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Patterns of topical corticosteroids prescriptions in children with asthma

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Abstract

Objectives: To study topical corticosteroid use in Dutch asthmatic children using pharmacy dispensing data and to assess whether Dutch physicians prescribe topical corticosteroids in this population according to clinical guidelines.

Methods: Medication histories of children using asthma medication were extracted from the pharmacy dispensing system in 100 Dutch community pharmacies. The incidence rate and the potency of topical corticosteroid prescriptions per age were assessed. The topical corticosteroid incidence rates of the different age groups were compared using the Pearson chi-square test. Generalized linear models were used to study the prescription behavior of general practitioners and atopic dermatitis-related specialists regarding different classes of topical corticosteroids.

Results: Thirty percent of the infants received a topical corticosteroid prescription, compared with 15%-18% of the children aged 4 and older. Similarly, the mean number of topical corticosteroid prescriptions in infants was 2.2 per year, compared with 1.6-1.9 in children aged 4 and older. In concordance with the clinical guidelines, we observed that atopic dermatitis-related specialists more often prescribed first prescriptions of potent and very potent topical corticosteroids than general practitioners (relative risk = 2.55, 95% confidence interval = 1.79-3.63). Statistically significant differences ($P < .01$) were found between potencies of prescribed topical corticosteroids.

Conclusion: Younger children receive more topical corticosteroid prescriptions than children aged 4 and older, and there is a statistically significantly higher prescription rate of topical corticosteroid for infants. Sometimes general practitioners do not follow guidelines and prescribe more-potent topical corticosteroids without a prior prescription of the same potency by a specialist.

KEYWORDS
asthma, atopic dermatitis, children, incidence, longitudinal, topical corticosteroids, treatment

*Deceased.

1 | BACKGROUND

Atopic dermatitis (AD) (also known as atopic eczema) is a common inflammatory, relapsing skin disease characterized by severe itching and eczematous skin lesions. Approximately, 30% of children with AD will develop asthma.[1] In a population of children who used asthma medication, we found a self-reported AD prevalence of 64%.[2] It remains unclear which mechanism drives this common coexistence.[3] Children with AD and asthma may have different interacting disease phenotypes than children with AD or asthma alone. This might affect the effect of pharmacologic interventions.

Standard medication for AD consists of emollients and topical corticosteroids (TCSs). Four classes of TCS strength are recognized, from mild (A) to very potent (D).[4] Topical calcineurin inhibitors (TCIs) and systemic immunosuppressive therapies such as oral corticosteroids, azathioprine, and cyclosporine can also be prescribed for AD treatment.[5]

The current Dutch clinical guidelines for general practitioners (GPs), last revised in 2014, advise that GPs should prescribe treatment only for mild disease (emollients and low-potency TCSs) in children.[6] If the disease cannot be controlled, the patient should be referred to a dermatologist, pediatrician, or other related specialist.[6] It is unclear whether physicians follow these guidelines. The aim of this current descriptive pharmacoepidemiologic study was to study AD medication patterns in Dutch children with asthma using pharmacy dispensing data and to determine whether Dutch physicians prescribe AD medication according clinical guidelines.

2 | METHODS

2.1 | Study population and data collection

Medication histories of children aged 4-12 using regular asthma medication were extracted from the pharmacy dispensing systems in 100 Dutch community pharmacies containing data from 1996 to 2013. The pharmacies were part of the UPPER Network of the Utrecht Institute for Pharmaceutical Sciences.[7] Regular asthma medication was defined as three or more prescriptions of asthma medication in the last 2 years and one or more prescriptions in the 6 months before inclusion (2009-2013).[8] Only children for whom medication history was available starting in the first year of life were included in this study.

2.2 | AD medication dispensing data

A TCS prescription was identified based on the Anatomical Therapeutic Chemical (ATC) code in the pharmacy dispensing system. All preparations starting with ATC code D07A (plain topical corticosteroids) were selected. To subdivide TCSs into potency classes, the next letter in the code was used. "A" represents a weak potency TCS, "B" a moderate potency TCS, "C" a potent TCS, and "D" a very potent TCS.

If two or more AD-related prescriptions were recorded on the same day (irrespective of the dosage), only the most potent TCS prescription was included in the analyses. Because combinations of TCS and an antifungal (ATC code: D07B) or antibacterial agent (ATC code: D07C) are used for treatment of infections, they were not counted as TCS therapy for AD.

We assessed the incidence rates of TCS prescriptions per person year (the number of years times the number of members of a population who were at risk for an event) in every age category. Information on the age at which each child received his or her first potent (class C) or very potent TCS (class D) was extracted. The duration of TCS use was estimated by counting the mean number of TCS prescriptions in children who received at least one TCS prescription per age category.

2.3 | Prescribers of AD medication

Information on prescribers was extracted from the pharmacy records. Prescribers were subdivided in three categories: GPs, AD-related specialists (dermatologists, pediatricians, allergists, pulmonologists, ophthalmologists), and non-AD-related specialists (e.g., urologists). The prescribed potency of TCSs was compared between two mutually exclusive groups of children: those prescribed TCSs only by an AD-related specialist and those prescribed TCSs only by a family doctor.

2.4 | Statistics

The TCS incidence rates of the different age groups were compared using the Pearson chi-square test. Generalized linear models were used to assess whether distinct categories of prescribers prescribed different classes of TCSs (SPSS version 20.0, IBM Corp., Armonk, NY).

3 | RESULTS

3.1 | Study population

Of 3575 children for whom medication histories were extracted, 2220 had medication histories available from the first year of life (Figure 1). The majority of these children who used asthma medications were boys (65.3%) and the median age was 8.3 years (interquartile range [IQR] 6.0-10.7 years) (Table 1). Overall, 62.8% of the children who regularly used asthma medication also received a TCS prescription at least once. Almost half of the children with a TCS prescription received a weak TCS (class A). The most potent TCSs (class D) were prescribed in only 3.2% of the study population. Prescriptions of TCIs were relatively rare (1%) in our study population. For 936 children, only GPs prescribed TCSs, and for 74 children only specialists prescribed TCSs.

3.2 | Age and TCS prescriptions

Older children received TCSs statistically significantly less frequently than younger children (Figure 2, Table S1, Figure S1). The amounts

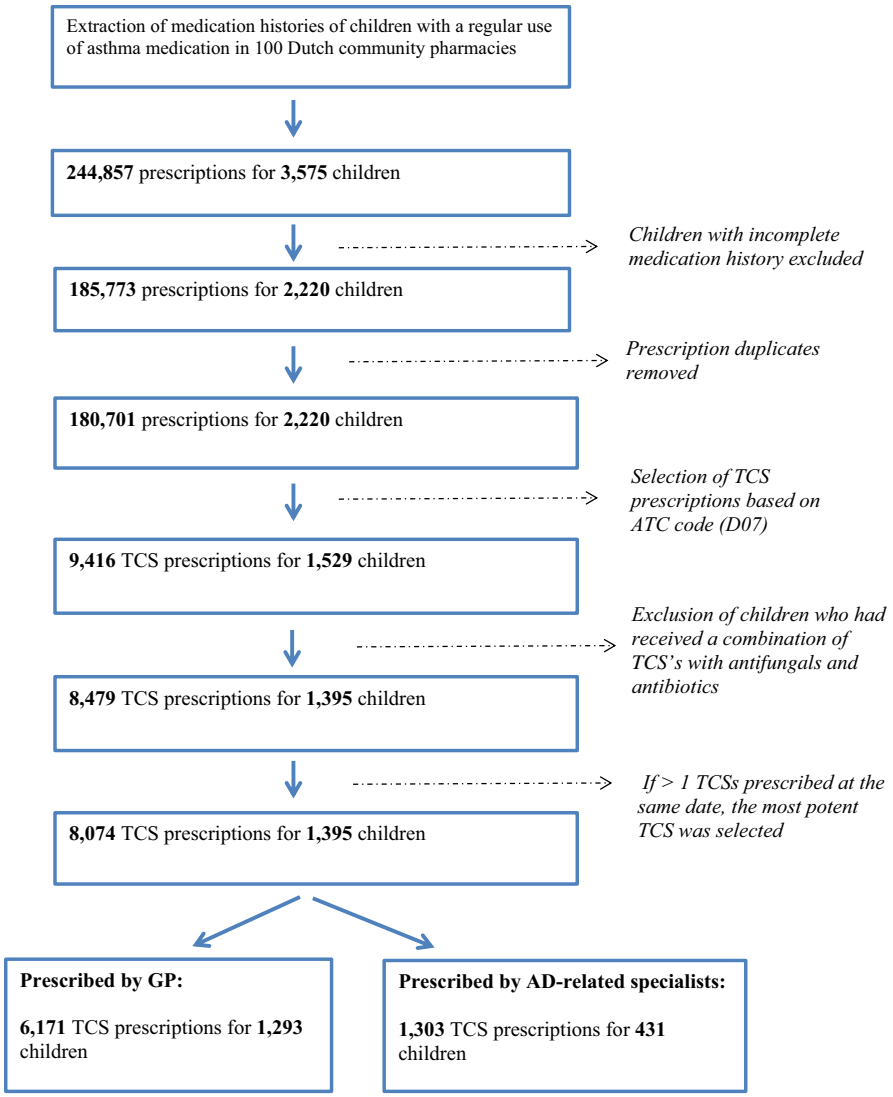

FIGURE 1 Flowchart of the data extraction. AD: Atopic Dermatitis, GP: General Practitioner, TCS: Topical Corticosteroids

TABLE 1 Study population characteristics: children with regular use of asthma medication and medication dispensing data available from the first year of life (N = 2220)

Characteristic	
Male, n (%)	1450 (65.3)
Age at time of data extraction, years, median (interquartile range)	8.3 (6.0-10.7)
Received ≥ 1 topical corticosteroid prescriptions, n (%)	1395 (62.8)
Weak (class A)	1084 (48.8)
Moderate (class B)	668 (30.1)
Potent (class C)	466 (21.0)
Very potent (class D)	56 (3.2)
Received ≥ 1 topical calcineurin inhibitor prescriptions, n (%)	23 (1.0)

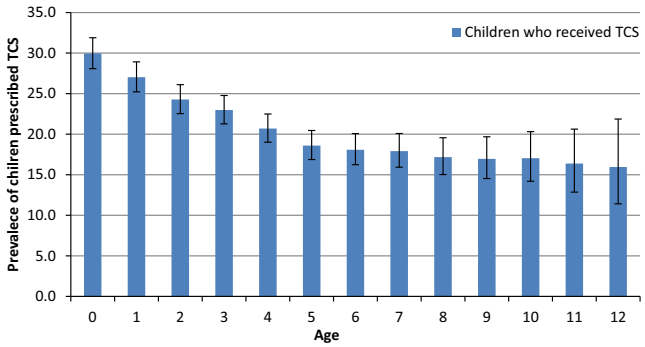

FIGURE 2 Prevalence of topical corticosteroid (TCS) prescriptions in children with regular use of asthma medication. The prevalence of TCS prescriptions in children with asthma was lower in older children. There was no significant difference in the amount of TCS prescriptions between boys and girls

of TCS prescriptions (in grams) stratified according to age category and year can be found in Table S2. Thirty percent of the infants received a TCS prescription, compared with 15%-18% of the children aged 4 and older (Figure S1). Infants were prescribed a mean of 2.2 TCS prescriptions per year, whereas children aged 4 and older were prescribed a mean 1.6-1.9 prescriptions per year

TABLE 2 Topical corticosteroid (TCS) prescriptions according to age year

Age, y	Weak (class A) Mean (range)	Moderate, (class B)	Potent, (class C)	Very potent, (class D)	Total
0	1.76 (1-9)	1.64 (1-7)	1.73 (1-8)	1.20 (1-2)	2.20 (1-14)
1	1.60 (1-10)	1.97 (1-10)	1.95 (1-10)	1.80 (1-5)	2.19 (1-17)
2	1.46 (1-7)	1.91 (1-12)	2.04 (1-11)	1.25 (1-2)	2.13 (1-13)
3	1.42 (1-8)	1.79 (1-7)	2.16 (1-10)	1.07 (1-2)	1.96 (1-12)
4	1.37 (1-7)	1.66 (1-9)	2.03 (1-9)	1.33 (1-3)	1.88 (1-9)
5	1.35 (1-10)	1.52 (1-8)	2.07 (1-10)	1.36 (1-2)	1.86 (1-14)
6	1.29 (1-11)	1.55 (1-7)	2.04 (1-8)	1.00 (1-1)	1.82 (1-14)
7	1.33 (1-9)	1.59 (1-12)	2.30 (1-10)	1.11 (1-2)	1.88 (1-13)
8	1.29 (1-5)	1.52 (1-5)	2.02 (1-8)	1.25 (1-2)	1.77 (1-12)
9	1.22 (1-3)	1.69 (1-7)	2.04 (1-8)	1.38 (1-3)	1.86 (1-9)
10	1.42 (1-6)	1.68 (1-10)	1.95 (1-8)	1.60 (1-3)	2.00 (1-10)
11	1.13 (1-2)	1.65 (1-5)	1.56 (1-5)	1.00 (1-1)	1.67 (1-5)
12	1.25 (1-3)	1.70 (1-4)	1.22 (1-3)	–	1.59 (1-4)

Potency class (A-D) based on Anatomical Therapeutic Chemical code of the TCS in the pharmacy dispensing system.

(Table 2). Young children received a prescription for a weak TCS more often than older children. From age 5, weak, moderate, and potent TCSs were used to a similar degree (Figure S1). There were no statistically significant differences in TCS prescriptions between boys and girls.

3.3 | AD medication prescribers

TCS prescribed by only GPs, only AD-related specialists, or both are reported in Tables S3 and S4. In concordance with the clinical guidelines, we observed that AD-related specialists more often prescribed first prescriptions of potent and very potent TCSs than GPs (relative risk [RR] = 2.55, 95% confidence interval [CI] = 1.79-3.63). Nevertheless, GPs prescribed potent and very potent TCSs for some patients (Figure 3). For both groups of prescribers, AD-related specialists and GPs, weak TCSs were the most commonly prescribed first TCS (Figure 3). Combined potent and very potent TCSs accounted for less than 10% of all first TCS prescriptions by GPs and almost 30% for AD-related specialists (Figure 3). Statistically significant differences ($P < .01$) were found between frequency of different potencies of prescribed TCSs using generalized linear models. First TCS prescriptions stratified according to TCS potency and prescriber specialty are listed in Figure S2.

When we divided first potent or very potent prescriptions according to age group, a statistically significant difference in prescription behavior between AD-related specialists and GPs was found only for children younger than 3 (RR = 2.86, 95% CI = 1.84-4.45), with AD-related specialists prescribing more potent or very potent TCS for young children (Figure S3). The incidence rate for prescribing a potent or very potent TCS was 12.6 prescriptions per 100 person-years for AD-related specialists and 4.4 prescriptions per 100 person-years for GPs.

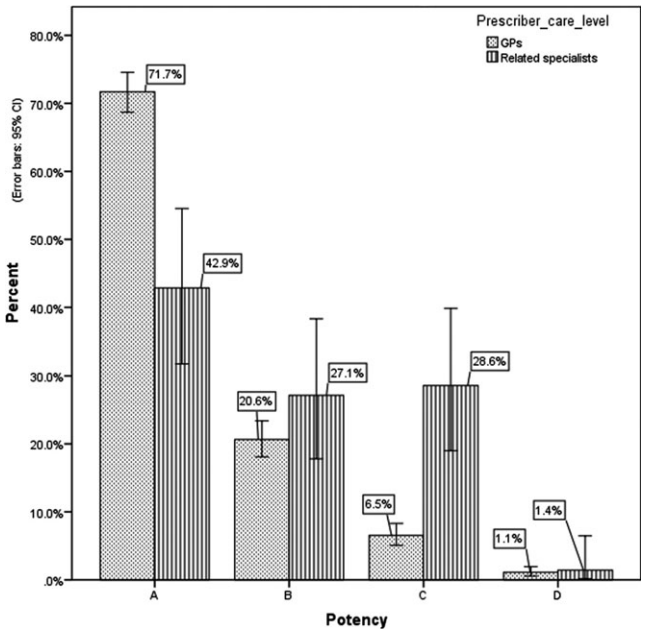

FIGURE 3 First TCS prescriptions stratified by TCS potency and prescriber. Prescribers have been classified into GPs and AD-related specialists (dermatologists, pediatricians, allergists, pulmonologists, and ophthalmologists). When focusing on the first TCS prescription a patient receives, GPs more often prescribe weak potency TCSs (class A), while AD-related specialists more often prescribe more-potent TCSs (class B-D).

4 | DISCUSSION

Atopic dermatitis and asthma often coexist. Children with AD have a high risk of developing asthma, but early asthma

symptoms, such as wheezing, may precede AD symptoms.[9] AD treatment with TCS is often required for months or years. This large pharmacy-based study provides insights into the number of TCS prescribed for AD in children with asthma symptoms and the TCS prescription behavior of GPs and AD-related specialists. We focused on TCS prescriptions, because TCS are considered to be the cornerstone of topical treatment of moderate to severe AD. Although it is unclear how many of these children had a physician diagnosis of AD, the number of children who received TCS (62.8%) was comparable with the patient-reported prevalence of AD (63.6%). Prospective cohort studies have shown that the disease often resolves when children get older.[9] This trend is also reflected in our study; children were prescribed fewer TCS as they became older. Previous studies have shown that AD is more prevalent in boys than girls,[10] but in our study the number of TCS prescriptions did not significantly differ between boys and girls.

Although younger children received TCS prescriptions more often, older children were generally treated with more potent TCS. In younger children, fear of corticosteroid use might play a bigger role.[11] Anxiety about the adverse effects of TCS use is common in TCS users[11] and might play a bigger role in parents of young children. Lack of knowledge of pharmacists or physicians regarding the safety and side effects of TCS use might also contribute to this anxiety and hesitation to prescribe more potent TCS.[12] Furthermore, older children often have more-persistent AD symptoms, which might also explain why they are more often treated with more potent TCS.

As expected, AD-related specialists prescribe potent TCS more often than GPs, although in some cases GPs prescribed potent TCS, even in children who, according to the pharmacy dispensing system, had not received a TCS prescription before. This is not in line with the Dutch GP guidelines.[6] The guidelines state that GPs should not prescribe very potent TCS if a specialist has not previously prescribed one, although we cannot exclude that patients received a previous potent TCS prescription outside their community pharmacy, for example in the hospital pharmacy.

Komura and colleagues showed in an economic assessment of prescriptions of AD drugs in children that mean drug costs per person with AD prescribed by dermatologists were significantly lower than the costs of drugs prescribed by pediatricians.[13] This supports our findings and suggests that patients with more severe AD should be referred to a dermatologist.

Some limitations of this study should be mentioned. We did not have data on physician diagnosis of AD. The presence or absence of a diagnosis could have influenced TCS prescription. It was not known either whether the TCS was prescribed for an indication other than AD.

This study has shown that younger children are more likely to be prescribed a TCS and that children aged 4 and older receive more prescriptions. There was a statistically significant difference in TCS prescribing patterns for infants, which is in accordance with the Dutch prescribing guidelines,[6] although contrary to the guidelines, GPs sometimes prefer to prescribe potent TCS without a prior prescription of the same potency by a specialist.

CONFLICT OF INTEREST

Jan A. M. Raaijmakers was a part-time professor at the Utrecht University, and he was Vice-president External Scientific Collaborations for GSK in Europe and had stock in GSK. Anke H. Maitland-van der Zee and Susanne J.H. Vijverberg have received an unrestricted grant from GSK in the past. The other coauthors report no conflict of interests.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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