

Letter to the Editor

Medication use in children with asthma in Finland from 1995 to 2006

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In 1994, after convincing documentation of the benefits of anti-inflammatory medication in long-term control of asthma,¹ Finland was one of the first countries to implement a national program aiming at targeting all aspects of asthma treatment. This program was shown in a 10-year follow-up to be highly successful in reducing the general burden of asthma in spite of an increasing occurrence.² The principles of pharmacotherapy were also readily adopted among pediatricians to change treatment guidelines during the 1990s.

All Finnish patients with a physician-diagnosed asthma fulfilling the nationally set criteria are entitled to special reimbursement for their medication cost. The Social Insurance Institution maintains a registry of these patients and of all the drug purchases from the pharmacies. This provided an interesting platform to study changes in the filling of prescriptions in childhood asthma medication from 1995 to 2006. Particular attention was paid to the use of 2 new classes of drugs, the long-acting β -agonists (LABAs) and leukotriene blockers.

From the registry, we collected information on all purchases of antiasthmatic drugs (Anatomical Therapeutic Chemical classification group R03) in children as old as 15 years with physician-diagnosed asthma. To analyze the trends in medication, we aggregated anti-inflammatory and LABAs into 5 groups: (1) inhaled corticosteroids (ICSs) plain, (2) cromones (sodium cromoglycate or nedocromil), (3) ICSs as a fixed combination with LABAs, (4) montelukast combined with any other drug, and (5) others. In each of the groups, concomitant symptom-relieving short-acting β -agonist could be used.

During the 1990s, a rapid growth was seen in the number of children diagnosed with asthma. The number of children with special reimbursement was 1.9 per 100 children at the beginning of the national program in 1994, rose steadily to reach the highest rate of 3.1 per 100 children in 2002, and thereafter slowed to 2.6 per 100 in 2006. This trend was roughly common to all subgroups by age.

Because wheezing is common among small children and this phenotype may differ from other children not only in pathological mechanisms of the symptoms but also in medication use, we analyzed those under 4 years of age separately. The next age group chosen was children below school age (more than 4 and less than 7 years of age), in which group atopic persistent asthma becomes the dominant phenotype but lung function is rarely measured, and the diagnosis is mainly clinical. Finally, all school-age children between 7 and 15 years of age were analyzed as 1 group, because for asthma diagnosis and for the special reimbursement, an objective documentation of bronchial reversibility documented by spirometry or peak flow measurement is a prerequisite.

Fig 1, A, shows the distribution of children with asthma age less than 4 years by medication groups. One year after the launching of the asthma program, in 1995, the proportion of patients using ICSs was 61%, and this share increased rapidly to 86%. After introduction of the fixed combination of fluticasone and salmeterol, the proportion of plain ICSs started to decrease, and use of the

fixed combination rose in 4 years to 22%. There was a tremendous regional variability in the use of fixed combinations; for example, in 2005, 13% of the small children in Helsinki area were using them, whereas in some areas, the corresponding share was 40%. Montelukast was accepted on special reimbursement list as late as in 2005, and the use of it was marginal preceding this time. In Fig 1, it is included in the group "others."

In the group of children 4 to 6 years old, use of ICSs also rose from 46% to 77% during the 1990s, and there was a clear decrease in those receiving cromones, from 13% to 1%. During the late 1990s, most guidelines still included cromones in the treatment options for mild persistent asthma. As with the youngest children, the share of fixed combinations grew in 5 years from less than 1% to 34%.

In the school-age children, cromones were still a significant drug class in 1995, when 19% of these children were using them as the main controller (Fig 1, B). Again, in parallel with the increase of ICSs, the proportion of cromones decreased to 4%, and the proportion of children using plain ICSs went from 43% to 62%. The most dramatic increase in the use of fixed combinations was seen in this age group of children, in 6 years, from 2% to 47%. The use of montelukast also increased in the last 3 years, mainly as add-on medication rather than monotherapy together with short-acting β -agonists.

Our study and findings resemble closely results published from Denmark recently in this Journal.³ However, our material adds information to the phenomenon, because only children above 6 years of age were included in the Danish study. In addition, children in our material were all patients with asthma diagnosed by a physician, usually a pediatrician, whereas the Danish study concerned all users of antiasthmatic drugs.

The most striking finding of our study was the high proportion (23%) of small children receiving a fixed combination of ICS/LABA. These drugs are neither indicated nor recommended for the youngest age group because of lacking evidence. A large proportion of all children with asthma were receiving inhalation glucocorticoids, but increasingly in combination with a LABA instead of plain preparations. Perhaps the fixed combination will finally be shown to be both effective and safe in young children, but at the moment, there is no such evidence.⁴

Early anti-inflammatory treatment is essential in the maintenance of lung function and control of symptoms.¹ ICSs were the major drug group used for this purpose in our material. Cromones and leukotriene antagonists also have anti-inflammatory properties. Of these, cromones were used rather commonly in Finland, but not in the other Nordic countries. These drugs kept their position until mid 1990s, but thereafter, their significance was rapidly lost. This was not unexpected, because increasing evidence indicated only moderate or no effect in pediatric asthma.⁵ Montelukast was introduced into the antiasthmatic pediatric drug market rather late, and its use remained insignificant in our material.

The Finnish Current Care Guideline of asthma were published in 2000. They recommend that children not adequately controlled with permanent ICSs (needing doses of more than 400 μ g/d either budesonide or beclomethasone or 200 μ g/d fluticasone) should be treated with add-on therapy. This may have sped up the use of fixed combinations since 1999, when they entered the market. It is difficult to assess the proportion of patients with moderate-to-severe

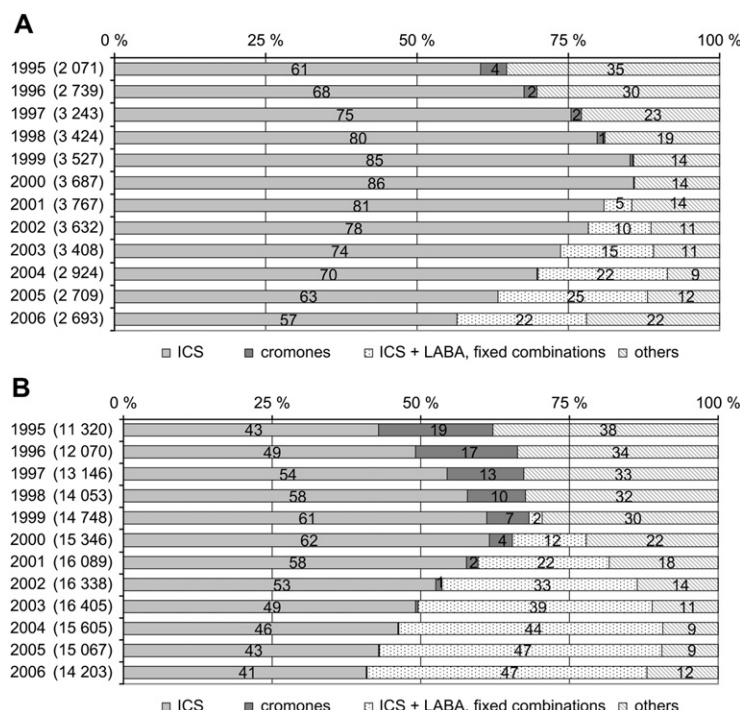


FIG 1. Proportion of children in Finland treated with different types of asthma drugs in the period 1995-2006. Children age 0 to 3 years (A) and 7 to 15 years (B). The numbers in parentheses are the numbers of subjects per year.

asthma, among whom fixed combinations should especially be used. Fuhlbrigge et al⁶ recently stated that the prevalence of moderate-severe asthma in children with asthma may actually be around 50% when the global asthma symptom burden is evaluated. In our data, 48% of the school-age children were on fixed combinations, which may reflect that physicians accurately categorize and treat their patients according to the recent guidelines.

As pointed out by Bisgaard,³ prescription practices of individual physicians are difficult to assess. Our study merely describes the large changes in medication especially during the last 5 years. The prescribing of medication is influenced by both individual factors including personal experience and knowledge, and external factors, such as marketing and published guidelines. It seems that data derived from mainly adult studies with fixed combinations have been extrapolated to children as such. This is not unusual in the pediatric age groups, in which evidence is often lacking and off-label use of drugs is common. Bisgaard³ encouraged a stronger emphasis on guideline implementation, but in Finland, the national asthma program has been widespread and widely accepted.² As can be seen from this evaluation report, management of childhood asthma was not the main topic in the program. Also, the national Current Care Guideline (<http://www.kaypahoito.fi>), after update in 2006, still includes managing both adult and childhood asthma. This may obscure the message especially for the youngest children, emphasizing the need for adequate international pediatric guidelines.

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