

Original Article

Albuterol Overuse: A Marker of Psychological Distress?

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What is already known about this topic? One-quarter of patients with asthma use 3 or more canisters of albuterol per year. Albuterol overuse is associated with worse asthma control and more frequent exacerbations. Among patients with asthma, depression is associated with more frequent symptoms, lower quality of life, and lower medication adherence.

What does this article add to our knowledge? Among adults with mild asthma, albuterol use on symptom-free days is the most important driver of overuse. Compared to those who use albuterol less frequently, overusers are at twice the risk for clinical depression.

How does this study impact current management guidelines? When albuterol overuse is suspected, depression should be considered as a potential comorbidity.

BACKGROUND: Albuterol overuse, 3 or more canisters per year, is associated with poor asthma control and frequent exacerbations.

OBJECTIVE: To describe albuterol use on symptom and symptom-free days and identify predictors of albuterol overuse and controller medication underuse.

METHODS: Secondary analyses of data from adults with mild asthma from the Trial of Asthma Patient Education were carried out. Based on albuterol use of 80% or more on symptom days and less than 20% on symptom-free days, participants were characterized as expected users, overusers, or underusers of albuterol. Good controller medication adherence was defined as 80% or more of prescribed doses. Data included demographic characteristics, diary data, spirometry, and scores from standardized questionnaires. Bivariate associations were examined between categorization of medication use and measured characteristics.

RESULTS: Of the 416 participants, 212 (51%) were expected users, 114 (27%) were overusers, and 90 (22%) were underusers of albuterol. No differences were observed among the user groups

by demographic characteristics or lung function. Expected users demonstrated the highest asthma-related knowledge, attitudes, and efficacy. Overusers reported the greatest symptom burden, worst asthma control, and highest frequency of symptom days. Overusers also had the highest burden of depression symptoms. More frequent symptom days accounted for 15% of overuse, greater use on symptom days accounted for 31%, and greater use on symptom free days accounted for 54% of overuse. Mean controller adherence was high across all groups, and there were no differences between the groups.

CONCLUSIONS: Although overusers experienced more frequent symptom days and used more albuterol on those days, most overuse was attributable to unexpected use on symptom-free days. High levels of comorbid depression were observed, particularly among overusers and among those nonadherent to controller medication. © 2015 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2015;■:■-■)

Key words: Asthma; Albuterol; Short-acting beta-agonist; Medication adherence; Depression

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This study was supported by the National Institutes of Health-National Heart, Lung, and Blood Institute (grant no. 5R01HL073494) and the American Lung Association. The study is registered at ClinicalTrials.gov: NCT00148408.

Conflicts of interest: T. F. Carr, C. Y. Wei, J. T. Holbrook, and L. B. Gerald have received research support for this study from the National Institutes of Health/National Heart Lung and Blood Institute (grant no. 35 5R01HL073494) and the American Lung Association. J. K. Gerald declares no relevant conflicts of interest. Received for publication June 4, 2015; accepted for publication June 16, 2015.

Available online ■■

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<http://dx.doi.org/10.1016/j.jaip.2015.06.021>

How patients take their prescribed asthma medications is an important predictor of asthma control and exacerbation risk. Underuse of controller medications leads to worse symptom control and more frequent exacerbations.^{1,2} Overuse of quick-relief medication (albuterol) is similarly problematic.³ Albuterol overuse is associated with more frequent symptoms, exacerbations, and health care utilization as well as lower mental and physical functioning.⁴⁻¹¹ Physiological and psychological dependence to albuterol is possible and can be challenging to distinguish from difficult-to-treat asthma.¹² Older age, male sex, white race, Hispanic ethnicity, coexisting medical conditions, lower educational attainment, current smoking, and physical inactivity have all been associated with albuterol overuse.^{6,7,9,11}

Albuterol overuse is an important problem. The 2009 Asthma Insight and Management Survey noted that 25% of patients relied on albuterol monotherapy to manage their persistent asthma and many used albuterol daily.¹³ The 2008-2010

Abbreviations used

ACQ- Asthma Control Questionnaire

ASUI- Asthma Symptom Utility Index

CES-D- Center for Epidemiological Studies-Depression

PEFR- peak expiratory flow rate

TAPE- Trial of Asthma Patient Education

Medical Expenditure Panel Survey noted that 15% of patients with asthma used more than 1 canister of albuterol per month.⁶ Several large claims databases have linked albuterol overuse with undesirable health outcomes. About 17% of Medicaid-insured patients and 25% of commercially insured patients filled 3 or more canisters of albuterol in a 12-month period.⁵ These patients had twice the risk of an asthma-related emergency department visit or hospitalization as compared with those who filled albuterol less frequently. Each canister filled beyond the first increased the exacerbation risk by 8% to 14% among adults and 14% to 18% among children. In another commercially insured population, 5% of patients with asthma were found to have filled more than 3 canisters of albuterol in a single fiscal quarter.⁴ These patients had 3 times the risk of an asthma-related emergency department visit or hospitalization as compared to those who filled albuterol less frequently.

Patients who overuse albuterol may have fundamentally different perceptions of their asthma.^{14,15} Overusers are more likely to focus on the mechanical effects of bronchoconstriction and the quick relief provided by albuterol rather than on the underlying inflammatory process and the prophylaxis provided by controller medications.¹⁵ In the schema described by Adams et al,¹⁴ patients who overuse albuterol are likely deniers/distanancers who perceive their diagnosis as negatively stigmatizing and therefore threatening to their self-image. These patients appear to have difficulty adapting to their diagnosis as evidenced by their tendency to express anger about asthma's impact on their lives, to underuse controller medication, to overuse albuterol, and to feel panicked when their albuterol inhaler is not available. In contrast, patients who have less difficulty adapting to their diagnosis (acceptors) tend to use their controller medication and albuterol more appropriately, to have more accurate asthma-related knowledge, to rate their health status more favorably, and to have a more positive self-image.^{14,16}

Although surveys and claims-based data provide important information on the magnitude of albuterol overuse they lack the granularity to describe the pattern of albuterol use in response to symptoms. To address these limitations, we used daily diary data collected from participants enrolled in the American Lung Association-Asthma Clinical Research Centers' Trial of Asthma Patient Education (TAPE).¹⁷ TAPE examined the impact of medication presentation on the response to a leukotriene receptor antagonist (montelukast) among adults with mild persistent asthma. Our goals were to describe the participants' pattern of albuterol use on symptom and symptom-free days and to identify characteristics associated with albuterol overuse and montelukast underuse.

METHODS

TAPE was a multicenter clinical trial that used a 2 × 2 factorial design to determine whether response to placebo or montelukast was augmented by messages that increased the expectation of benefit. A

TABLE I. Classification of participants by albuterol use on symptom and symptom-free days (N = 416)

Use on symptom-free days	Use on symptom days	
	≥80%	<80%
≤20%	212 (51%) Expected users	90 (22%) Underusers
>20%	114 (27%) Overusers	*

*A total of 11 participants in this category were excluded.

TABLE II. Mean albuterol actuations per day, symptom day, and symptom-free day

Actuations	Mean ± SD albuterol puffs per day			P value
	Underuser	Expected user	Overuser	
Overall	0.44 ± 0.52	0.88 ± 0.85	2.43 ± 1.40	<.0001
Symptom days	0.88 ± 0.85	2.17 ± 1.03	3.31 ± 2.00	<.0001
Symptom-free days	0.04 ± 0.10	0.05 ± 0.11	1.83 ± 1.32	<.0001

fifth group (usual care) was also followed to estimate the impact of clinical trial enrollment on the primary outcome of peak expiratory flow rate (PEFR) after 4 weeks of treatment. Participants were 15 years or older, had physician-diagnosed asthma, had previously used controller medication, had an FEV₁ of more than 75% of predicted, and had 1 or more indicators of poor asthma control. The study was approved by the institutional review boards at each center; patients provided written consent.

The analytic sample comprised 416 of 601 TAPE participants who reported both symptom and symptom-free days, and who had complete diary data. Most (174) participants were excluded because they reported only symptom days or only symptom-free days. Data included demographic characteristics, daily diary data, spirometry, and scores from the Mini Asthma Quality of Life Questionnaire,¹⁸ the Asthma Symptom Utility Index (ASUI),¹⁹ the Asthma Control Questionnaire (ACQ),²⁰ the Knowledge, Attitude, and Self-Efficacy Asthma Questionnaire,²¹ the Short-form Health Survey,²² the Shortness-of-Breath Questionnaire,²³ and the Center for Epidemiological Studies-Depression (CES-D) questionnaire.²⁴ All data were obtained from the baseline visit except for diary data, which were recorded during the 4-week treatment period.

Participants recorded their albuterol use, montelukast or placebo use, and asthma symptoms on daily diary cards. Although pill counts were recorded, adherence assessment was restricted to diary reporting of number of albuterol actuations and use/no use of controller medication on each day. Participants were instructed to record only rescue albuterol use and not preexercise use. Symptom days included any with symptoms including nighttime awakenings. *A priori*, we expected albuterol to be used on 80% or more of symptom days and on less than 20% of symptom-free days. Based on symptom and symptom-free day albuterol use, participants were characterized as expected users, overusers, or underusers (Table I). A fourth category of participants who used albuterol on less than 80% of symptom days and 20% or more of symptom-free days was excluded because few participants (n = 11, 3%) met these criteria. Adherence to montelukast or placebo was characterized as adherent if 80% or more of the doses were taken. Adherence was not recorded among usual care participants.

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