Proposed:

It Is non Ethical to Treat Children Under 3 years with Inhaled Corticosteroids

Summary of the Con Position

Inhaled corticosteroids have become the maintenance medication with the greatest degree of efficacy. In pre-school age children with persistent asthma, these agents can be effectively delivered, by both metered dose inhaler via a valved holding chamber and by nebulizer, with efficacy in decreasing asthmatic symptoms.\textsuperscript{1,2,3} Although there is evidence for dose-related systemic effects,\textsuperscript{4} conventional low doses have an established safety record.\textsuperscript{5,6} A minimal degree of hypothalamic-pituitary axis suppression and a small degree of transient growth suppression is detectable at modest doses, but neither clinically detectable adverse effects nor sustained effect on growth are apparent except at higher doses.\textsuperscript{7}

However, convincing data have demonstrated that these agents, at least in conventional doses, do not prevent exacerbations of asthma from viral respiratory infections.\textsuperscript{8,9,10} Bronchoalveolar lavage studies show no evidence of airway inflammation in children with a history of intermittent non-atopic asthma during their symptom-free periods, while airway inflammation seems to persist in patients with atopic asthma even when they are asymptomatic.\textsuperscript{11,12} Nor are there any other currently available therapeutic measure that can, as safe maintenance therapy, prevent viral respiratory infection induced asthma.\textsuperscript{13} Since viral respiratory infections are the major contributors to acute care requirements for asthma,\textsuperscript{14,15,16,17,18} especially in young children who have an especially high frequency of these common cold viruses,\textsuperscript{19} the use of inhaled corticosteroids in children whose asthma is limited to being induced by viral respiratory infections is not justified based on evidence from controlled clinical trials.
Moreover, inflammation from viral respiratory infection-induced asthma is predominantly non-eosinophilic in contrast to the eosinophilic airway inflammation characteristic of atopic children with asthma. This indicates different inflammatory mechanisms between these asthma phenotypes.\textsuperscript{20,21,22,23,24,25}

While the most common asthma phenotype in children under the age of 3 is the nonatopic viral respiratory infection induced pattern, atopy does present clinically in that age group. Wilson et al found cockroach sensitivity in 29\%, dust mite in 10\%, cat in 10\%, and Alternaria in 4\% among 49 asthmatic infants under one year of age.\textsuperscript{26} For children under age 3 with evidence for atopy, inhaled corticosteroids reduce symptoms and are therefor of clinical value even for those under one year of age.\textsuperscript{3} While attempts to utilize early administration of inhaled corticosteroids to alter the natural history of young atopic children with asthma have been unsuccessful, those studies nonetheless demonstrated clinical improvement in symptoms during the period of administration.\textsuperscript{27,28}

The controversy regarding the use of inhaled corticosteroids appear to arise from confusion as to what is to be called “asthma.” Some appear to consider children with pre-school wheeze limited to viral respiratory infections as not asthma.\textsuperscript{29,30,31} However, limiting asthma to typical atopic asthma is an excessively narrow definition and is certainly not universally accepted. The complexity and challenge of defining asthma has been discussed extensively by Sears.\textsuperscript{32} In examining the 12 definitions and references in his review, a common theme to all is the presence of airway disease that varies over time either spontaneously or as a result of treatment. A committee of the American Thoracic Society agreed upon the definition that “Asthma is a disease characterized by an increased responsiveness of the trachea and bronchi to various stimuli and
manifested by a widespread narrowing of the airways that change in severity either spontaneously or as a result of therapy.” This definition was expanded by a subsequent committee of the American Thoracic Society to include “The major symptoms of asthma are paroxysms of dyspnea, wheezing and cough, which may vary from mild and almost undetectable to severe and unremitting...” That definition and others, most notably that of Simon Godfrey, added to the definition that the airflow obstruction and clinical symptoms are largely or completely reversed by treatment with bronchodilators or corticosteroids.

Moreover, while a high percentage of those young non-atopic children whose asthma is limited to induction by viral respiratory infections remit by school age, about half continue to have some degree of episodic asthma with viral respiratory infections well into adult life. When age of onset of asthma is assessed in a population, most are found to have begun during the first years of life. And it is those early years that are associated with the highest rate of hospitalization.

Rather than attempting to diagnose asthma in young children by what their subsequent course will be, it is more reasonable to consider asthma as a type of end-organ response with different phenotypes that can be identified by the clinical pattern. Intermittent viral respiratory infection induced asthma at any age appears not to be reliably prevented by inhaled corticosteroids, although it is generally accepted as responsive to systemic corticosteroids. This clinical pattern of asthma which dominates in children under age 3 do not benefit from inhaled corticosteroids. However the minority with persistent symptoms, most of whom have evidence of atopy do benefit from inhaled steroids by the reduction of symptoms even if that treatment does not alter the long-term clinical course.
In conclusion, it is ethical to treat children under 3 years with inhaled corticosteroids if careful evaluation identifies them as having persistent asthma, which in most cases will be associated with evidence of atopy. However, this asthma phenotype is much less common than the typical non-atopic viral respiratory infection induced pattern of asthma at this age, where inhaled corticosteroids have little benefit and their use is not justified.

References


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