Original Article

Burden of Chronic Oral Corticosteroid Use by Adults with Persistent Asthma

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What is already known about this topic? Chronic oral corticosteroid (C-OCS) use in asthma is an indicator of disease severity, but factors associated with C-OCS use in adults with persistent asthma need to be identified.

What does this article add to our knowledge? Patients with asthma requiring C-OCS use have significant disease burden, comorbidities, and elevated blood eosinophil counts. Prior C-OCS use was the strongest independent predictor of future C-OCS use.

How does this study impact current management guidelines? Population care management programs need to identify C-OCS users to institute more intensive patient management and treatment.

BACKGROUND: Chronic oral corticosteroid (C-OCS) use in asthma is an indicator of disease severity, but its risk factors are largely unknown.

OBJECTIVE: To describe patient characteristics and disease burden associated with C-OCS use by adults with persistent asthma.

METHODS: We identified 9546 patients aged 18 to 64 years in a large managed care organization who met the Healthcare Effectiveness Data and Information Set 2-year criteria (2009-2010) for persistent asthma. A subgroup had blood eosinophil counts. We calculated cumulative OCS dispensed per patient in 2010 and examined the distribution of disease characteristics by average daily amounts of OCS dispensed. C-OCS use was defined as 2.5 mg/d or more. Baseline factors (2010) associated with C-OCS use during follow-up (2011) were investigated by multivariable Poisson regression.

RESULTS: At baseline, 782 (8.2%) patients were C-OCS users. Compared with patients who received no or less than 2.5 mg/d OCS, C-OCS users were older and more often female and ethnic minorities; and had more comorbidities, asthma specialist care, greater step-care level, controllers, asthma exacerbations, and greater blood eosinophil counts (all $P < .01$). Baseline factors significantly associated with C-OCS use in the follow-up year included (1) demographic characteristics: older age, females, blacks versus whites, and whites versus others/unknown ethnicities; (2) disease burden: more asthma emergency department or hospitalization visits, greater step-care level, excessive short-acting β_2-agonist dispensed, theophylline use, asthma specialist care, and nasal polyposis; (3) greater blood eosinophil counts; and (4) most strongly, C-OCS use.

CONCLUSIONS: C-OCS use was associated with more asthma burden, comorbidities, and greater blood eosinophil counts. Prior C-OCS use was the strongest predictor of future C-OCS use. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;■:■-■)

Key words: *Administrative data; Corticosteroid; Comorbidities; Allergist; Asthma specialist; Asthma control; Blood eosinophil count; Chronic oral corticosteroid use; Controller medication; Exacerbations; Asthma guidelines; Managed care; Persistent asthma; Short-acting β_2-agonists*

Refractory, uncontrolled asthma is estimated to account for less than 5% of all cases of asthma.[1] We have reported a prevalence of severe uncontrolled asthma of 2.4%, defined by 2 or more asthma exacerbations and high controller medication dispensing in a managed care organization.[2] Moreover, patients with severe asthma use more oral corticosteroid (OCS) for their asthma treatment.[2,3] However, patients with frequent or chronic oral corticosteroid (C-OCS) exposure may be refractory to

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Abbreviations used
C-OCS- Chronic oral corticosteroid
ED- Emergency department
GINA- Global Initiative for Asthma
HEDIS- Healthcare Effectiveness Data and Information Set
ICS- Inhaled corticosteroid
OCS- Oral corticosteroid
RR- Risk ratio
SABA- Short-acting β_2-agonist

standard asthma treatments or adhere poorly to present therapy regimens. Regardless of reason, patients requiring high OCS use may be at increased risks for severe exacerbations, as well as increased morbidity and mortality.[3,4] A longitudinal study of patients with asthma at least 12 years of age from a US Medicaid registry who received at least 5 mg of prednisone equivalent per day for 6 months reported a significant exposure-response relationship between C-OCS use and risk of future asthma exacerbations, OCS-associated adverse effects, and cost of care.[4] A confirmatory cross-sectional observational study in the United Kingdom noted that OCS-related adverse effects, including diabetes, osteoporosis, gastric ulcer disease, and cataracts, were more common in severe than in mild to moderate asthma.[3]

We and others have demonstrated that an elevated blood eosinophil count is an independent predictor of future exacerbations in adults[5] and children[6] with persistent asthma in a US managed care cohort and for adolescents and adults with asthma in a UK primary care cohort.[7] Although the eosinopenic effect of OCS is understood,[8,9] it is unknown whether lowering of eosinophil concentrations by chronic OCS use mitigates the relationship of eosinophil concentration as a predictor of asthma exacerbations.

Nevertheless, studies are few and findings are inconsistent for the risks associated with C-OCS use in asthma.[4,10] As such, it is important to determine for adults with persistent asthma the prevalence, patient characteristics, disease burden, comorbidities, and corticosteroid-related complications of C-OCS use, as well as the factors (including blood eosinophil count) that may be associated with future C-OCS use. We hypothesized that prior C-OCS exposure would be the predominant independent predictor of future chronic use for adults with persistent asthma.

METHODS

Study population and setting

The present study was a retrospective observational cohort study of adults with persistent asthma.[5] We used longitudinal, administrative pharmacy and health care utilization data captured from the Kaiser Permanente Southern California Research Data Warehouse to identify the study patients (Figure 1, *A*). The Kaiser Permanente Southern California Institutional Review Board approved the study with waiver of written consent.

We identified 9546 patients aged 18 to 64 years who met the Healthcare Effectiveness Data and Information Set (HEDIS) 2-year criteria (2009 and 2010) for persistent asthma and had continuous health plan enrollment and pharmacy benefit from 2009 to 2011 (no gap of >45 days within each calendar year). The HEDIS definition for persistent asthma required 1 of the following criteria to be met in both calendar years 2009 and 2010: an asthma hospitalization, an asthma emergency department (ED) visit, 4 or more asthma outpatient visits and 2 or more asthma drugs dispensed, or 4 or more asthma drugs dispensed. Exclusions included encounter diagnoses of chronic obstructive pulmonary disease and other chronic conditions (see this article's Online Repository at www.jaci-inpractice.org).[5]

OCS use determination

OCS use was determined as average daily amount in baseline (2009) and future outcome (2010) years. The average daily amount of OCS dispensed (mg/d) was calculated as follows: The total milligrams of prednisone equivalent for each OCS dispensing were calculated by multiplying the number of pills by their strengths. The total cumulative milligrams of prednisone equivalent dispensed in a year (the sum of all OCS dispensed in a year) was then divided by 365 days to yield the average daily OCS use. Through a sensitivity analyses, we also studied OCS use by examining the number of courses of OCS, captured as the sum of the number of separate OCS dispensed prescriptions. There was no differentiation between OCS courses dispensed for long-term maintenance or for treatment of acute exacerbations.

Definition of covariates

An asthma exacerbation was defined as either (1) an ED visit or hospitalization with a primary asthma diagnosis or secondary asthma diagnosis with a primary respiratory diagnosis based on *International Classification of Diseases, Ninth Revision* coding or (2) worsening asthma requiring systemic corticosteroids within 7 days before or after an outpatient visit using Kaiser Permanente Southern California extension codes indicating uncontrolled asthma (ie, acute exacerbation, status asthmaticus, acute asthma attack, not controlled asthma, or asthmatic bronchitis). A period of at least 8 days between episodes defined a new exacerbation.[11]

Socioeconomic information, including head of household education level and household income, was determined by geocoding address information to the census block level, and then linking the level to census-based block group-level. Determination of a patient's Global Initiative of Asthma (GINA) medication step-care level and dosage of inhaled corticosteroid (ICS) at baseline (2010) was based on a published algorithm and formula.[12] We determined the number and frequency of asthma controller medication and short-acting β_2-agonists (SABAs) using the number of individual canisters dispensed. Classification of ICS dosing into low, medium, and high dosages was based on National Asthma Education and Prevention Program guidelines. The Asthma Medication Ratio was defined as the number of dispensed asthma controller units (inhaled controller medication canisters or 30-day supplies of oral controller medications) divided by the total number of controller units and SABA canisters dispensed. The Asthma Medication Ratio is a validated administrative-data quality marker predictive of future asthma ED or hospital care.[13] An Asthma Medication Ratio of 0.5 or more is the minimum quality measure cutoff point set by HEDIS to define adequate controller medication dispensing.[14] Prescribing 9 or more units of controllers per year, equivalent to at least 75% adherence,[15] was used as a proxy for adherence to treatment.

Specific comorbidities were determined from *International Classification of Diseases, Ninth Revision* codes (see this article's Online Repository at www.jaci-inpractice.org) and overall comorbidities by Charlson comorbidity index.[16] Asthma-related comorbidities included gastroesophageal reflux disease, pneumonia, rhinitis, chronic sinusitis, acute upper respiratory tract infection, nasal polyps, eczema, and urticaria.[17] Potential OCS-related comorbidities