Use of Inhaled Anti-inflammatory Medication in Children With Asthma in Managed Care Settings

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Background: Many factors affect use of inhaled therapy in asthma. Relatively little is known about current patterns of use of anti-inflammatory medication in children with asthma and whether variations occur with age and use of bronchodilator medication.

Objective: To study the factors associated with dispensing of anti-inflammatory (controller) asthma medication to children in 3 managed care organizations (MCOs).

Methods: Using automated databases, a 1-year cross-sectional study of children with asthma aged 3 to 15 years cared for in 3 MCOs was used to evaluate the association of age and other factors with controller medication use.

Results: A total of 13352 children were studied. Significantly fewer children aged 3 to 5 years were dispensed any (≥1) controller medication than older children (P<.001). Among children dispensed 6 or more β-agonists, only 39% also received 5 or more controller dispensings, with adolescents significantly less likely than younger children to receive 5 or more controllers (33%; P<.001). Significant differences were seen among MCOs in proportions of patients dispensed controller medication. In a multiple logistic regression model, controlling for frequency of β-agonist dispensing and MCO, significantly lower dispensing of any controller medication was seen for those aged 3 to 5 years (odds ratio [OR], 0.8; 95% confidence interval [CI], 0.7-0.9) and for girls (OR, 0.9; 95% CI, 0.8-0.96). In contrast, for repeated (≥5) controller dispensing there were significantly fewer dispensings to adolescents (OR, 0.7; 95% CI, 0.6-0.9) and girls (OR, 0.8; 95% CI, 0.7-0.9).

Conclusions: There may be differences in the use of preventive asthma medication in children that are affected by age, sex, and health care organization. Few children with frequent symptoms are using controllers regularly, as is recommended by national guidelines.

POPPULATION AND METHODS

SETTING

This is a 1-year cross-sectional analysis of data collected for the PAC-PORT II trial, a multicenter trial of implementation strategies for the NAEPP guidelines for the diagnosis and management of children with moderate to severe asthma. As part of the initial phase of this project, clinical care for children with asthma within the primary care practice settings at each of the health plans was characterized.

All subjects were members of one of the MCOs participating in the PAC-PORT II, located in 3 geographically varied US metropolitan areas. Each MCO provides a number of managed care products. We report data from 4 different care delivery systems within the 3 MCOs. The 4 systems are herein referred to as MCOs 1 to 4. MCO 1 is organized as a staff-model, closed panel MCO with approximately 400,000 enrollees. MCOs 2 and 3 are 2 formerly separate divisions of approximately equal size that have now been amalgamated into one organization, with an overall enrollment of approximately 1.2 million people. We report results from these 2 divisions separately. MCO 2 is a group-model MCO and MCO 3 is a network-model system. Data for MCO 4 come from only the staff-model system of this mixed-model MCO with about 400,000 members. Approximately 90% of all members of each plan have prepaid drug coverage that provides up to a month's supply of medicine for a nominal copayment ($5-$10 per prescription).

There is little recent information regarding the potential side effects of ICS in young children, because no nebulized ICS formulations were available during the study period and because of concern regarding the potential side effects of ICS in young children. We examined whether these practice patterns were continuing despite more than a decade since the initial dissemination of the guidelines.

RESULTS

Dependent variables were categorical in nature, and thus chi-square tests were performed to test for differences in the data. To control for factors associated with potential selection bias, we used logistic regression techniques. Each significant variable in the bivariate analyses was tested in the multiple logistic regression model. A variable was included in the final model if it was associated with the outcome at the 2-sided 0.05 level.

Eligibility criteria were satisfied by 13,352 children, with 3082 children from MCO 1, 2,852 from MCO 2, 6033 from MCO 3, and 1385 from MCO 4. The average age of the children was 9.3 years, and there was a predominance of boys (59%) in the sample overall. The distribution of age and sex was similar across MCOs.

ANALYSIS BY AGE

Dispensing of controller therapy varied among age groups. Significantly fewer children aged 3 to 5 years received 1 or...
controller therapy included ICSs (referred to as “inhaled steroids”) and inhaled cromolyn sodium or nedocromil (referred to as “cromolyn”). Oral antileukotrienes were rarely dispensed at any age, and have been omitted from the analysis. β-Agonists included inhaled or pediatric oral preparations and included anticholinergics, but excluded long-acting β-agonists such as salmeterol, as use of these drugs during the period under study was minimal.

STATISTICAL ANALYSIS

The main outcome of interest was frequency of asthma controller therapy dispensing. The frequency of β-agonist dispensing served as a surrogate for asthma severity and was used as the main variable for stratification in the analysis. Potential covariates included age, sex, and MCO. Information on race was unavailable for a substantial proportion of the population and was therefore not considered in this analysis. Pharmacy data included any initial dispensing and refills of all prescription medications.

Differences in the proportion of children dispensed any controller therapy in each stratum were assessed for significance by χ² tests and Mantel-Haenszel methods. β-Agonist dispensing rates were collapsed into 4 categories (0, 1-2, 3-5, ≥6 dispensings). These categories were viewed as proxies for measurements of disease severity. This method has been successfully used in previous studies to stratify risk of morbidity.17,18 Leone et al19 reported a monotonic relationship between a pharmacy-based severity classification and future inpatient resource utilization for asthma. Six or more dispensings of β-agonists provides at least 1200 observations for the outcomes of (1) any controller dispensing, (2) 3 or more controller dispensings, and (3) 5 or more controller dispensings. Three controller canisters during 1 year would provide less than 2 inhalations per day, while 5 controller canisters are the minimum number that could indicate nearly daily use of medication, at an average of 2 to 3 inhalations per day. Differences by patient age were evaluated by stratified analysis and by inclusion of interaction terms in the logistic model.

Approval for this study was obtained from institutional review boards at each study site.

more dispensings of a controller therapy than did children in older age groups (P <.01) (Figure 1). Although a similar proportion of 3- to 5-year-olds were dispensed cromolyn as 6- to 8-year-olds, fewer younger children were dispensed ICSs (Figure 1). In all age groups the proportion of children receiving controllers increased with more frequent dispensing of β-agonists. Overall, 60% of children who received 3 or more β-agonists also received some controller medication (Figure 2), and this figure increased to 77% in those with 6 or more β-agonist dispensings (Figure 3). The pattern of age differences in controller use changed among children with more frequent dispensing of β-agonists. Among children who received 6 or more β-agonists, a similar proportion of 3- to 5-year-olds (70%) as older children (71%) received a controller medication (Table 1). Preschool-age children in the 3 or more and 6 or more β-agonist groups continued to receive cromolyn more frequently than older children, and more frequently than they were dispensed ICSs. However, in multivariate analysis, controlling for frequency of β-agonist dispensing, sex, and MCO, 3- to 5-year-olds were less likely to receive a dispensing of controller therapy than older children (odds ratio [OR], 0.8; 95% confidence interval [CI], 0.7-0.9; P = .01) (Table 2).

The pattern of repeated (≥3 or ≥5) controller dispersions showed few children received controllers regularly, even among children with frequent β-agonist use (Table 3). Only 12% of all children were dispensed 5 or more canisters of controller over 12 months. Few children at any age who were infrequent β-agonists users were regular users of controllers (Table 4). Among those dispensed 6 or more β-agonists, 58% received 3 or more, and 39% received 5 or more controllers of any type. Significantly fewer adolescents (12- to 15-year-olds) than younger children who received 6 or more β-agonists were dispensed either 3 or more (54% vs 61%; P = .001), or 5 or more controllers (33% vs 43%; P <.001). Only 21% of adolescents in this group of frequent β-agonists users received 5 or more dispensings of ICSs. This pattern was confirmed in multivariate analysis, controlling for other factors as above. Children aged 12 to 15 years were significantly less likely to be dispensed 3 or more (OR, 0.8; 95% CI, 0.70-0.94; P = .005) or 5 or more controllers (OR, 0.7; 95% CI, 0.6-0.9; P <.001) than younger children. Children 6 to 8 years old were more likely to receive repeated (≥3) controller dispensations than preschool-age children (OR, 1.3; 95% CI, 1.1-1.6; P = .008). When the analysis was restricted to only those who had been dispensed some controllers (n = 5237), a similar pattern was seen. Using 3- to 5-year-olds as the reference group, the OR for repeated (≥5) controller dispensings in 12- to 15-year-olds was 0.6 (95% CI, 0.5-0.8; P <.001), and for 6- to 8-year-olds was 1.3 (1.1-1.6; P = .03) (data not shown).

ANALYSIS BY SEX

Over the year of the study, a significantly lower proportion of girls (37%) received any controller therapy than did boys (41%; P <.001). A difference of similar magni-
A similar pattern was seen for repeated (≥5) controller dispensing (10% vs 13%; P=.001). Among children dispensed 6 or more β-agonists, significantly fewer girls than boys received any controllers (75% vs 79%; P=.006) or repeated (≥5) controller dispensings (39% vs 43%; P=.005). In the group with 6 or more β-agonist dispensings, the sex discrepancy for repeated controller dispensing was greatest in children aged 3 to 5 years (34% vs 48%; P=.001) and was also seen in 9- to 11-year-olds (41% vs 46%), but was absent in 12- to 15-year-olds (35% vs 36%). In the multivariate analyses, controlled for age, organization, and β-agonist use, girls were significantly less likely than boys to receive any controller therapy (Table 2). Girls were also less likely than boys to receive 5 or more dispensings (OR, 0.8; 95% CI, 0.7-0.9; P=.004), or 3 or more dispensings (OR, 0.9; 95% CI, 0.8-0.97; P=.01) of controllers. In the analysis restricted only to those dispensed some controller, a similar result was found, with girls significantly less likely to receive repeated (≥5) controller dispensing (OR, 0.8; 95% CI, 0.7-0.95; P=.03).

**EFFECT OF ORGANIZATION**

Differences in controller use were evident among MCOs. Children at MCO 1 were more likely than children at MCO 4 to receive ICSs (33% vs 23%; P<.05) and less likely to get cromolyn (15% vs 25%; P<.05). This pattern was seen across all age groups. Differences in controller use among MCOs persisted among children dispensed 6 or more β-agonists. At MCO 3, 69% who received 6 or more β-agonists were also dispensed at least 1 controller, compared with 85% at MCO 1 and 83% at MCO 4. The multivariate model for any controller dispensing showed children at MCO 3 were significantly less likely than children cared for at other MCOs to receive any controllers (Table 2). Those cared for at either MCO 1 or 2 were more likely than those from MCO 4 to be dispensed any controller. However, the model for repeated (≥5) controller dispensing showed different results. Children from MCO 3 were significantly more likely (OR, 1.3; 95% CI, 1.1-1.7; P=.02) and those at MCO 1 less likely (OR, 0.8; 95% CI, 0.6-0.99; P=.05) than those at the reference group of MCO 4 to be dispensed 5 or more controllers. A similar result was evident for dispensing of 3 or more controllers. When the analysis was restricted to those with some controller dispensing, MCO 3 children were significantly more likely to have repeated controller dispensing (OR, 1.7; 95% CI, 1.3-2.1; P<.001) than those from MCO 1 (OR, 0.7; 95% CI, 0.6-0.98; P=.03) or the reference group of MCO 4.

**COMMENT**

Nearly a decade after the distribution of national guidelines for the management of asthma, few children with symptomatic asthma use controller therapy regularly in the diverse managed care settings that we studied. The current NAEPP guidelines clearly recommend the regular use of controller medication for children whose high β-agonist use indicates symptoms throughout the year. Six or more β-agonists per year will provide on average more than 3 inhalations per day of quick-relief medication. Few of these children will not have persistent asthma. Although nearly three quarters in this group were dispensed a controller at least once, only around two fifths had 5 or more dispensings of controller. Among these children with more frequent β-agonist use, only a little more than half were dispensed 3 or more controllers; in no age category did the proportion dispensed 5 or more controllers exceed 50%.
controllers reach 50%, and in adolescents this proportion dropped to one third. Conversely, there were few children who were regular users of controllers but infrequent β-agonist users, suggesting that the group with persistent asthma who was well controlled was small.

As anticipated, children of preschool age were less likely to be initiated on anti-inflammatory medication, and fewer adolescents were regular users of anti-inflammatories. Our results provide similar findings to earlier studies of overall controller use that were conducted during the first years of life.
after the initial dissemination and promotion of the national guidelines. 7,9,10 Halterman et al10 found that in the years 1991 to 1994, 26% of children with moderate-to-severe asthma reported using inhaled controller therapy in the previous month. However, unlike these authors we found significant sex differences in controller use. In addition, although preschool-age children were less likely to be initiated on controller therapy, similarly to the findings of Goodman et al,9 we found that adolescents are less likely to use them regularly. The varied nature of the practice types in the MCOs we studied, as well as their geographic diversity, suggests that our results can be extrapolated more generally. Our findings indicate that current systems of care for children with asthma lead to less than ideal asthma management, and that the passage of time is not substantially altering this situation. The sharp discrepancy seen among frequent β-agonist users between any dispensing of a controller and more regular use suggests that attention needs to be focused more on the barriers to long-term use of controllers by patients and families than on simply getting clinicians to prescribe “a controller” for chronic asthma.

A number of factors may explain why children with more frequent symptoms are apparently not receiving adequate asthma therapy. That there are many children who have both frequent dispensings of bronchodilators and one dispensing of controller, but do not receive refills of controllers, suggests that limited patient adherence plays a major role.20,21 Adherence with treatment declines in adolescence, and most deaths from childhood asthma occur in adolescents.13 External influences can have major effects; in a recent study,22 26% of adolescent inhaler users were not allowed to carry their medication on their person while at school. It is also possible that less frequent physician visits could explain the lower regular use of controllers in adolescents. Adolescents initiate visits to physicians at much lower rates than do younger children.23 It is also possible that physicians do not, or are unable to, schedule routine and timely follow-up visits to monitor the clinical situation for children started on controller medication, as is recommended in the guidelines.4 Hence, children, especially adolescents, may be using prescriptions with long-term refills or requesting telephone refills without physicians’ complete awareness of their frequent β-agonist use. More effective systems of monitoring and of providing feedback to physicians of patterns of patient drug usage are possible methods for improving this situation.

Concern about adverse effects may also reduce the ICS use, both from a reluctance of physicians to prescribe ICSs and of families to continue using them.24 Such concerns do not explain the concomitant underuse of alternative medications such as cromolyn. An alternative explanation why children may be dispensed 1 or 2 controllers per year is that physicians may be using them to manage exacerbations. This management strategy is unproven and would not accord with current guideline recommendations.23

Most cases of asthma in children are identified by the age of 5 years.26 Therapy for preschool-age children differs from that for older children in several ways. Overall, controller use is lower in children aged 3 to 5 years, adjusted for β-agonist use, and this age difference is greater in those needing less frequent bronchodilator treatment. Cromolyn is used more often in younger children, a pattern seen with more frequent β-agonist use as well as in children needing less bronchodilator treatment. There are several likely reasons for these differences. Delivery methods for ICSs currently available in the United States may limit their use in this younger age group.27 Although the use of metered-dose inhalers with close-fitting masks has been shown to be effective28,29 and some experts would recommend them as the first-choice device,20 the lack of a corticosteroid formulation for use via nebulizer in the United States may lead clinicians to favor cromolyn in preschool-age children. The severity of asthma may be underestimated in younger children.28,30 Less frequent β-agonist use (1–3 dispensing per year) may indicate intermittent asthma in which controllers are not indicated, and intermittent disease may be more common in preschool-age than older children. Finally, concern over the potential long-term adverse effects of ICSs may cause physicians to use cromolyn in young children. However, the majority of preschool-age children dispensed 6 or more β-agonists were not using cromolyn regularly. In young children (<5 years old) with frequent symptoms, low use of ICSs is not being compensated by increased use of cromolyn.

Although the relative differences in use of controllers between boys and girls are small, this discrepancy would still lead to large absolute numbers of inadequately treated girls with asthma. Several reasons can be postulated as to why we found differences in the frequency of controller dispensing in girls and boys. Dysapnic growth of airways and lung parenchyma may show sex differences, leading boys to have smaller airways for the same lung volume than do girls, with consequently more frequent airway obstruction.31 Symptoms of wheezing are more likely to be treated as asthma than symptoms such as persistent nocturnal cough,32 and there may be sex differences in types of asthma symptoms. Kühni and Semmhauser33 found that in Swiss children, for all asthma symptoms except wheeze, approximately twice as many boys as girls received bronchodilator treatment. Boys have also been reported to be more likely than girls to receive medication, regardless of the frequency of wheezing.34 Psychosocial influences may be important. Physicians, parents, and children may have different perceptions of symptoms and different attitudes toward treatment of girls and boys. For instance, exercise limitation in boys may be perceived as a problem that requires treatment more often than it does in girls. In this regard, it is interesting to note that a previous study based on self-report did not show sex differences in use of controller therapy.10 The large sex difference for repeated controller use among preschool-age children dispensed 6 or more β-agonists, a group for whom symptoms are likely to be a significant problem that will attract the attention of parents and physicians, suggests a role for psychosocial factors. Quality improvement efforts may need to focus on sex differences in asthma management, and further work is needed to explore this area.

The strength of our study lies in the diverse practice-type settings of the MCOs studied, as well as their geographic spread. However, this study has a number of limitations. The absence of individual clinical data limits the conclusions that can be drawn regarding the appropriateness of medication regimens for many children in our study, as we lack an independent definition of severity. However, in the
group of children with frequent β-agonist dispensings, we can be confident that the large proportion not regularly using controllers represents less than ideal use of asthma therapy. We used medication dispensing as a surrogate for actual medication consumption. The effect of this may be varied, as some children will not use the dispensed medication, while others will obtain medicine from non-pharmacy sources, such as physician samples or family members. It is likely that our estimates of the amount of medication for regular use is an overestimation of the actual duration of use, as some medication will not be used and some will be used at higher doses than 2 to 3 puffs a day but for shorter periods. The advantage of this method over patient self-report is that recall bias and the tendency for people to give socially desirable responses are limited. The reliability of the automated data in capturing the dispensing of medications has been demonstrated previously in these systems. The proportion of children receiving no prescription therapy for asthma was similar to that found by Buchner et al using similar methods of claims data analysis in MCOs. No adjustment was made for dosage of controller medication, nor was any weighting performed to adjust for potency of different inhaled steroids. The effect of this is probably minimal as the use of fluticasone or budesonide is very small, and the recommended doses of other ICSs are very similar. A lack of data on factors such as race, smoking, and detailed socioeconomic status measures is also a limitation of the study’s conclusions. The cross-sectional design and the absence of data from other periods make it difficult to discern temporal trends in dispensing patterns.

In the diverse managed care settings we studied, most children with frequent symptoms, as judged by their use of bronchodilators, have received some pharmacotherapy to combat airway inflammation. However, at any age the majority of children with frequent need for bronchodilators are not using sufficient controller medication to be considered “regular” users of preventive therapy, as recommended in national guidelines. Adolescents are at particular risk for suboptimal asthma management. Clinicians also need to be aware of potential sex differences in asthma management. Organizations and clinicians need to focus on strategies that encourage greater medication adherence with regular maintenance asthma therapy among patients and families.

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