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[Intervention Review]

Ciclesonide versus other inhaled corticosteroids for chronic asthma in children

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ABSTRACT

Background

Inhaled corticosteroids (ICS) are the cornerstone of asthma maintenance treatment in children. Particularly among parents, there is concern about the safety of ICS as studies in children have shown reduced growth. Small-particle-size ICS targeting the smaller airways have improved lung deposition and effective asthma control might be achieved at lower daily doses.

Ciclesonide is a relatively new ICS. This small-particle ICS is a pro-drug that is converted in the airways to an active metabolite and therefore with potentially less local (throat infection) and systemic (reduced growth) side effects. It can be inhaled once daily, thereby possibly improving adherence.

Objectives

To assess the efficacy and adverse effects of ciclesonide compared to other ICS in the management of chronic asthma in children.

Search methods

We searched the Cochrane Airways Group Register of trials with pre-defined terms. Additional searches of MEDLINE (via PubMed), EMBASE and Clinical studyresults.org were undertaken. Searches are up to date to 7 November 2012.

Selection criteria

Randomised controlled parallel or cross-over studies were eligible for the review. We included studies comparing ciclesonide with other corticosteroids both at nominally equivalent doses or lower doses of ciclesonide.

Data collection and analysis

Two review authors independently assessed trial quality and extracted data. Study authors were contacted for additional information. Adverse effects information was collected from the trials.

Main results

Six studies were included in this review (3256 children, 4 to 17 years of age). Two studies were published as conference abstracts only. Ciclesonide was compared to budesonide and fluticasone.



Ciclesonide compared to budesonide (dose ratio 1:2): asthma symptoms and adverse effect were similar in both groups. Pooled results showed no significant difference in children who experience an exacerbation (risk ratio (RR) 2.20, 95% confidence interval (CI) 0.75 to 6.43). Both studies reported that 24-hour urine cortisol levels showed a statistically significant decrease in the budesonide group compared to the ciclesonide group.

Ciclesonide compared to fluticasone (dose ratio 1:1): no significant differences were found for the outcome asthma symptoms. Pooled results showed no significant differences in number of patients with exacerbations (RR 1.37, 95% CI 0.58 to 3.21) and data from a study that could not be pooled in the meta-analysis reported similar numbers of patients with exacerbations in both groups. None of the studies found a difference in adverse effects. No significant difference was found for 24-hour urine cortisol levels between the groups (mean difference 0.54 nmol/mmol, 95% CI -5.92 to 7.00).

Ciclesonide versus fluticasone (dose ratio 1:2) was assessed in one study and showed similar results between the two corticosteroids for asthma symptoms. The number of children with exacerbations was significantly higher in the ciclesonide group (RR 3.57, 95% CI 1.35 to 9.47). No significant differences were found in adverse effects (RR 0.98, 95% CI 0.81 to 1.14) and 24-hour urine cortisol levels (mean difference 1.15 nmol/mmol, 95% CI 0.07 to 2.23).

The quality of evidence was judged 'low' for the outcomes asthma symptoms and adverse events and 'very low' for the outcome exacerbations for ciclesonide versus budesonide (dose ratio 1:1). The quality of evidence was graded 'moderate' for the outcome asthma symptoms, 'very low' for the outcome exacerbations and 'low' for the outcome adverse events for ciclesonide versus fluticasone (dose ratio 1:1). For ciclesonide versus fluticasone (dose ratio 1:2) the quality was rated 'low' for the outcome asthma symptoms and 'very low' for exacerbations and adverse events (dose ratio 1:2).

Authors' conclusions

An improvement in asthma symptoms, exacerbations and side effects of ciclesonide versus budesonide and fluticasone could be neither demonstrated nor refuted and the trade-off between benefits and harms of using ciclesonide instead of budesonide or fluticasone is unclear. The resource use or costs of different ICS should therefore also be considered in final decision making.

Longer-term superiority trials are needed to identify the usefulness and safety of ciclesonide compared to other ICS. Additionally these studies should be powered for patient relevant outcomes (exacerbations, asthma symptoms, quality of life and side effects). There is a need for studies comparing ciclesonide once daily with other ICS twice daily to assess the advantages of ciclesonide being a pro-drug that can be administered once daily with possibly increased adherence leading to increased control of asthma and fewer side effects.

PLAIN LANGUAGE SUMMARY

Ciclesonide compared to budesonide and fluticasone in the treatment of asthma in children

Asthma is a common disease in childhood. Most children with chronic asthma are treated with inhaled corticosteroids (ICS) to control airway inflammation and reduce asthma symptoms. Although these drugs are considered to be very safe and effective, not all children achieve full asthma control and some parents are concerned about the possibility of reduced growth or local side effects such as hoarseness. The challenge for newer ICS is to achieve improved asthma control with fewer side effects. This could be achieved by small-particle-size ICS, leading to better lung deposition as they penetrate deeper into the small airways. Therefore, asthma control could be achieved with lower daily doses and with fewer side effects. In children, particle size of ICS might be even more important because of their smaller airways.

Ciclesonide is a new small-particle-size ICS. The smaller particle size may make the corticosteroid go deeper into the lungs. Potential advantages are a lower required dose to achieve asthma control, once daily instead of twice daily dosing, and reduced local (oral thrush) and systemic (growth suppression) side effects.

We found six studies comparing ciclesonide with either budesonide or fluticasone in 3256 children (aged four to 17 years) with chronic asthma. After three months of treatment with ciclesonide compared to budesonide or fluticasone, no relevant differences could be found on asthma symptoms, exacerbations or side effects. Ciclesonide compared to a double dose of fluticasone was assessed in one study and no differences were found in asthma symptoms, use of rescue medication and adverse effects. However, children receiving ciclesonide experienced more asthma exacerbations than children in the fluticasone group.

The results of this review regarding the efficacy and safety of ciclesonide compared to other ICS are not conclusive. Relatively few studies were found, different inhalers were compared and treatment and follow-up time (12 weeks) was too short for the assessment of relevant outcomes such as exacerbations and growth retardation. Future studies should pay attention to those aspects.