Symptom-driven or regular use of inhaled corticosteroids in childhood asthma?

The global burden of asthma. In children is immense. The Global Initiative for Asthma (GINA) strategy, used worldwide, is advocating a radical shift in the management of asthma. In a new symptom-driven approach, GINA recommend that Inhaled corticosteroids (ICS) are used only when someone with asthma feels like they need a bronchodilator, rather than as regular preventer therapy. For adolescents and adults the new recommendation is to use, as rescue therapy, inhalers combining ICS with fast-acting, long-acting beta-agonist (LABA) such as formoterol. For children under 12 the recommendation is to use ICS when short-acting beta agonist (SABA) is required, but in separate inhalers. The rationale behind this change is that over-reliance on SABA rescue therapy for asthma symptoms, when taken without ICS, is associated with a risk of death. By using ICS/LABA, in a symptom-driven approach people would in essence titrate their steroid dose according to their need. In this paper we consider the potential implications of this for children.

The evidence comes from four recent high quality randomised controlled trials (RCTs), involving nearly 9,000 adolescents and adults. These studies compared symptom-driven use of ICS/LABA as required with the traditional approach of using ICS as preventer and SABA as reliever in separate inhalers. There appears to be no significant difference in the rates of asthma exacerbations between the groups, although overall asthma control appeared better in those people taking ICS regularly. For adults and adolescents with mild asthma, using ICS/LABA may offer a useful alternative to regular ICS and rescue SABA. For children younger than 12 years, however, things are less clear-cut.

Symptom-driven and regular ICS strategies have been compared in two RCTs in children. Neither study was focussed on steroid-naïve children at the time of diagnosis. In the larger study, of 843 children, the primary outcome was the time to first exacerbation: this was lower in children taking regular ICS than those taking intermittent ICS, and the authors conclude that “rescue beclomethasone can lower the risk of exacerbations and treatment failures, but to a lesser degree than does daily beclomethasone”. In the other study, of 206 African-American children, the primary outcome of asthma control was not different between children taking regular or intermittent ICS.

Results of RCTs examining ICS in adults are not directly transposable into paediatric guidelines, because they may underestimate the benefit of ICS in this age group. In adults, there are phenotypes which are less responsive to corticosteroids but these are rare in children. The issue of asthma control requires clarification, as this is an important outcome in childhood. Asthma control reflects underlying inflammation which, in children, can lead over time to permanent airway remodelling and damage. The most concerning problem is the absence of an inhaler containing both ICS and bronchodilator which is easy for children to use. The dry powder inhalers containing ICS/LABA are technically challenging for children to use, hence the recommendation for younger children is to use ICS whenever SABA is required. The logistics of doing this, when children don’t always even carry their salbutamol inhaler, may preclude the reliable use of intermittent ICS. This predisposes them to overuse of SABA without ICS – the very problem that the new GINA guidelines are trying to prevent.

What needs to happen next? Large, pragmatic RCTs are required to determine the safety of using symptom-driven approaches to ICS in childhood asthma. The key goal is to determine whether not taking ICS regularly increases the risk of asthma exacerbations, and secondary questions remain around asthma control. Any future studies should be conducted in primary care, preferably using routinely collected data rather than additional appointments, to reflect outcomes in routine care. A cost-effectiveness analysis is necessary to identify whether ICS/LABA inhalers (which are significantly more expensive to purchase than separate ICS and SABA inhalers) are prohibitively expensive in low resources settings.

The likely situation is that some children may benefit from regular ICS and others may be fine with a symptom-driven approach to treatment. As we move into an era of personalised medicine for asthma, reflecting better understanding of underlying phenotypes, there is a need to identify strategies for accurately tailoring care to individual children.