

What is the preferred treatment for a child with mild persistent asthma?

EVIDENCE-BASED ANSWER

Low-dose inhaled corticosteroids are the preferred treatment for children with mild persistent asthma because they demonstrate superior reduction in severity and frequency of asthma exacerbations compared with alternatives (strength of recommendation [SOR]: **A**, based on multiple randomized controlled trials). As add-on therapy, nedo-

cromil, theophylline, and cromolyn have all demonstrated a modest benefit in symptom control; leukotriene receptor antagonists are also recommended based on data from older children (SOR: **B**, cohort study). Unlike treatment of moderate or severe asthma, long-acting beta-agonists are not recommended (SOR: **A**, randomized trials).

CLINICAL COMMENTARY

Clear medication choices for mild asthma are supported by good evidence

Physicians who routinely treat children with asthma are fortunate to have the body of evidence outlined in this review. Clear medication choices are supported in most instances by relatively clear comparisons with alternatives. In my practice, where many children can be classified in the “mild persistent” category, I am always surprised at how many patients’ families lack a clear understanding of the factors that trigger a child’s asthma and how to avoid them.

Another common clinical scenario among children and adolescents is exercise-induced asthma. Depending on the sport, the asthma can be classified as “mild persistent” or “mild intermittent.” For true intermittent symptoms, my clinical experience (and often parental preference) argues for pre-activity treatment with short acting beta-agonists as the most practical therapy.

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Evidence summary

Mild persistent asthma is defined as forced expiratory volume over 1 second (FEV_1) $\geq 80\%$ predicted, with daytime symptoms more than twice per week but less than once daily, and nighttime symptoms more often than twice monthly.¹

Low-dose inhaled corticosteroids

Two large randomized trials support using low-dose inhaled corticosteroids in these children. The Childhood Asthma Management Program (CAMP) study, which included 1041 children, evaluated treatment with either budesonide or nedocromil vs placebo. Patients

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FAST TRACK

Low doses of inhaled steroids are far better at reducing exacerbations of mild persistent asthma

taking budesonide had a lower rate of urgent care visits (absolute risk reduction [ARR]=10%; number needed to treat [NNT]=10; $P=.02$) compared with children taking nedocromil (ARR=6%; NNT=17; $P=.02$). The urgent care visits were reported as number of visits per 100 person-years.

In practical terms, this means that in order to decrease 1 urgent care visit, 1 patient would need to take budesonide for 10 years. However, because rates are not necessarily homogenous over time, the number of visits decreased during the first year may be different than the number of events decreased throughout the tenth year.

Children taking budesonide experienced 21.5% more episode-free days than those taking placebo ($P=.01$). No change was observed in the nedocromil group.² In the inhaled Steroid Treatment As Regular Therapy (START) in early asthma study, budesonide demonstrated a 44% relative reduction in time to first severe asthma related event, compared with placebo (95% confidence interval [CI], 0.45–0.71; NNT=44; $P=.0001$).³

Theophylline

Theophylline is considered an alternative to inhaled corticosteroids. One study compared beclomethasone with theophylline in 195 children. This study found near-equivalent efficacy in doctor visits, hospitalizations, monthly peak expiratory flow rates, and FEV₁; however, beclomethasone was superior to theophylline in maintaining symptom control and decreasing the use of inhaled bronchodilators and systemic steroids.

When compared with beclomethasone, theophylline was linked to 14% more central nervous system adverse effects ($P<.001$) and 17% more gastrointestinal disturbances ($P<.001$). Although beclomethasone induced more oral candidiasis compared with theophylline (8.9% vs 2.4%; $P<.001$), the incidence of this infection can be reduced by using a spacer.

Long-term systemic effects

The potential long-term adverse systemic effects of inhaled corticosteroids on growth, bone metabolism, and pituitary-adrenal function call for longer-term studies.⁴ A systematic review of 15 trials reported that the protective effect of leukotriene receptor antagonists is inferior to inhaled corticosteroids for adults (relative risk [RR]=1.71; 95% CI, 1.40–2.09); however, evidence is insufficient to extrapolate this to children.⁵

Beta-agonists

Evidence does not support use of long-acting beta-agonists as monotherapy or in combination with other medications for children with mild persistent asthma. Although 1 study showed an improvement in lung function for children taking budesonide plus formoterol compared with budesonide alone, the rate of severe exacerbations was lower for those taking budesonide alone (62% decrease vs 55.8% decrease; $P=.001$). Both groups had a 32% decrease in the number of rescue inhalations per day when compared with placebo ($P=.0008$).⁶

Recommendations from others

Recommendations are listed in the **TABLE**.^{1,7,8} Unlike the NAEPP and GINA asthma guidelines, the BTS/SIGN asthma guidelines define no objective measurement or staging classification to diagnose asthma among children. Diagnosis is determined by a child's response to medication.⁸ Independent of any daily controller medication use, all children should have a short acting bronchodilator on hand in case of an acute attack.^{1,8,9}

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TABLE

Recommendations for treating mild persistent asthma

GUIDELINE	DAILY CONTROLLER MEDICATION	ALTERNATIVE TREATMENT
National Asthma Education and Prevention Program (NAEPP) ¹	Low-dose inhaled corticosteroids	Children <5: cromolyn, LTRAs Children >5: cromolyn, LTRAs, nedocromil, sustained release theophylline
Global Initiative for Asthma (GINA) ⁷	Low-dose inhaled corticosteroids	All children: Sustained released theophylline, Cromone, LTRAs
British Thoracic Society/ Scottish Intercollegiate Guidelines Network (BTS/SIGN) ⁸	Inhaled steroids	All children: LTRAs, theophylline Children >5: cromones, nedocromil

LRTA, leukotriene receptor antagonists.
Sources: NAEPP, *J Allergy Clin Immunol* 2002¹; GINA, *Guidelines and Resources* 2005,⁷ and BTS/SIGN, *Thorax* 2003.⁸

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