



Correspondence

Combination of inhaled corticosteroid and a long-acting β -agonist Proceed with caution



Spahn¹ describes the long and winding road related to the controversies of the inhaled corticosteroid (IC) LABA combination. He states that the large studies demonstrating the safety of the combination are compelling.^{2–4} However, because those studies specifically excluded patients with previous life-threatening reactions, I want to draw attention to the observations my colleague and I previously reported in 2 boys, aged 10 and 15 years, with a previous history of life-threatening asthmatic exacerbations while receiving a LABA with an IC.⁵ They experienced life-threatening bronchospasm with exertion not prevented with a short-acting β_2 -agonist (SABA) until use of the LABA was discontinued. Loss of bronchoprotective effect of a SABA from regular use of a LABA has been previously reported⁶ and is not prevented by the simultaneous use of an inhaled corticosteroid.^{7,8}

I have since observed clinically a few other patients in whom adding a LABA to an IC caused deterioration rather than the much more usual added benefit. Until proven otherwise, we should consider that there is a small subset of patients at risk for the serious adverse effect documented in the 2 boys described in our previous publication.⁵ Because it is highly unlikely that those 2 boys are the only ones with such a profound apparent down-regulation of the β_2 -adrenergic receptor from addition of a LABA to an IC. The way to detect such patients is to monitor the clinical course when a LABA is added to an IC. The clinical course of asthma frequently varies. Consequently, clinically identifying the uncommon situation where

a LABA is the cause of worsening asthma will be more difficult when the combination is added de nouveau than when the LABA is added when control of asthma is inadequate with an IC. Because many patients have their asthma controlled with a usual dose of an IC alone, the need for a combination is not routine; however, this does not belie the convincing data that LABAs are the most effective add-on therapy—when needed.

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Disclosure: Author has nothing to disclose.

Author response



Dr Weinberger disagrees with my assertion that large studies^{1–5} demonstrating the safety of combination inhaled glucocorticoid (IGC) and long-acting-agonist (LABA) therapy are compelling because they did not include patients with life-threatening asthma. Dr Weinberger describes a case report he published in 2006 of 2 children with poorly controlled asthma despite high-dose IGC and LABA combination therapy who developed life-threatening episodes of bronchospasm after exercise that were not prevented by albuterol pretreatment.⁶ Only after discontinuing use of the LABA did albuterol provide adequate bronchoprotection, suggesting that LABA therapy resulted in a complete inhibition of the bronchoprotective effect of albuterol.

Although tachyphylaxis develops after long-term LABA therapy, its clinical relevance remains to be fully determined. For example,

in the study Dr Weinberger cites describing loss of the bronchoprotective effect of short-acting β -agonists in patients receiving regular LABA therapy,⁷ patients taking LABAs still had significant improvements in lung function after albuterol, although larger doses were required to achieve the same degree of bronchodilation.^{6,7} In a study Dr Weinberger did not cite, the bronchodilator effect of albuterol was evaluated in patients receiving LABA therapy who presented to the emergency department with acute asthma.⁸ Patients not receiving LABA therapy served as controls. No difference in the bronchodilator effect of albuterol was noted between the LABA and control groups (39% vs 50% improvement in peak expiratory flow in the control vs LABA groups, respectively). In addition, no difference was found in the number of patients who required hospitalization between the 2 groups.

Dr Weinberger also states that it is highly unlikely that the 2 children he describes are the only ones who develop profound

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