For the second part of the study, samples of MDIs (Flovent, Serevent, albuterol, and Qvar) were obtained from the manufacturers and studied in the laboratory. They evaluated the MDIs to determine how many actuations could be emitted and obtained weights during the process. They evaluated the usefulness of floating the MDIs in water to determine if they were full or empty, as has been suggested in the past for tracking the content of MDIs.

Results. The survey revealed that 72% of subjects determined that their MDI was empty when they could no longer hear a sound when actuated. Another 20% said they replaced it when it was “old” without giving specific details, although most said “within a month or so” or “after a while.” Four patients stated that they were told to float their MDI in water to determine if it was full (sinks to the bottom) or empty (floats), although none had actually done it. The majority (78%) said they knew they were supposed to shake the MDI before using it, but only half shook the MDI when their technique was evaluated later. In the laboratory, MDIs had similar flotation patterns, with mean flotation angles of 27.6 to 31.7° when empty. Water obstructed the valve or collected near the valve during this procedure 27% of the time. The chlorofluorocarbon inhalers (Flovent, Serevent, and albuterol) had a mean of 86% more audible puffs and Qvar 54% more than the stated manufacturer actuations. Shaking the MDI before actuation increased the doses available for the chlorofluorocarbon inhalers significantly.

Conclusions. Most patients studied did not know how to tell if their MDI was empty, and many did not shake the MDI before actuation, which can limit the amount of drug delivered. These results may in part explain the poor adherence with refills for MDIs, because patients may not realize that they are not receiving a full dose of active drug (because all of the MDIs studied had significantly more actuations than noted on the canister), which the authors termed “pseudo-adherence.” The only way to truly track the number of remaining doses in MDIs is to count each dose. Most MDIs will emit more drug doses if the device is shaken before actuation. Floating MDIs in water is not accurate for assessing remaining doses and often will clog the valve.

Reviewer’s Comments. This article demonstrates one of the limitations of MDIs in the inability of patients to accurately assess when they are empty without counting each dose. It illustrates the need for better devices to track doses remaining (an advantage of dry-powder inhalers).

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MEDICAL THERAPIES

DOUBLING THE DOSE OF INHALED CORTICOSTEROID TO PREVENT ASTHMA EXACERBATIONS: RANDOMISED CONTROLLED TRIAL


Purpose of the Study. The investigators proposed to determine if doubling the dose of inhaled corticosteroids (ICSs) to treat deteriorating asthma control reduced the need for starting oral corticosteroids.

Study Population. The study population included 390 nonsmoking individuals aged ≥16 years, with stable asthma requiring regular ICS use and a course of oral corticosteroids or doubled dose of ICS in the past 12 months.

Methods. Participants recorded their daily morning peak flow and daytime symptom score on a 4-point scale. After a 2- to 4-week run-in period, an independent pharmacist randomly allocated participants to receive active or placebo study inhalers, matched to their usual ICS, inhaler type, and dose. Participants were stratified into low-to-moderate–dose (equivalent of beclomethasone dipropionate, ≤1000 µg/day) and high-dose groups based on their dose of ICS at study entry. They continued their usual ICS and added the study inhaler for 14 days if their morning peak flow fell by 15% or their daytime symptom score increased by 1 point compared with the run-in period means. Participants took 10 days of oral prednisolone (30 mg/day) if their peak flow fell 40% from the mean run-in value or if their asthma control deteriorated to where they would usually start oral corticosteroids.

Results. Of the 192 participants in the active-inhaler group, 110 started their study inhaler (88 in the low-to-moderate–dose group), and of the 198 participants in the placebo-inhaler group, 97 started their study inhaler (74 in the low-to-moderate-dose group). Twenty-two participants (11%) in the active-inhaler group and 24 (12%) in the placebo group started prednisolone, for a risk ratio of 0.95 (95% confidence interval [CI]: 0.55, 1.64). Prednisolone was started because of a 40% peak-flow drop in 6 participants in the active group and 4 controls. In the low-to-moderate–dose group, 13 of 158 in the active group and 17 of 162 in the placebo group started prednisolone, for a risk ratio of 0.8 (95% CI: 0.4, 1.6). Doubling the dose of ICS led to a small reduction in the mean maximum fall of peak flow but did not change the time taken for peak flow or symptom scores to return to the baseline.

Conclusions. These findings do not support the effectiveness of doubling the dose of ICS to prevent the need for oral corticosteroids during asthma exacerbations.

Reviewer’s Comments. This randomized, control trial questions a recommendation that is part of many asthma-exacerbation-management plans. Although the results of at least 1 other study support these findings, a longer study following individuals beyond their first need for oral corticosteroids, involving larger increases as well as doubling of ICS doses, evaluating objective measures such as peak flow and symptom scores in all patients at the time of starting oral corticosteroids, and including younger patients and those with milder disease may reveal a benefit to increasing the ICS dose in some situations and subgroups of asthmatics. However, if this study’s findings can be consistently replicated in children, we may need to modify our recommendations for early management of asthma exacerbations.
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