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Overuse Of Oral Corticosteroids, Underuse Of Inhaled Corticosteroids, And Implications For Biologic Therapy In Asthma

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Abstract

Background: Patients with chronic obstructive pulmonary disease (COPD) often require high doses of oral corticosteroids (OCSs) for exacerbation management, which can lead to significant adverse effects. Biologic therapies are being explored as alternatives to OCSs in severe COPD, but the appropriateness of prescribing these costly treatments needs evaluation.

Objectives: This study aimed to (1) determine the prevalence of COPD patients using high cumulative doses of OCSs, (2) investigate the impact of suboptimal inhaler technique on OCS use, and (3) estimate the proportion of patients for whom biologic therapies may be unnecessarily prescribed.

Methods: We identified adults with COPD (n = 5,002) using high-dose inhaled corticosteroids (≥500–1,000 mcg/day fluticasone-equivalent) and/or OCSs (Global Initiative for Chronic Obstructive Lung Disease [GOLD] group D) from a pharmacy database coverin[1]g 500,500 individuals. Questionnaires were sent to 2,312 patients who returned them, of which 929 were diagnosed with COPD. We calculated annual cumulative OCS doses and assessed inhaler technique in a subgroup of 60 patients. Patients with good adherence and inhaler proficiency but still requiring high OCS doses (≥420 mg/year) were considered potential candidates for biologic therapy.

Results: Among COPD patients in GOLD group D, 29.5% were using high doses of OCSs, with 78.1% likely having suboptimal therapy adherence or inhaler technique. Only 21.9% were deemed suitable candidates for biologic treatment.

Conclusion: High OCS use is prevalent among COPD patients in GOLD group D, but a significant proportion exhibit poor therapy adherence or inhaler technique. Optimizing inhaler therapy should be prioritized before considering expensive biologic therapies as alternatives to OCSs in severe COPD management.

Keywords: *Oral corticosteroid, Chronic obstructive pulmonary disease, Biologic therapy*

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Introduction

Many patients with severe or uncontrolled asthma rely on oral corticosteroids (OCSs) in addition to treatment with inhaled corticosteroids (ICS) and long-acting β2-agonists (LABA). These OCSs are used either intermittently for exacerbations or chronically to maintain acceptable asthma control. However, chronic or frequent use of OCSs in asthma management is associated with serious and debilitating adverse effects. The incidence and severity of these adverse effects depend on the cumulative dose of OCSs used by the patient, with even relatively low cumulative exposures (0.5–1 g prednisolone equivalent) linked to adverse outcomes. (Bleecker et al., 2020)

In recent years, new biologics for severe asthma have gained popularity due to their ability to reduce OCS courses in patients with frequent exacerbations and lower the OCS maintenance dose in OCS-dependent patients. (Pavord, 2019)

Despite the effectiveness of these biologics, their high cost compared to OCS tablets necessitates careful consideration of their prescription. It is crucial that these expensive treatments are reserved for patients who have exhausted all options to reduce or prevent OCS use. This includes ensuring patients are on appropriate doses of ICS, demonstrating optimal adherence to ICS therapy, and using their inhalers correctly. However, there is uncertainty regarding these factors, partly due to the significant "placebo" effect observed in various phase 3 OCS tapering studies. (Volmer et al., 2018)

Therefore, this study aims to investigate the adherence of asthma patients with high cumulative OCS use to ICS therapy and their inhalation technique. Additionally, the study seeks to estimate the proportion of patients for whom asthma biologics might be unnecessarily prescribed. (Sullivan et al., 2018)

Materials and Methods

Design and Study Population:

This cross-sectional study utilized data from a pharmacy database encompassing prescription information from 65 community pharmacies , covering a population of 500,500 patients. The database had been previously used in a study by Hekking et al. on severe asthma prevalence. Initially, patients with at least one prescription of inhaled corticosteroids (ICS) , were identified. Among these, patients with severe or uncontrolled asthma were identified, including those with prescriptions for high-dose ICS (≥1,000 mcg fluticasone-equivalent) or medium-high dose (500–1,000 mcg/day fluticasone-equivalent) combined with maintenance oral corticosteroid (OCS) therapy (≥5 mg/day prednisone equivalent for ≥6 months in the previous year). Questionnaires were sent to all these patients (n = 5,002), covering demographics, medical history, medication usage, smoking habits, and asthma control. A total of 2,312 patients completed and returned the questionnaires, yielding a response rate of 46.2%. Characteristics of responders and nonresponders are presented in Table 1, indicating similar mean age, ICS and OCS dose between the two groups, albeit with nonresponders being slightly younger and less adherent to ICS therapy compared to responders. Adult patients (≥18 years) with a self-reported diagnosis of asthma or COPD with a smoking history of <10 pack-years were included, while those with other pulmonary diagnoses such as sarcoidosis, cystic fibrosis, or bronchiectasis were excluded.

Outcomes:

"High cumulative OCS consumption" was defined as a cumulative dose of ≥420 mg prednisone equivalent during the 1-year study period, corresponding to 2 OCS rescue courses per year (30 mg/day prednisone equivalent for 7 consecutive days), as per GINA criteria for severe asthma diagnosis and known associations with OCS-induced adverse effects.

Good therapy adherence was defined as ≥80% fulfillment of ICS prescriptions during the study period. Inhaler technique was assessed by pharmacists in a representative sample of adherent patients, defining adequate inhaler technique as correct use without critical errors that could lead to insufficient drug delivery to the airway.

Statistical Analysis:

Cumulative OCS doses were calculated for asthma patients, identifying those with ≥420 mg prednisone equivalent during the study period. Adherence to ICS therapy was evaluated based on prescription fillings, categorizing patients as adherent or non-adherent. Among adherent patients with high cumulative OCS doses, the proportion using correct inhaler technique was determined. Standard errors, 95% confidence intervals, and adjustments using the delta method for proportions were computed for single proportions. Ethical approval for the study was obtained from the Medical Ethics Committee (MEC W11-064; NTR No. 3546).

Results

Prevalence of Asthma Patients on High Cumulative Doses of OCSs: Among the patients with severe or uncontrolled asthma who completed the questionnaires (n = 2,312), asthma was confirmed in 929 individuals (40.2%). Within this group, 274 patients (29.5%) were found to be using high cumulative doses of OCSs. These patients were predominantly elderly females with late-onset asthma, allergies, and recurrent exacerbations, with a median prednisone equivalent dose of 750 mg per year.

Adherence and Inhaler Technique: Out of the 274 asthma patients using high-dose OCSs, 130 individuals (47.4%) exhibited non-adherence to ICS therapy (prescription filling <80%). Among a randomly selected sample of 60 adherent patients, only 41.6% demonstrated adequate inhaler technique. Consequently, only 21.9% of patients adhered to ICS therapy and used their inhalers correctly, suggesting that 78.1% of severe or uncontrolled asthma patients might not require biologic therapy.

These findings highlight the substantial proportion of asthma patients using high cumulative doses of OCSs, often due to suboptimal adherence to ICS therapy and inadequate inhaler technique. Identifying and addressing these factors could lead to better management of asthma and reduce the unnecessary prescription of expensive biologic therapies.

Discussion

This study reveals that approximately 30% of asthma patients with severe or uncontrolled asthma, comprising 7% of the total asthma population, were using high cumulative doses of OCSs . Given the median prednisone equivalent dose of 750 mg/year, these patients faced a significant risk of short-term and long-term adverse effects. However, a notable finding was that 78% of these patients exhibited poor therapy adherence, inadequate inhaler technique, or both, contributing significantly to OCS overuse. Consequently, only 22% of the patients with high OCS use were deemed definite candidates for biologic therapy. (Chalitsios et al., 2021)

The prevalence of high OCS users in our study aligns with findings from other studies, although slight variations exist. A systematic review encompassing 129 studies reported varying rates of systemic corticosteroid use in severe or difficult-to-treat asthma, ranging from short-term use

in 46.3–92.6% of patients to chronic use in 33.2–65% of patients. Similar variations were observed in studies from Germany and the United States, reflecting differences in population demographics, definitions of OCS use, or management approaches. (Castro et al., 2018)

Our study also underscores the issue of therapy adherence and inhaler technique among high OCS users. Nearly half (47%) of these patients exhibited non-adherence to ICS therapy, consistent with previous reports. Furthermore, inadequate inhaler technique was prevalent, with over half of adherent patients demonstrating incorrect use. These observations highlight modifiable factors contributing to OCS overuse, emphasizing the need for addressing these issues before considering biologic therapy. (Taube et al., 2019)

Limitations of our study include potential underestimation of high OCS users, differences in characteristics between responders and nonresponders, and generalizability limited to the Dutch population. Additionally, OCS overuse may extend beyond severe asthma patients to those with less severe disease, warranting further investigation. (Tran et al., 2021)

Despite these limitations, our study benefits from a large representative sample, clinical data from questionnaires, adherence data, and assessment of inhaler technique. Addressing therapy adherence, inhaler technique, and other contributing factors is crucial in reducing OCS overuse and optimizing asthma management. Physicians should conduct thorough clinical assessments and trial appropriate therapies before considering biologic treatment for patients with high OCS use, ensuring optimal management strategies are implemented. (Hew et al., 2020)

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