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Levalbuterol has not been established to have therapeutic advantage over racemic albuterol

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To the Editor:

We read with interest the clinical trial recently published by Milgrom et al.¹ comparing the safety and efficacy of nebulized levalbuterol with that of racemic albuterol in children with asthma. They concluded that levalbuterol (the R-isomer of racemic albuterol) was effective at a lower dose that resulted in fewer adverse effects than the standard 2.5-mg dose of racemic albuterol; however, their results did not support this conclusion. In addition, their discussion did not address clinical studies demonstrating that the S-isomer is inactive.² It does not produce adverse systemic effects,^{3 4} an increase in airway reactivity,⁵ or tolerance.⁶ Available evidence indicates that all beneficial and adverse effects of albuterol in human beings are a consequence of the R-isomer only.

Essential to an investigation attempting to compare relative potencies of β -agonists is, first and foremost, that a dose-response relationship be demonstrated. This was not the case in the report by Milgrom et al.¹ Specifically, there were no significant differences in the peak change in FEV₁ after doubling doses of either the levalbuterol or the racemic formulation. If

they were unable to distinguish differences in bronchodilation between doubling doses of levalbuterol, they cannot conclude that 0.31 mg of levalbuterol was as potent as 1.25 mg and 2.5 mg of racemic albuterol. Inasmuch as the dose-response curves were flat in their subjects, giving a smaller dose would be expected to produce the same effect as giving a larger dose.

Accordingly, the authors' data with regard to safety of the 2 formulations shows only that as you decrease the β_2 -adrenergic agonist dose, the propensity for adrenergic mediated adverse effects also decreases. That is, 0.31 mg of levalbuterol (which contains only pure R-isomer, the systemically active component of albuterol^{3 4}) produces less of a systemic effect than the 1.25-mg and 2.5-mg doses of racemic albuterol (which contain 0.63 mg and 1.25 mg of R-isomer, respectively) that were tested in the report by Milgrom et al.¹ We suspect that a dose of racemic albuterol containing an amount of the R-isomer equivalent to that in 0.31 mg of levalbuterol (ie, 0.63 mg) would yield results that are not statistically different from those obtained in this investigation for 0.31 mg of levalbuterol.

Given the greater cost of levalbuterol, the routine use of this product has the potential to increase the cost of asthma care without identified benefit. Prescribing lower doses of generic, preservative-free racemic albuterol aerosols can prevent minor transient adverse effects if the standard dose is not well tolerated.

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