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Corticosteroid prescription in children with respiratory symptoms: A real-life study

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Abstract
Asthma is one of the most common childhood diseases. Most children respond to low doses of corticosteroids and/or anti-leukotrienes. However, a small percentage remain symptomatic. They require high doses of inhaled corticosteroids (ICS) and anti-leukotrienes, sometimes with long-acting bronchodilators (LABA) and occasionally systemic corticosteroids (SC). However, we frequently observe that the only treatment they receive for exacerbations is short-acting beta-agonists (SABA) and oral corticosteroids (OC) without adding ICS as a maintenance treatment to prevent new episodes. This leads to frequent exacerbations, airflow limitation, and significant alterations in the quality of life. In addition, this results in high resource consumption, frequent emergency room visits, and school absenteeism, leading to absence from work for caregivers. A descriptive, retrospective, observational, and multicenter study was carried out on patients under 12 years of age, who attended pediatric allergy consultations for the first time. The main objective was to determine the consumption of SCs because of respiratory exacerbations in the year before the first consultation. Data were obtained from 144 children, 58.3% male, with a median age of 5 years. It was found that during the year before

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attending our clinic, 70% had perennial symptoms and were only prescribed with salbutamol on demand when they presented with respiratory symptoms. They had not been prescribed with ICS or anti-leukotrienes. They required attention in the emergency room of their nearest health center or hospital on an average of three times per year. During these exacerbations, almost 75% received SCs(prednisolone), with an average of 2.6 annual cycles (0–12) prescribed in more than half of the cases in the emergency room. In over 80% of the cases, the effects of SC abuse were not previously monitored. The overuse of SC in atopic children with respiratory symptoms was confirmed in our group, which requires considering behavioral changes.

Introduction

Asthma in children is one of the most common chronic respiratory diseases worldwide. It affects approximately 334 million people of all ages[1], causing 250,000 premature deaths related to the disease per year.[2] In Spain, it affects approximately 5% of adults and 10% of the pediatric population. Asthma is one of the chronic diseases with the greatest impact on the quality of life of children[3-5], and its prevalence is increasing. Currently, there are no significant geographical variations in the prevalence of asthma in Spain. However, certain regions show higher rates consistently, with boys being predominantly affected during school age and girls during adolescence, as demonstrated by the ISAAC study.[4-7]

While most patients achieve control of symptoms with low doses of inhaled corticosteroids (ICS) and/or leukotriene receptor antagonists (GINA steps 1 and 2), a subset of patient's experiences persistent severe symptoms.[8,9] The AIRE (Asthma Insight and Reality in Europe) study demonstrated poor asthma control in children in Western Europe. Only 5.3% of the general population achieved the GINA goals.[9] They required higher doses of ICS, often combined with long-acting beta-agonists (LABA) or additional treatments such as leukotriene receptor antagonists or, in some cases, systemic corticosteroids (CS). In such cases, asthma control and treatment strategies must be closely monitored during each consultation.[10-15]

In clinical practice, however, we frequently observe an overuse of short-acting beta-agonists (SABA) and SCs as the only treatment during exacerbations without subsequently prescribing a maintenance ICS. This approach is linked to frequent exacerbations and poor quality of life for both themselves and their families. These patients instead reported an excessive utilization of healthcare resources, including frequent emergency room visits and school absenteeism. These factors also lead to absence from work among caregivers.[16-18]

Oral corticosteroids (OC) have long been used in asthma management for their anti-inflammatory properties. However, they are now reserved for step 5 of the GINA guidelines because of their potential for significant adverse effects, such as adrenal insufficiency, weight gain, psychological impacts (e.g., depression and anxiety), cataracts, cardiovascular issues, fractures, or increased susceptibility to infections.[19-21]

Despite these risks, protocols for monitoring these adverse effects are rarely implemented in routine clinical practice. There are few published studies on the abuse of OCs in children during episodes of respiratory exacerbations. Such data are crucial for understanding current trends and optimizing the management of childhood asthma.

Therefore, our main objective was to determine the consumption of SCs because of respiratory exacerbations in the year before the first consultation.

Material and Methods

In our study, carried out according to real-life clinical practice and distributed throughout much of Spain, we conducted an observational, retrospective, and descriptive study. The Asthma Committee of the Society of Allergology and Clinical Immunology (SEAIC) also collaborated in the study. Data were collected from the medical records of all patients who attended the pediatric allergy clinics for the first time, and parents were given a questionnaire about medical data that collected data on the happening in the child's life in the previous year. The selected patients were aged up to 12 years. Data collection was done from March 2023 to February 2024. The patients came with respiratory symptoms (wheezing, cough, or dyspnea) or a diagnosis of asthma. The diagnosis was made according to current guidelines based on clinical history and a bronchodilator test after spirometry.[4] This could only be determined in selected children over 5 years of age. They came to our clinics for the first time, and we wanted to collect data from the year before coming to the clinics (number of exacerbations, drug use, and number of visits to the emergency room or their pediatrician at the health center).

They were subsequently prescribed an appropriate treatment and were reviewed after 1 month to assess their progress, but that was not part of our study.

Patients were included in this study by allergists and pediatricians from Spanish hospitals (eight public and private hospitals throughout Spain). Data were collected at the first visit to the clinic.

Study population

We collected, in collaboration with the patients, sociodemographic data, personal medical history; breastfeeding; type of delivery; exposure to tobacco; comorbidities like nasosinusal polyposis, urticaria, angioedema, eosinophilic

esophagitis, or drug allergy; date of asthma onset; and bronchiolitis during the first year of life. We also registered clinical and biological data during the last 12 months (symptoms, exacerbations, body mass index, sensitivity to allergens, peripheral blood eosinophilia, total IgE levels, the blood cortisol level, measurement of exhaled nitric oxide (FeNO), and spirometry test plus bronchodilator test which had been performed in children >5 years old). Normal levels of FeNo are 5–15 ppb. We tried to record whether blood cortisol levels had been determined in the previous year. We also sought to find out whether the possible adverse effects that multiple OC regimens can produce, such as weight gain, diabetes, high blood pressure, skin disorders, etc., were taken into account. Regarding the respiratory symptoms for which the patient comes to our clinic, we recorded all the medication received in the year before the visit. We recorded both during exacerbations and maintenance treatment. The use of ICS or OCS, bronchodilators, and anti-leukotrienes was noted, as well as the doses, the duration, and who had prescribed that treatment. We also considered whether the parents had administered it without a prescription.

Data collection and statistics

The methodology for collecting data for the study was a questionnaire that the parents filled out on the first day of the consultation. This questionnaire is shown in the documentation attached to the article. It includes demographic data, personal and family history of the patient, as well as clinical data and treatments received from the previous year until the time of consultation. In addition, data were taken from the patient's clinical history or from the patient's digital records. The variables were collected in a computerized database designed for this project. This database will not store personal data, as they will be coded in the data collection process from the clinical history. Each patient was coded according to a code given the numerical assignment to each center participating in the study with a consecutive patient number.

Independent quantitative and qualitative variables were studied. Statistical analyses were performed using IBM SPSS version 29 software. Descriptive statistics were used, using tables, representing the absolute and relative values of the qualitative variables, as well as measures of central tendency and variability for the quantitative variables.

The assumption of normality of the quantitative variables was verified using the Shapiro–Wilk or Kolmogorov–Smirnov test. We compared the groups using Pearson's x^2 test or Fisher's exact test, when necessary, for qualitative variables.

Statistical significance was considered significant if the p-value <0.05.

Ethical consent has been developed in accordance with the ethical principles of the Declaration of Helsinki with the standards of Good Clinical Practice and the legal regulations in force during its duration. The privacy and custody of the data obtained during the study is guaranteed, in accordance with Organic Law 3/2018 of the personal data protection and the Guarantee of Digital Rights.

All parents and children aged more than 12 years signed the informed consent. The study was approved by the corresponding ethics committees.

Results

A total of 144 patients were enrolled, with 58.3% boys and 41.7% girls. The mean age was 5.86 years. Concerning atopic manifestations, 52.2% of the patients had symptoms of rhino conjunctivitis, 49.6% had atopic dermatitis, and 18% had food allergy. Almost all the patients (99%) had no other comorbidities.

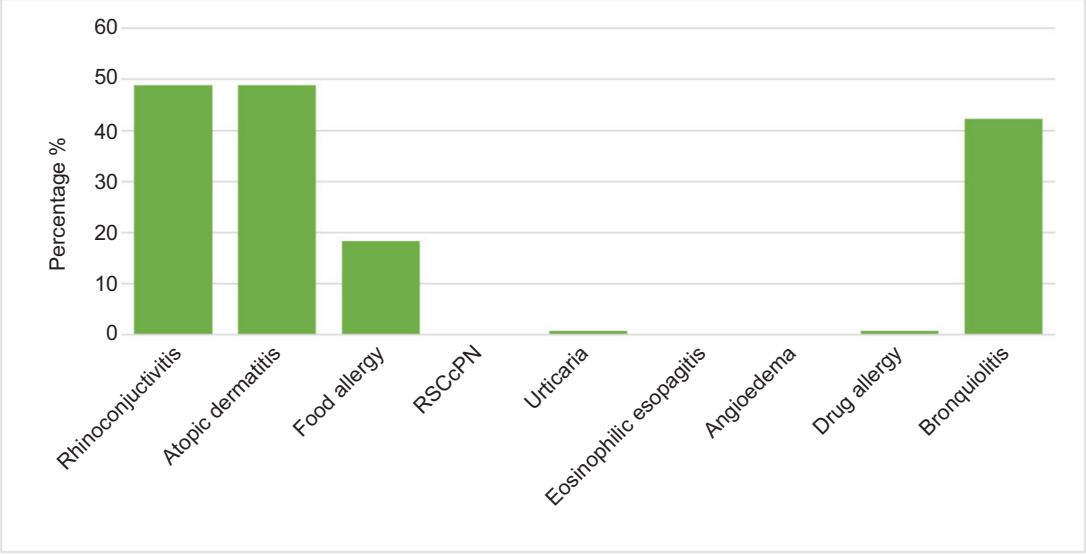

Figure 1 Comorbidities.

Most of them (70%) had a family history of atopy, reported in one parent (39.4% in father, 28.7% in the mother), 20.2% in both parents, and 7.4% in one sibling.

The BMI was 16. Most of them (66%) were exclusively breastfed; 18.8% had formula milk and the rest had mixed feeding. Regarding the family structure, 35% had no siblings, 0.6% had one sibling, and 19.4% had two or more siblings. They were exposed to tobacco reported in 19% and to pets in 31.9%.

Regarding medical history, 43% of the children had bronchiolitis during their first year of life and 11% had been diagnosed with respiratory syncytial virus infection. If we focus on respiratory symptoms, most of the included children's patients (73%) had perennial symptoms. Regarding the causal allergen, 6.3% were allergic to fungi, 17.4% to mites, and 20% to epithelia. About half of them (45%) reported seasonal symptoms and were allergic to the grass pollen.

With regard to the biological findings, the mean peripheral blood eosinophil count was 522 eosinophils/microliter and the median of total IgE was 328 kU/L.

Concerning spirometric findings, pulmonary function data were obtained in 39% of the cases because of the young age of most of the patients. They did not know how to perform spirometry correctly.

The mean FEV1 data obtained were normal in all patients who were able to complete spirometry. FeNO was only determined in 18% of cases (mean 23.44). Basal cortisol and vitamin D were determined in very few cases, only in 3.5% (mean 16,48 mcg/dL) and 2.8%, respectively.

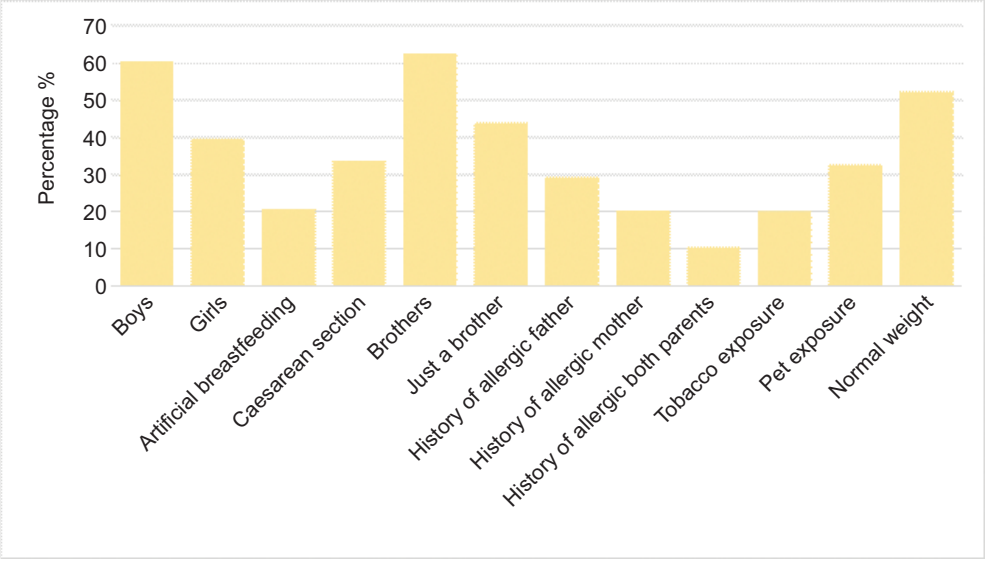

Figure 2 Demographic characteristics, personal history, and family history.

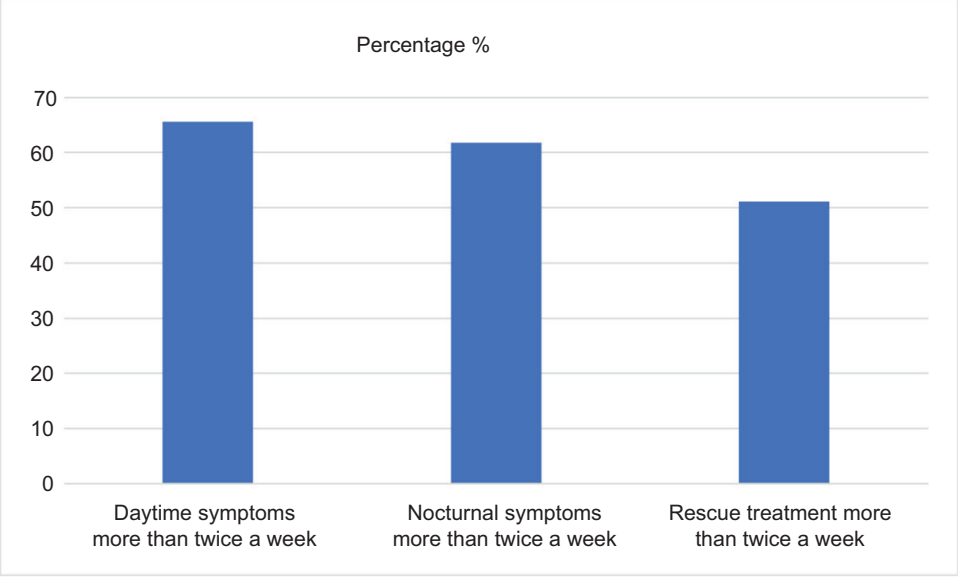

Figure 3 Symptoms and rescue treatment by week.

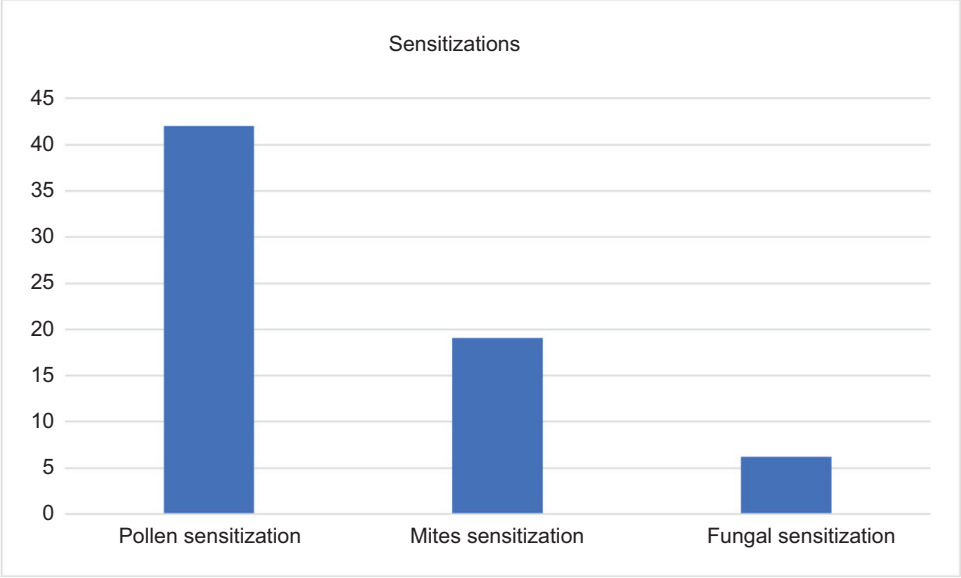

Figure 4 Sensitizations.

Table 1 Daily treatment for asthma when patients arrived at the allergy clinic.

Treatment in the previous year	
Salbutamol only	68%
Inhaled corticosteroids (IC)	31.1%
Anti-leukotriens	8.4%
IC+LABA	8.3%
Tiotropium	4.2%

The monitoring of side effects of SCs was carried out in 12.5% of the total sample. Concerning asthma daily treatment for when they arrived at the allergy clinic, we can see in Table 1. No patient had biological therapy when they arrived at the clinic.

Of all patients, 74.3% had received OCs during asthma exacerbations in the previous year. Oral methylprednisolone was the corticosteroid used in 72.9% of cases. The average number of cycles received during the asthma exacerbations in the previous year was 2.57. They were prescribed from the emergency room in 58,9% of cases. The average number of visits to the emergency room per year was 3.19 (0-15) times with a hospital admission in 15.3%.

After the assessment in our clinics, the previous treatment was modified in 64.6% of patients. The ICS were prescribed in 61.8% of cases (budesonide in 70% of cases). Anti-leukotrienes were also added in 23% and tiotropium in 2%.

In Spain, the biological drugs approved according to the Gema guideline for severe asthma are Omalizumab, Mepolizumab and Dupilumab (4). Only one patient was started on biological treatment after coming to our clinics.

No statistical significance was found in the relationship between patients who received OCs during asthma exacerbations. No correlation was found between the onset of asthma and breastfeeding, history of allergy, tobacco exposure, or obesity. We have also found no relationship between asthmatic patients and their history, such as the type of delivery they had (vaginal or cesarean), the type of breastfeeding (breastfeeding or bottle feeding), the total number of siblings they had, or the position they occupied among them. In our series, the majority of patients (80.6%) who had no exposure to pets in childhood had not received SCs. And, 36.2% of those who had exposure to pets received OCS (p:0.046). Only 13.1% of children with dust mite allergy received OCS (p:0.023).

Discussion

ICS are the first line of treatment. In children over 3 years of age, the efficacy of daily corticosteroids is sufficiently proven, with improvement in clinical, functional, and bronchial inflammation parameters, with a better quality of life, and a reduction in the risk of exacerbations and hospitalizations.[4]

Short courses of OCS are indicated only for the treatment of children with asthma in severe-moderate exacerbations, and maybe it should be considered in mild exacerbations with insufficient response to bronchodilators or if the child has a history of severe crisis.[19] In the case of preschool children with acute episodes of wheezing, they would only be indicated in severe crisis, as their use is questioned in mild or moderate crises caused by viruses.[22]

On the other hand, the adverse effects that SC can cause in children are well known, even at low doses, so their use should be optimized.[20, 21] The use of frequent cycles of oral or injected corticosteroids is the most common cause of adrenal suppression in the pediatric population, and the risk of acute adrenal insufficiency is the most serious potential adverse effect. The World Allergy Organization issued a call for attention regarding the optimization of CS use in patients with asthma and the consideration of alternative therapies when possible. SCS are a highly effective

treatment for acute exacerbations and long-term symptom control in asthma. Primary prevention of exacerbations and improvement of asthma control is a key first step in achieving SCS stewardship, by optimizing maintenance asthma medications and addressing modifiable risk factors, such as adherence and inhaler technique.[21]

In our study, conducted according to real-life clinical practice across a large part of Spain, it is noteworthy that the average age of the children was 5.86 years and that 75% had received OCS during exacerbations in the previous year with an average of 2.6 short courses of OCs per year, prescribed in more than half of the cases by emergency services.

We had been observing an overuse with cycles of oral or injected corticosteroid treatment during exacerbations in pediatric patients who came to our clinics, and we aimed to demonstrate this, as we have done, to raise awareness of current clinical practices. In fact, 68% of the children who came to our clinics for the first time had received treatment with salbutamol on demand in the previous year exclusively, and only 31.1% were taking ICS as maintenance treatment. In addition, 8.4% were on anti-leukotrienes, and 8.3% were on ICS combined with LABA. The cortisol test is used to diagnose or rule out medical conditions that cause too much or too little cortisol, such as Cushing's syndrome, Addison's disease, or secondary adrenal insufficiency. It is not routinely performed. It is performed only when one of these conditions is suspected. In our sample, despite the fact that patients received frequent courses of SCs, blood cortisol was only determined in 3.5%. Monitoring for the possible side effects of SCs, as discussed above, was carried out in only 12.5% of the total sample.

There is ongoing concern about the long-term use of ICS in children. Systematic reviews have found no greater benefit from OCs than ICS in children with asthma exacerbations. Comparisons are made in terms of rates of hospital admission, unscheduled visits for asthma, and the need for an additional course of SCs.[20]

Furthermore, the benefits of ICS, prescribed and used correctly, outweigh their possible adverse effects.

Asthma remains the most common chronic disease in childhood. Most clinical guidelines refer to children with asthma in the following age categories: 2–5 years (preschool), 5–12 years, 12–18 (adolescents; usually regarded as adults for management). The most effective maintenance therapies reduce the inflammation in the airways by using ICS (topical. Inhaled long-acting beta-agonists (LABAs) added in combination with ICS are now frequently used as preventer therapy, and this combination is effective in controlling more severe asthma. For such patients, new biologic agents (namely, monoclonal antibodies to various inflammatory pathways such as IgE and Interleukins including anti-iL5 and Il4/IL13) have proven efficacy in reducing asthma exacerbation rates.[23-25]

We believe that just as there are concerns regarding the overuse of SCs in adult asthmatic patients, similar warnings should be established for pediatric patients. Protocols for the management of adverse effects in this group should also be proposed.

In making a final analysis of our study, we should highlight positive and negative points. The abuse of short courses of OCs without maintaining a continuous treatment with ICS to avoid possible relapses has been confirmed in our group. As a positive point, we should highlight the need to establish a starting point to know what the real clinical practices and, in accordance with the recommendations of the WAO. We should look for possible strategies to optimize the use of OCs for the repeated exacerbations suffered by some asthmatic children.

Conclusions

In our study, we detected an excessive use of OCs in children with asthma and inadequate maintenance treatment in most patients. We believe it is necessary to establish guidelines for the use of OCs during asthma exacerbations.[26] We should propose subsequent maintenance treatment with ICS or anti-leukotrienes to prevent new relapses.

In addition, in children who receive frequent cycles of SCs, close monitoring for possible adverse effects would be essential.

Disclosure

This work has been approved for oral poster defense at the next SEAIC national congress.

Authors Contributions

All authors contributed equally to this article.

Conflicts of Interest

None.

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