantages for VI/FF, in combination, compared with placebo, particularly for forced expiratory volume in one second (FEV_1) and peak expiratory flow; however, the variety of questions addressed in the included studies did not allow review authors to draw firm conclusions. Information was insufficient for assessment of whether once-daily VI/FF was better or worse than twice-daily FP/SAL in terms of efficacy or safety. It is clear that more research is required to reduce the uncertainties that surround interpretation of these studies. It will be necessary for these findings to be replicated in other work before more robust conclusions are revealed. Only five of the 13 included studies provided data on health-related quality of life, and only six recorded asthma exacerbations. Only one study focused on paediatric patients, so no conclusions can be drawn for the paediatric population. More research is needed, particularly in the primary outcome areas selected for this review, so that we can draw firmer conclusions in the next update of this review.

PLAIN LANGUAGE SUMMARY

Vilanterol and fluticasone furoate for chronic asthma in adults and children

Review question

We considered in this review whether the combination of vilanterol (VI) and fluticasone furoate (FF) is better than placebo for people with asthma. We also compared VI and FF with other inhaled steroids and long-acting $beta_2$-agonist medications.

Background

Asthma is an inflammatory lung condition whereby the pathway through the airways may become very restricted. By the year 2025, it is estimated that 400 million people will have this condition. Asthma can very seriously affect people's quality of life, and the combination of VI and FF may help to reduce difficulties related to the impact on everyday life of breathlessness and other associated symptoms.

Study characteristics

We included 14 studies in this review, involving a total of 6641 participants. All studies lasted between two and 78 weeks. All people included in these studies had received a diagnosis of asthma. Trials included both men and women, and one study included children and young people.

All studies looked at VI and FF versus another medication or placebo. In all studies, the VI/FF combination was taken through a dry powder inhaler.

Key results

We found that participants who received a combination of FF and VI therapy had improved lung function compared with those given placebo, but evidence was insufficient to permit any other conclusions because researchers attempted to answer too many different questions. Evidence was lacking on whether the combination of VI and FF therapy once-daily is better or worse than a twice-daily alternative. More studies are needed, so that we can gain a better understanding of the evidence overall.

Quality of the evidence

Overall, the evidence presented in this review is taken from well-designed studies at low risk of bias in terms of decisions on who received which treatment, blinding and how to report outcomes for participants who did not finish the study. However, because we were not able to combine results for many of our outcomes of interest, or because the outcome was rare, we judged the quality of the evidence overall to be low to moderate.