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Daily Asthma Controller Therapy and a Written Action Plan: Keys to Good Asthma Management

Québec City - Asthma is a chronic, underlying inflammatory condition that requires daily controller therapy to maintain symptomatic control. Unfortunately, it is often treated as an episodic illness, with parents citing fear of side effects as the reason why they use treatment only intermittently. However, not all inhaled corticosteroids (ICS) behave the same: physicians must explain to parents that some formulations are inherently safer than others and that fear of side effects need not detract from the benefits of controller ICS use. Experts here at the CPS outlined how a written asthma plan can be an important component of a self-guided management strategy and they discussed studies showing how these plans can improve compliance and asthma control over usual prescriptions alone.

Chief Medical Editor: Dr. Léna Coïc, Montreal, Québec

Physicians must convince parents, patients and perhaps even themselves that asthma is a chronic, ongoing inflammatory disease that requires daily, not intermittent, controller therapy, and a written action plan (WAP) to keep children well and out of the hospital due to worsening asthma can be very helpful.

Dr. Denis Bérubé, Assistant Professor of Paediatrics, Université de Montréal, noted that a survey carried out in 2008 (IMS Sept 2008) showed that out of approximately 600 respondents, only about 25% of patients (or parents of children with asthma) used daily medication, despite the fact that approximately half of patients surveyed had moderate to severe asthma. "When you ask parents if there is anything that keeps them from using daily medication, 71% of them said they worry about side effects (SEs) even though half of them have no idea what SEs they are worried about," Dr. Bérubé reported to delegates here at the CPS. Patients might use a controller medication for a few weeks, as they would to treat an acute infection; once symptoms resolve, they stop the medication, only to restart it when asthma worsens, he explained.

Even physicians find intermittent use of inhaled corticosteroids (ICS) attractive, according to Canadian guidelines on the management of asthma (*Can J Med* 2005;173:S1-S55). Until relatively recently, there was scant evidence supporting daily use of controller medication as the optimal strategy for asthma control.

However, in the Prevention of Asthma in Children (PAC) study, Bisgaard et al. (*N Engl J Med* 2006;354(19):1998-2005) randomized 411 1-month-old infants to either budesonide 400 µg/day or placebo for 2 weeks after each 3-day episode of wheezing over 3 years. Virtually identical numbers at 83% for the budesonide group and 82% of placebo controls experienced symptom-free days over the 3-year follow-up while 24% of children in the ICS group vs. 21% of placebo controls had persistent wheezing. The mean duration of acute episodes was 10 days in both groups, again over a 3-year follow-up. The conclusion, as Dr. Bérubé emphasized, was that intermittent ICS therapy

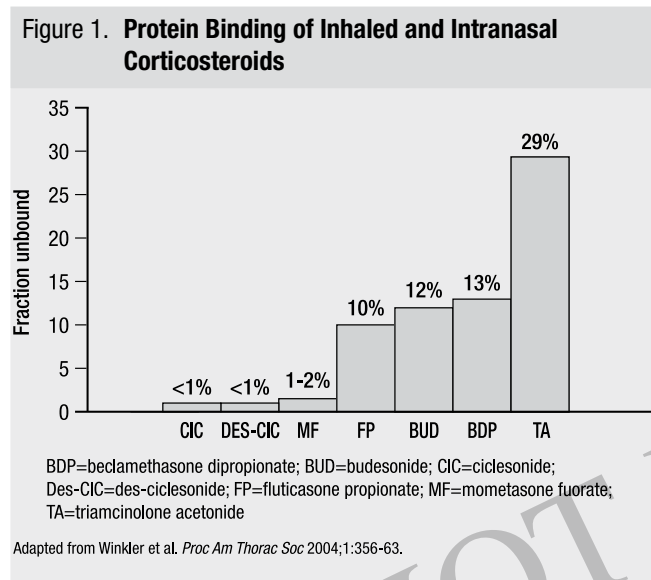
had no effect on the progression from episodic to persistent wheezing and offered no short-term benefit during episodes of wheezing in the first 3 years of life.

Bachanier et al. (*J Allergy Clin Immunol* 2008;122:1127-35) again examined the effectiveness of episodic ICS use vs. montelukast in preschoolers with moderate to severe intermittent wheezing. In a randomized fashion, 238 children received either 7 days of budesonide inhalation suspension (1 mg b.i.d.), montelukast (4 mg q.d.) or placebo plus albuterol on each identified respiratory tract illness. At the end of 12 months, the proportion of children who had episode-free days did not differ between the 3 treatment groups at 76% for the budesonide group, 73% for montelukast group and 74% for conventional therapy. Nor did the 3 groups differ in oral corticosteroid use, health care use, quality of life or linear growth. These observations again support the concept that episodic use of either an ICS or a leukotriene receptor antagonist in this patient population does not increase the proportion of episode-free days or decrease oral corticosteroid use over a 12-month period. "Intermittent ICS are useless against exacerbations," Dr. Bérubé re-iterated.

Low- to Moderate-dose ICS

Dr. Bérubé noted that most of the benefit from ICS controller therapy is derived from low- to moderate-dose ICS, the objective being to get the medication to the lungs. "Patients are getting at best 50% of whatever comes out of the metered dose inhaler (MDI) into the lungs," he noted, and at least part of the rest goes to the oropharynx, where it can give rise to potential SEs. Medication left in the oropharynx will eventually end up in the systemic circulation, he added; once there, it will be partly protein-bound but the part that is not bound is the part that gives rise to SEs. "The more protein-bound a medication is, the less likely SEs will occur," Dr. Bérubé stated. With a pro-drug such as ciclesonide, the drug has no steroid effect until it is activated in the airways where the disease is, so there is less risk of SEs, Dr. Bérubé explained.

In a comparison of fractions of the different ICS that are absorbed into the systemic circulation but which remain unbound (Winkler et al. *Proc Am Thorac Soc* 2004;1:356-63), ciclesonide had the highest protein-binding affinity of all the ICS, “so it again limits SEs because there is less free medication in the blood stream,” he added. It also has among the shortest half-lives of the ICS “and the shorter the time the medication stays in the blood, the better it is for SEs,” Dr. Bérubé confirmed (Figure 1). He added, “If parents are worried about SEs, the safest ICS is ciclesonide.”



Written Action Plan

Here at the CPS, Dr. Francine Ducharme, Professor of Paediatrics, CHU Sainte-Justine, Université de Montréal, Québec, noted that despite having effective medications for asthma and free access to health care services, asthma remains one of the leading causes of health care resource consumption in Canada. A major contributor to this resource consumption is poor adherence. According to the Global Initiative for Asthma (GINA), patients with asthma should know how to both prevent and manage deteriorating symptoms and acute exacerbations; to that end, they need a guided self-management plan.

In an overview of studies comparing self-management with usual care, Dr. Ducharme pointed out that self-management reduces hospitalization rates, emergency room (ER) visits, unscheduled visits, work absenteeism and nocturnal asthma

(Gibson et al. *Cochrane Database Syst Rev* 2003;1:CD001117). Guided self-management consists of a number of components, key among them a WAP. A WAP spells out for patients what they need to do on a daily basis; when and how and for how long they need to increase treatment; and when to get help.

In her own WAP, Dr. Ducharme and colleagues developed the plan that would not take more time to write up than a usual prescription, simply by merging the action of writing the prescription at the same time as physicians write the WAP (*Am J Respir Crit Care Med* 2011;183(2):195-203). Hypothesizing that a WAP designed to promote guided self-management would increase short-term adherence to asthma controller medication, Ducharme and colleagues randomized 219 children between the ages of 1 and 17 to receive a WAP plus a prescription (WAP-P) or an unformatted prescription (UP). The objective was to determine if the WAP-P would improve adherence to fluticasone prescribed in the ER along with other recommendations.

“Both groups showed a similar drop in adherence in the initial 14 days,” Dr. Ducharme observed. However, between days 15 and 28, 50% of children who had received a WAP-P remained adherent to fluticasone vs. 34% of those with UP. “Surprisingly, as well, the WAP-P really improved physicians’ recommendations,” Dr. Ducharme added: some 83% of WAP-P patients consulted with their usual physician following the ER physicians’ recommendation to do so vs. 44% of the UP group. Not unexpectedly, asthma control measures were significantly better in the WAP-P group compared with the UP group, with significantly more of the WAP-P children taking more of their ICS, more of their oral steroids when prescribed, and more with better asthma control than those given the UP.

“The WAP definitely improved compliance to treatment, probably by improving communication,” Dr. Ducharme noted. “And because the pharmacist gets exactly what the physician has prescribed, they know exactly what the physician has told the patient to do and they can reinforce this message as well.”

Summary

Asthma is a costly disease that precipitates many unnecessary visits because of poor disease control. Improving patient asthma control must be a priority for all physicians as with daily controller medication, asthma can be well managed. Reassuring patients that some ICS are less likely to cause SEs than others may be key to promoting daily use of controller therapy and with it, better outcomes. □

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Medical Education Network Canada Inc. 132 chemin de l’Anse, Vaudreuil, Quebec J7V 8P3

