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Reliever inhaler overuse, asthma symptoms and depression

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The need for reliever medication, such as the inhaled short-acting beta₂-agonist (SABA) albuterol, along with day-time symptoms, night-time waking and activity limitations, is used to assess symptom control in asthma and to estimate the risk of future exacerbations (1). The inclusion of reliever inhaler use in assessments of asthma control in adults is based on evidence that overuse of SABA medication is associated with poor symptom control (2), increased risk of exacerbations (3, 4) and death from asthma (5, 6). Both national and international asthma guidelines use similar criteria to define SABA overuse (1, 7). In the GINA guideline, the use of a reliever inhaler for symptoms more than twice per week in the past 4 weeks is classified as partly controlled asthma and if symptoms and activity limitation due to asthma are also present is classified as uncontrolled asthma (1). Excess SABA inhaler use greater than one 200-dose canister per month is a risk factor for exacerbations (1) and for death from asthma (5, 6). Overuse of reliever inhalers is a common problem in people with asthma, which is highlighted by the Medical Expenditure Panel Survey finding that 15% of the asthmatic population in the United States used more than one reliever inhaler canister per month (8). In addition to increased albuterol use in patients with poorly controlled asthma, several demographic factors are associated with reliever inhaler overuse including male gender, black race, current smokers, lower educational level and lower income (8).

In the current issue of *The Journal Allergy and Clinical Immunology: In Practice*, Gerald and colleagues (9) report the results of a study designed to describe the pattern of albuterol use on symptom and symptom free days and to identify characteristics associated with albuterol overuse in adolescents and adults with mild asthma previously enrolled in the American Lung Association-Asthma Clinical Research Centers' Trial of Asthma Patient Education (TAPE)

(10). A *post hoc* analyses was undertaken of demographics and daily diary data including albuterol use as well as generic and asthma specific quality of life, asthma control and clinical depression questionnaire scores. Participants were characterized as over-, expected-, or under-users of albuterol based on albuterol use of $\geq 80\%$ on symptom days and $< 20\%$ on symptom free days. Four hundred and sixteen patients were recruited, of whom 212 (51%) were expected-users, 114 (27%) were over-users, and 90 (22%) were under-users of albuterol. The over-user group reported the greatest symptom burden, worst asthma control and lower asthma quality of life. Of particular interest was the unexpected finding that the frequency of albuterol use in the over-user group was greater on symptom free days (approximately half of the overuse) compared to symptomatic days. The reason(s) for the excess use of albuterol on symptom-free days is not explained by the study, although possible factors might include psychological dependence on SABAs, heightened perception of symptoms or associated co-morbidities such as dysfunction breathing or psychiatric disorders such as anxiety or depression. Gerald and colleagues (9) propose that one of the goals of management of over-users should be to reduce inappropriate use of albuterol on symptom-free days since excessive beta₂-agonist use has been associated with paradoxical adverse effects (11).

Both anxiety and depression commonly occur in people with asthma (1). Depression is associated with worse asthma outcomes and poor adherence with medication (12). Using the Center for Epidemiological Studies-Depression threshold score of ≥ 16 to identify participants at risk of clinical depression, Gerald and colleagues (9) found that 32% of albuterol over-users were at risk of clinical depression compared to 17% of expected-users. The finding that the risk of depression in albuterol over-users was almost twice that found in

the expected-users emphasises the importance that clinicians should consider depression in patients with mild asthma who over-use albuterol.

Although interesting, the study by Gerald and colleagues (9) has some limitations. The findings may not be generalizable to a 'real-life' population of patients with asthma that include a higher proportion of older subjects, current smokers, and subjects with a history of poor adherence with controller medications. The participants were mainly female and had mild disease and the pattern of reliever inhaler use may differ in males or in patients with severe disease. Also, the findings were from a short-term study lasting 4 weeks and may not reflect longer-term albuterol use. A further consideration is that self-reported inhaler use may not accurately reflect actual use, with over-users of SABAs tending to underreport their use and under-users of controller inhalers tending to overreport their use (13). Even if the participants in the study by Gerald and colleagues (9) underreported their use of albuterol, this is unlikely to affect the main conclusions on the pattern of reliever inhaler use. Finally, the psychological assessment did not include measures of anxiety status, psychosocial stress or personality traits which may influence reliever use. Further research is indicated to confirm and expand on the findings reported by Gerald and colleagues (9) by recruiting 'real-life' populations of people with asthma as well as those with severe disease. Future clinical studies should be undertaken for a longer duration, include objective measures of asthma outcomes, use electronic monitoring devices to measure inhaler use and include more detailed assessment of mental health including anxiety status.

What are the clinical implications of the study by Gerald and colleagues (9) for the management of patients with asthma who overuse reliever medication? The preliminary

nature of the results temper any definitive conclusions on clinical management.

Nevertheless, the findings suggest that when assessing patients with mild asthma suspected of reliever inhaler overuse, clinicians should consider that a proportion of albuterol use might be inappropriate, due to administration on symptom-free days and that depression may be an underlying co-morbidity. In the clinic, strategies to improve asthma control highlighted by reliever inhaler overuse include ensuring that the diagnosis of asthma is correct, starting or stepping-up controller therapy, improving adherence with controller therapy as well addressing co-morbidities, educational issues and self-management (1).

Although depression may contribute to reliever inhaler over-use, poorly controlled asthma and poor adherence with controller medication, the best methods for treating psychological problems in patients with asthma are not clearly established (14). Of interest, relaxation therapy may decrease the use of reliever medication (14). Formal psychiatric assessment is indicated if clinical depression is suspected (1). Administrative-based asthma outreach programs are a novel intervention reported to reduce over-dispensing of SABA canisters without compromising asthma control (15). In conclusion, the study by Gerald and colleagues (9) on the pattern of overuse of albuterol in mild asthma and the association with depression provides a stimulus for further research into understanding the influence of psychological factors on asthma control and medication use and to developing effective strategies to manage reliever inhaler overuse.

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