Coprescription of Antibiotics and Asthma Drugs in Children

WHAT'S KNOWN ON THIS SUBJECT: Antibiotics and asthma drugs are the most frequently prescribed drugs in most age categories and in most countries.

WHAT THIS STUDY ADDS: In this study, antibiotic use was found to be 1.9 times more frequent in children who were treated with asthma drugs than those who were not. Among children who received an asthma drug, 35.6% were dispensed an antibiotic on the same day.

abstract

FREE

BACKGROUND: In children, antibiotics as well as asthma drugs are frequently prescribed. We investigated the effects of the codispensing of antibiotics and asthma drugs to children.

METHODS: Using a health insurance database, we examined dispensing and codispensing of antibiotics and asthma drugs for the period of a 1 year in 892 841 Belgian children aged <18 years.

RESULTS: For a 1-year period, an antibiotic was dispensed to 44.21% of children: 73.05% aged <3 years; 49.62% aged 3 to 7 years; and 34.21% aged 8 to <18 years. An asthma drug was dispensed to 16.04% of children: 44.81% aged <3 years; 17.90% aged 3 to 7 years; and 7.64% aged 8 to <18 years. Overall, an antibiotic was dispensed without an asthma drug to 38.62% of children versus with an asthma drug to 73.50% of children ($P < .0001$). More frequent dispensing of antibiotics to children who received an asthma drug (odds ratio: 1.90; 95% confidence interval: 1.89–1.91) occurred in all age categories ($P < .0001$). In 35.64% of children with an asthma drug dispensed, an antibiotic was dispensed on the same day.

CONCLUSIONS: In all age groups, dispensing of antibiotics is more likely in children who have an asthma drug dispensed in the same year. In all age groups, codispensing of antibiotics and asthma drugs is a common practice. Efforts to decrease antibiotic use in children could be improved by focusing on children who are being treated with asthma drugs. *Pediatrics* 2011;127:1022–1026

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KEY WORDS
asthma drugs, antibiotics

ABBREVIATIONS
ICS—inhaled corticosteroids
DPI—dry powder inhaler
CI—confidence interval

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In children antibiotics are the most frequently prescribed drug in all age categories.[1] This overuse of antibiotics in the treatment of pediatric patients is a well-known practice. For instance, in preschool children with asthma-like symptoms such as recurrent episodes of wheezing, cough, and shortness of breath, it has been reported that treatment more often consists of antibiotics and cough medicines than asthma drugs.[2]

Asthma drugs are also frequently prescribed to children, and in several age categories of pediatric patients the frequency of the use of asthma drugs is second only to that of antibiotics.[1] This high prescription rate is not surprising because wheezing is a common symptom at all ages and asthma is a frequent diagnosis during childhood.[3] Asthma drug use is highest, however, in preschool children,[1,4] the age category during which the least evidence for asthma drug efficacy has been documented.[5]

Although antibiotics and asthma drugs are both frequently prescribed, there is no information available on the frequency of coprescription of these drugs. Collection of medical history data in patients with respiratory symptoms alerted us to the frequent coprescription of antibiotics and asthma drugs by referring physicians. The aim of the current study was therefore to investigate codispensing of antibiotics and asthma drugs in a large sample of Belgian children. We investigated the frequency of dispensing antibiotics and asthma drugs to children. We divided the population into those who had and those who had not received asthma medication and examined the pattern of antibiotic use. In particular we looked at whether there was codispensing of antibiotics and asthma drugs on the same day.

METHODS

We used the database of Christelijke Mutualiteiten, the health care insurer that covers 44% of the Belgian population, to analyze all dispensing of antibiotics and asthma drugs to children younger than 18 years for a period of 1 year (October 1, 2005, to September 30, 2006). All Belgian citizens are entitled to health care insurance, which is mandatory in Belgium. To evaluate the consistency of findings and as an internal validation, we performed the same analysis using data of the period from October 1, 2006, to September 30, 2007. Data were extracted on the basis of the Anatomic Therapeutic Chemical Classification System codes, with J01 as the code for antibiotics and R03A through R03D as the codes for asthma drugs (β-agonists, inhaled corticosteroids [ICS], ipratropium, and leukotriene receptor antagonists). The full coding of the Anatomic Therapeutic Chemical classification was available for all drugs prescribed. This coding indicates not only the first level, which indicates the anatomic main group, but also the second through fifth levels, which indicate, respectively, the therapeutic main group, the therapeutic/pharmacological subgroup, the chemical/therapeutic/pharmacological subgroup, and the chemical substance. In addition, every type of dose and formulation has a unique pharmacological product number. Therefore all subcategories of antibiotics and asthma drugs could be reported. Each individual child was tracked over the course of the year so that the number and percentage of children who had an antibiotic or an asthma drug dispensed were calculated. Codispensing was studied by calculating the percentage of subjects with an asthma drug dispensed who had an antibiotic dispensed on the same day as well as throughout the same year.

We further assessed asthma drug use by calculating the number and percentage of children who had an ICS dispensed during the year in combination with other drugs or as monotherapy. We estimated the prevalence of recurrent/chronic use of ICS by calculating the number of subjects with at least 3 prescriptions dispensed, just as in a recent study.[1] Also for ICS, the proportion of all prescriptions dispensed as a pressurized metered dose inhaler, dry powder inhaler (DPI), and automatic inhaler and nebulization solution was calculated in each age category.

The following age categories were defined: younger than 3 years; 3 to 7 years; and 8 to $<$18 years. Subjects were categorized on the basis of their age at the end of each registration period. Age categories chosen were justified as follows: In 2006, 60.4% of Belgian children younger than 3 years attended day care and $>$90% of children aged 3 years and older attended preschool (source: year report 2006, Child and Family, the Belgian governmental organization with the mission to protect child health and welfare)[6]. In children aged 8 years and older, an asthma diagnosis is easily supported by use of spirometry, and nearly all children in this age category are able to correctly use DPIs.[7]

We further assessed health care utilization by calculating the mean number of outpatient visits to general practitioners and pediatricians per year according to medication group.

RESULTS

Drug-dispensing data were analyzed in 892 841 Belgian children aged between 0 and 18 years (first study year). The analysis in the second study year included data from 880 969 children and was used for internal validation. The percentage of children with medication use was slightly but statistically significantly lower during the second observation year, during which we observed a 3.12% decrease in dispensing

TABLE 1 Dispensing and Codispensing of Antibiotics and Asthma Drugs to Belgian Children in 3 Age Categories During the First Study Year

	Age Category, y			
	<3	3 to 7	8 to <18	All
Total cohort, *n*	137 126	234 135	521 580	892 841
% Of cohort	15.36	26.22	58.42	100
Antibiotic in year of study, *n*	100 170	116 182	178 407	394 759
% Of age category	73.05	49.62	34.21	44.21
95% CI	72.82–73.28	49.42–49.82	34.08–34.34	44.11–44.31
Asthma drug in year of study, *n*	61 443	41 917	39 826	143 186
% Of age category	44.81	17.90	7.64	16.04
95% CI	44.55–45.07	17.74–18.06	7.57–7.71	15.96–16.12
Plus antibiotic on same day, *n*	23 444	15 629	11 964	51 037
% Of treatment group	38.16	37.29	30.04	35.64
95% CI	37.77–38.54	36.82–37.75	29.59–30.49	35.40–35.89
Plus antibiotic in same year, *n*	48 501	31 896	24 844	105 241
% Of treatment group	78.94	76.09	62.38	73.50
95% CI	78.62–79.26	75.68–76.50	61.90–62.86	73.27–73.73
No asthma drug in year of study, *n*	75 683	192 218	481 754	749 655
% Of age category	55.19	82.10	92.36	83.96
95% CI	54.93–55.45	81.94–82.26	92.29–92.43	83.88–84.04
Antibiotic in same year, *n*	51 669	84 286	153 563	289 518
% Of treatment group	68.27	43.85	31.88	38.62
95% CI	67.94–68.60	43.63–44.07	31.75–32.01	38.51–38.73

of antibiotics and a 0.21% decrease in dispensing of asthma drugs. The decrease in prescription of antibiotics was present in all age groups (95% confidence intervals [CIs] did not overlap). A significant decrease in asthma drug use in year 2 was evident only in children in the age category 3 to 7 years (−0.74%). We report here only the data recorded during year 1 of the study (Table 1). For data from year 2 see Supplemental Table 3.

In all age groups antibiotics were dispensed to a larger subset of children than were asthma drugs. A steep decrease of dispensing with age was seen for asthma drugs and to a lesser degree for antibiotics: asthma drug dispensing was 44.81% in children younger than 3 years and dropped to 7.64% in children aged 8 to <18 years, whereas for antibiotics the decrease was from 73.05% to 34.21%. In all age categories, the vast majority of children with an asthma drug dispensed also had an antibiotic dispensed during the same year, and approximately one third of subjects had an antibiotic dispensed on the same day as the asthma drug. Overall, an antibiotic was dispensed to 73.50% of the children with an asthma drug dispensed versus 38.62% of children without an asthma drug dispensed during the year. If children had an asthma drug dispensed, the odds that they had also been given an antibiotic were 1.90 (95% CI: 1.89–1.91) compared with children who had not had an asthma drug. Conversely, if a child had an antibiotic the odds of having had an asthma drug were 3.50 (95% CI: 3.46–3.54). The significantly higher dispensing rate of antibiotics to children who had an asthma drug dispensed was present in all age categories (χ^2 $P < .0001$). Penicillin antibiotics were dispensed most often (64.4% of all antibiotic use: amoxicillin, 37.7%; amoxicillin plus clavulanic acid, 24.5%; other, 2.2%), followed by macrolides (14.2%) and cephalosporins (12.2% total: first generation, 3.3%; second generation, 8.9%).

In 38.63% of the children with an asthma drug dispensed, the drug(s) delivered included an ICS; in 9.55% of subjects an ICS was the only drug dispensed. Of the children with an ICS dispensed, only the minority had evidence of chronic use: >2 packs were delivered to 28.06% of the children younger than 3 years and to 11.65% of the children aged 8 to 17 years (Table 2). In the youngest age group, 54.54% of all ICS were delivered as nebulization solution.

The mean number of outpatient visits per year was 7.34 in children who received an asthma drug and 3.04 in children who did not receive an asthma drug; it was 8.45 in children who received an asthma drug and an antibiotic on the same day and 4.48 in children who were prescribed an antibiotic but no asthma drug in that same year.

DISCUSSION

Antibiotics are more commonly dispensed to children who have had an asthma drug dispensed than in children who did not get an asthma drug. Our report is the first to highlight this link as well as the strong tendency for health care providers to coprescribe antibiotics and asthma drugs, sometimes even on the same day.

Our data on close to 1 million children are nearly identical in 2 separate years of analysis, which strengthens the validity of the findings. The strength of

TABLE 2 Dispensing of ICS to Belgian Children in Different Age Categories for a 1-Year Period

	Age Category, y		
	<3	3 tot 7	8 to <18
Subjects whose asthma drug included ICS, %	36.80	43.21	36.64
Subjects to whom >2 packs of ICS were dispensed, %	28.06	20.16	11.65
ICS packs in age category			
As pMDI	44.62	60.64	25.27
As solution	54.54	10.11	2.33
As DPI	0.23	21.51	47.58
As automatic inhaler	0.61	7.73	24.83

pMDI, pressurized metered dose inhaler.

our study was the size of the data set and the similar findings in 2 consecutive years of analysis. A weakness of this investigation was that we had no data on diagnoses for which drugs are dispensed and that the data are cross-sectional. Our observation of a high prescription rate of asthma drugs in young children, which decreased toward adolescence, is consistent with Italian data.[4] In that study 22.6% of children aged 0 to 13 years had an asthma drug dispensed during the year 2000, and asthma drugs were dispensed to 30% to 35% of children younger than 2 years. The Belgian and Italian data document a higher prescription rate compared with that observed in the Dutch study by Zuidgeest et al.[8] In that study, an evaluation of 74 580 children, asthma drugs were prescribed to 11.7% of the children aged 0 to 2 years and to 5.1% of the children aged 15 to 17 years.[8] In our evaluation as well as in previously reported studies,[4,8] asthma drug prescription was found to be most frequent in children in the youngest age group, despite guidelines that highlight the very limited evidence to support the effectiveness of these drugs in preschool children.[5,9]

The high prescription rate of antibiotics in all age groups in our study is also consistent with other reports.[1,10] In a study performed by Marra et al[10] to investigate the association of antibiotic use to later asthma development, 43.3% of the subjects aged up to 9 years were treated with antibiotics over the course of a year. This percentage is somewhat lower than our finding that 58.27% of Belgian children younger than 8 years were treated with antibiotics.

Our report is the first to highlight the current practice of coprescription of asthma drugs and antibiotics. The fact that coprescription of antibiotics and asthma drugs was obvious in all age groups provides further confirmation of the prevalence of this practice. To what extent the conclusions of this analysis can be applied to other resource-rich countries is not known. Other investigators have reported the frequent use of antibiotics in subjects with respiratory symptoms. Thirty-five percent of episodes of respiratory tract infections are treated with antibiotics,[11] despite the fact that these infections are mostly commonly viral in origin and trigger wheezing in young children.[9] In preschool children across Europe and the United States, wheezing with persistent cough and wheezing with breathlessness are more often treated with antibiotics (34%) than with asthma drugs.[2] Campaigns to decrease the frequency of antibiotic use might be made more effective by focusing on children with repeated episodes of cough, wheezing, and shortness of breath. It should be stressed that episodes of wheezing are mainly associated with viral infections, and physicians should be discouraged from routinely coprescribing asthma drugs and antibiotics. When faced with a child with respiratory symptoms, the physician should distinguish between children who have wheezing and shortness of breath and may be helped with an asthma drug and those who have fever and signs of bacterial airway infection that may warrant treatment with an antibiotic. In addition, focusing efforts during autumn and winter, when asthma symptoms[12] and asthma drug use[13] reach a peak secondary to rhinovirus and respiratory syncytial virus infections might be most effective. In our study population, the yearly cost of the antibiotics dispensed amounted to 6 568 996 Euros. Because of the lack of efficacy and high cost of coprescription of antibiotics and asthma drugs, the negative aspects of the "coprescription habit" should become a focus of health education.

In the current study, we found that children who have an asthma drug prescribed have more frequent doctor visits than children who do not have an asthma drug prescribed. This finding is not surprising and most likely reflects the fact that these children are more symptomatic. Undoubtedly some of the antibiotic prescriptions to children who receive an asthma drug are given for appropriate indications. That antibiotics are prescribed twice as frequently to children who receive asthma drugs, however, must in part be attributable to inappropriate practice, as has been reported previously.[2,11] The coprescription of antibiotics in one third of the children who are prescribed an asthma drug is particularly hard to justify or understand. Because these children frequently present for treatment at outpatient clinics, physicians who provide outpatient treatment should be targeted for education concerning indications for antibiotic prescriptions in this group. This education should specifically stress prescribing practices for children aged 8 to 18 years because coprescription continues to be a common practice in this age group, despite the relative ease with which asthma and bacterial infections can be differentiated.

As a secondary aim to this study, we explored chronic ICS use and the modality of ICS use. We found that chronic ICS drug use was uncommon in all age groups, and especially in children in the older age group, in whom a diagnosis of asthma is more straightforward. Again, our data are in line with those of previously published studies. In an Italian cohort[4] only 26% of the children received at least 3 prescriptions in 1 year. In a Dutch study chronic asthma drug use was also limited in children: only 8% of 1074 first-time ICS users received their asthma drug for a full year.[14] A low proportion of repeated asthma drug prescriptions was also

reported in a multinational European survey.[1] Concerning the mode of inhalation prescribed in the current study, the major conclusions are that nebulized ICS solution is still overused in children in the young age category, and DPI and automatic inhalers are underused in children aged 8 to 18 years. Overuse of ICS via nebulization was also reported in the Italian population,[4] and underuse of DPI in children older than 8 years was noted in the Dutch study by de Vries et al, in which 35,6% of children older than 8 years were not using a DPI.[15]

CONCLUSIONS

In our study population many young children were exposed to antibiotics and asthma drugs. The rates and types of prescriptions we observed are in line with previously reported results. However, we are the first to report the very common coprescription of asthma drugs and antibiotics in children. This finding highlights the need for educational opportunities to inform clinicians that such coprescription should be limited.

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