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Article

Most Children Who Receive Oral Glucocorticoids in Outpatient Care Do Not Deserve It

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Abstract: Background and objectives: Glucocorticoid bursts have been used for various paediatric conditions without concern until it was recently reported that they are associated with potential subsequent harm. Thus, our aim was to explore the prescribing indications of glucocorticoid short courses in paediatric ambulatory care on an island in Southeast Spain. **Methods:** A retrospective analysis of short-term glucocorticoid prescription was conducted in a health area of 27,000 people. All children aged seven and twelve who attended the paediatric clinic during their well-child visits between Spring and Fall 2022 were recruited. In parallel, data on the attending physicians and on the episodes that led to glucocorticoid prescriptions was taken from case notes. According to current guidelines and meta-analyses, the resulting prescriptions were classified as appropriate or inappropriate indications. **Results:** Each child received, on average, five and a half days of oral glucocorticoids in roughly eleven years of life. Forty-five (47.3%) of the 95 children received at least one glucocorticoid burst, with a range of 1- 10 bursts per child. Children with diseases of the respiratory system were the most frequent targets of short-term glucocorticoid use. The indication of glucocorticoids was deemed inappropriate for 60% of all prescriptions. Physicians in out-of-hours settings may exhibit a higher likelihood of prescribing glucocorticoid bursts ($P=0.056$). **Conclusion:** The inappropriate prescription of glucocorticoids to children in our community is a common finding. In this regard, continuing professional training seems essential to ensure that most of the prescriptions for these drugs will reflect appropriate indications in the future.

Keywords: primary care physicians; out of hours medical care; inappropriate prescription; wheezing; steroids.

1. Introduction

Since short-term use of oral glucocorticoids (GC) (defined as courses for ≤ 14 days) was considered safe, its prevalence has rarely been measured. However, there is mounting evidence of its detrimental impact. Seminal research reported in 2017 that within 30 days of initiating GC bursts, the risk for fracture, thromboembolism, or sepsis was doubled, tripled, or increased by a factor of five, respectively [1]. Subsequently, these findings have been confirmed in systematic reviews [2]. To conclude, descriptive research on over one million children who were prescribed GC bursts has proved truly alarming in concluding that this treatment increases the risk of pneumonia or sepsis by about 100% within one month of starting the therapy at issue [3].

Hence, our first objective was to explore whether there is an unnecessary prescription of GC bursts to outpatient children in our area, and our secondary objective was to explore variations of GC bursts dispensing linked to physicians' settings.

2. Materials and Methods

Design and setting. This is a retrospective cohort study to evaluate GC outpatient prescriptions for children. It is a secondary analysis of a pilot research study on paediatric heart rhythm disturbances between Spring and Fall 2022 [4] undertaken at La Vileta General Practice, Mallorca. La Vileta includes ambulatory clinics and emergency care for 27,000 people, of whom 4,500 are children under 15. We recruited all children aged seven and twelve who attended three paediatric clinics of our medical centre during the follow-up that is scheduled for every healthy child. Only children under prescriptions for long-term GC treatment were excluded from this study.

Data Collection

We extracted details on oral glucocorticoids (dexamethasone, methylprednisolone, prednisolone, and hydrocortisone) and inhaled salbutamol treatment of these children from birth to their well-child visits at the age of 7 or 12 from the local admission dataset. Ambulatory by-appointment and out-of-hours (OOH) prescriptions of inhaled salbutamol in this sample were taken as a proxy of these two types of consultations in our study, given that 98% of ten-year-old European children have received inhaled salbutamol at some point [6]. Majorcan proportion of out-of-hospital by-appointment and OOH medical care was taken from the local public health care register [5] to confirm the previous estimation based on salbutamol prescriptions.

Definitions

Wheeze is a sign of bronchiolitis, bronchitis, and asthma that indicates airflow limitation. There is no agreed-upon definition of wheeze. This paper accepts wheeze as a high-pitched intrathoracic sound heard and recorded by a health care professional [7]. In addition, we have classified wheezing episodes as mild when they meet the requirement of rapid symptom relief, according to a proposal by the updated 2024 GINA Report [8] for a commonly used definition with obvious clinical utility in primary care.

Statistical Analysis. *We used convenience sampling of subjects* who participated in the original research, which enabled this secondary analysis of previous data. We analysed the data using R Version 4.3.3. The chi-square test was used for dichotomous variables, and the t-test was used for continuous variables.

Ethics

The Balearic Institutional Review Board approved the study's protocol for Health and Medical Research (ECIAP-2023), and the parents of all children were required to give formal written consent.

3. Results

We recruited 95 children, who received, on average, five and a half days of GC in roughly eleven years of life. In total, the children of our sample have received 102 GC prescriptions, 12 for rash (12 children), 45 for croup (16 children), 59 for wheezing (20 children), and 7 for upper airway infection. Sometimes there was overlapping of diagnoses, a few prescriptions were due to the child having more than one of these diagnoses at the same time. Forty-five children (47.3%) received at least one GC burst. We found no significant differences in baseline or somatometric characteristics between ever and never-GC-prescribed children (Table 1). Among GC users, the median number of days per short course was 3, and the range of short courses was 1-10 (Table 2).

Table 1. Demographic and somatometric data by glucocorticoid prescription. Data are mean (SD) unless otherwise specified.

VARIABLE	No prescribed oral glucocorticoids	Prescribed oral glucocorticoids	P value
Number	50	45	
Age (years)	11.18 (3.00)	11.00 (3.03)	NS
Girls/boys	22/28	25/20	NS
Weight percentile	51.80 (28.09)	58.25 (26.67)	NS
Height percentile	63.76 (27.07)	65.10 (24.54)	NS
BMI percentile	46.24 (27.73)	49.47 (27.01)	NS

ABBREVIATIONS: BMI, body mass index; NS, non significant.

Table 2. Oral glucocorticoids prescription (days and short courses) to 95 children of our sample. Data are mean (SD) unless otherwise specified.

Illness	Days of oral glucocorticoids	Short courses of oral glucocorticoids
Wheezing	2.14 (5.68)	0.66 (1.86)
Croup	2.28 (9.76)	0.52 (1.50)
Rash	0.82 (2.41)	0.15 (0.39)
Total	5.55 (1.50)	1.51 (2.63)

The most common indication for GC bursts was wheezing, followed by croup, and rash. Five out of twenty children on short courses of GC had moderate or severe wheezing; only one of them was of school age. Most children prescribed GC for skin conditions had an insect bite or dermatitis (42% and 33%, respectively), and the remaining 25% were equally divided between urticaria, cellulitis, and miliaria (Table 3).

Table 3. Oral glucocorticoid use for acute cutaneous disease. Data are mean (SD) unless otherwise specified.

gender	Age (years)	season	diagnosis	prescribing physician's specialty
girl	2	spring	Atopic dermatitis	Primary care Paediatrician
girl	10	summer	Atopic dermatitis	Primary care Paediatrician
boy	1	winter	Atopic dermatitis	Emergency physician
girl	11	winter	Atopic dermatitis	Unknown
girl	7	spring	Urticaria	Emergency physician
boy	10	winter	Miliaria (sweat rash)	Primary care Paediatrician
boy	7	summer	Insect bite	Primary care Paediatrician
boy	3	winter	Insect bite	Primary care Paediatrician
girl	2	winter	Insect bite	Primary care Paediatrician
boy	3	spring	Insect bite	Unknown
boy	6	summer	Scarlet fever	Emergency physician
boy	6	winter	Cellulitis (dermis infection)	Primary care Paediatrician

A reasonable estimate of paediatric treatments prescribed by OOH services in our area has been derived from figures of the population at large (children and adults): primary care consultations by appointment account for 85.4%, and OOH consultations account for 14.6% of the ambulatory health care burden [6]. The 17.4% proportion of paediatric salbutamol prescriptions by OOH services in our sample confirms this estimate [OR=0.962; 95%CI:0.615-1.503; P=0.862]. Conversely, our 22.4% of OOH GC prescriptions deviates from the overall proportion of OOH consultations, and shows a trend toward a higher prescription of GC during OOH visits compared to scheduled primary care visits [OR=0.638; 95%CI:0.401-1.016; P=0.056] (Table 4).

Table 4. Comparison between nominal figures of medical care and actual salbutamol or oral glucocorticoids orders by outpatients’ setting.

	Primary care	Out-of-hours
Salbutamol paediatric prescriptions	119 (84%)	23 (16%)
Annual medical consultations <i>versus</i> salbutamol paediatric prescriptions	P=0.862	
Ambulatory annual medical consultations ¹	5,922,161 (85.4%)	1,101,542 (14.6%)
Annual medical consultations <i>versus</i> oral glucocorticoids paediatric prescriptions	P=0.056	
Oral glucocorticoids paediatric prescriptions	79 (77%)	23 (23%)

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4. Discussion

Among our prescription of GC over time and space have been described. There is an annual rise in GC use, with a 30% increase in the UK over two decades and a 14% increase in France over one decade [9]. GC prescription rates vary from region to region from 0.5%-21% [10]. Until aged eleven, 11% of Swedish children [11] and 26% of Dutch children have been prescribed GC [6], which is less than our findings. Besides that, our prevalence is lower than 13% or 24% 1-year prevalence of GC use among Italian or French children, respectively [12,13].

Wheezing

Twenty children in our sample were prescribed GC bursts to treat wheezing, and most of them received repeated GC prescriptions. These findings align with previous reports of 15%-50% of children receiving more than one GC prescription [6]. The use of GC, given for decades to treat wheezy toddlers, was based on an extrapolation from studies conducted in asthmatic older children and adolescents who responded to this class of drugs. It is worth emphasizing that the response to GC differs depending on the different phenotypes of wheezing in childhood; in preschool wheezers, airway inflammation is mostly due to a neutrophilic response to viral triggers, while school-age children more frequently present with eosinophilic, highly steroid-responsive airway infiltration A meta-analysis on the role of GC in toddlers with wheezing exacerbations [14] found no difference between GC and placebo regarding unscheduled visits, and that outpatient toddlers treated with GC had a higher hospitalization rate. Accordingly, current guidelines remind us of the strong evidence against GC bursts in preschool children with acute wheezing [15]. For schoolchildren, guidelines state that although clear evidence is lacking to support GC use for those with mild exacerbations, closely monitored GC should be a part of the initial treatment in case of moderate to severe asthma [16]. Just one of the GC prescriptions in our sample was indicated for a school-aged child with a moderate wheezing crisis.

Croup

Sixteen (17%) of 95 children in our cohort received at least one GC burst to treat croup. The 2023 Cochrane systematic review on this topic concluded that it reduces croup symptoms, length of hospital stays, and the rate of return consultations [17]

Rash

Eleven children in this study were treated with GC for skin conditions: 42% for insect bites, a third for dermatitis, and a quarter for cellulitis, urticaria, or miliaria (Table 3). Current guidelines recommend against GC in atopic dermatitis [18]. Whether GC are beneficial in acute urticaria is controversial [19]. There is strong evidence on the efficacy of concurrent systemic steroid use in

children with orbital cellulitis. We have not found references to support GC prescription against miliaria or insect bite inflammation.

To summarize, GC bursts did follow current guidelines in one wheezy child, in sixteen children with croup, and in one child with cellulitis, which totals 18 appropriate indications out of 45 participants (40%) that were prescribed GC. These findings deepen previous reports on the inappropriate use of GC in primary care, which may account for 63% of total prescriptions, especially by young physicians or patients under 15 [20].

Health Care Setting

The escalation of inappropriate GC prescriptions has been linked to multimorbidity, economic and geographical factors, or physicians' preferences. Parents who make appointments for acute conditions are usually seen within 24 hours in our health area. This is quite adequate when comparing OOH services with scheduled primary care. We have found one-third more GC prescriptions in OOH than in scheduled primary care consultations. While our results, at the $P=0.056$ level, do not reach statistical significance, they show a trend towards greater ease in prescribing GC by emergency physicians compared to paediatricians in primary care. The data presented in this study are limited to Southeast Spain and, therefore, cannot be considered representative of GC's short-term usage. Our conclusions may be limited by the sample size, and the fact that we investigated GC misuse indirectly through medical records prescriptions. The retrospective nature of this study does not permit causal inferences. Finally, accurate estimation of the dose and treatment duration is beyond the scope of our work.

5. Conclusions

It is unclear whether the ubiquitous use of GC, from neonatal to pubertal stages, can be attributed to the incidence of these medications' approved indications or to irrational outpatient drug use. There is a trend towards higher rates of GC prescriptions the further away from Northern Europe and the closer to Southern Europe. Most ever-GC-prescribed wheezy children in our study received repeated doses of GC, a red flag for poor bronchospasm control. This study's most extensive indications for prescribing GC do not conform to currently available recommendations and evidence. Emergency physicians are more likely to prescribe GC bursts than primary care physicians.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Balearic Islands Review Board (ECIAP-2023)

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study

Data availability statement: The data underlying this article will be shared on reasonable request to the corresponding author.

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Conflicts of Interest: The authors declare no conflicts of interest.

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