infection. Symptoms began 2 months after the beginning of treatment with etanercept, which seemed early for the development of disseminated MAC infection. Reports from the HIV literature\(^4\) derived from the early 1990s stated that the mean period of time until the appearance of disseminated MAC infection was at least 8 months after making the diagnosis of HIV. Another observation seen was the distinct two-tiered improvement, which was possibly not emphasized adequately with the original report.\(^5\) A clear improvement first occurred during the week immediately after stopping etanercept therapy, with no additional clinical change demonstrated until prednisone was added.

Inhibitors of tumor necrosis factor and corticosteroids have been shown to impair defense mechanisms directed toward mycobacterial infection.\(^4,5\) Even if immunity was restored after stopping etanercept therapy, the effect was transient since prednisone was implemented by week 4. Under these conditions, a spontaneous and sustained remission of disseminated MAC would be unlikely. Admittedly, treatment with steroids can impact the illness severity of mycobacterial infection, for which reason it is sometimes used as an adjunct to antimicrobial therapy.\(^6\) Complete resolution of the pathology extending from mycobacterial disease would not be expected with prednisone alone, unless the Mycobacterium was linked to hypersensitivity pneumonitis.

Our patient had no exposure to hot tubs or swimming pools, which have been linked to MAC hypersensitivity pneumonitis.\(^7\) Moreover, the case descriptions of this relatively new entity appear to be comparable to extrinsic allergic alveolitis. A major characteristic of extrinsic allergic alveolitis is that the pathology is limited to lung tissue.\(^8\) For our patient, the granulomatous inflammation was systemic, seen in specimens from both lung and skin biopsies. The combination of systemic pathology with no inhalation exposures strongly argues against a diagnosis of mycobacterial hypersensitivity pneumonitis.

In summary, our case is unique to those reporting MAC hypersensitivity pneumonitis in that the inflammation was systemic. Discriminating between disseminated MAC infection and drug-induced injury can be more of a challenge. In retrospect, blood cultures may have been helpful and are recommended for future cases presenting in a similar manner. The temporal features, along with the response to the therapeutic interventions, favor a diagnosis of etanercept-induced lung injury. The MAC isolated in our case is more likely to represent colonization.

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Levalbuterol vs Racemic Albuterol
Science or Drug Company Propaganda?

To the Editor:

With regard to the article by Truit et al (January 2003),\(^1\) I would like to raise the following concerns: this was a retrospective study; the placebo factor and other confounding factors were not taken into account; other differences in treatments were not considered; and sicker patients were enrolled in the control group.

In retrospective studies, care must be taken to ensure that nothing changed between the two treatment groups. During this study, the pressure to treat patients in the outpatient setting may have changed, and new medications were introduced. Additionally, the physicians changed the protocol, suggesting that they believed the medication was safer and more effective, and perhaps was influencing them to send patients home earlier. Furthermore, the authors admit that they cannot track other treatments that may have changed.

When a therapy is changed in the “real world,” there are always questions from patients. It would be interesting to know how this change was presented to the patients. I doubt that my patients who were accustomed to treatment every 4 h would graciously accept a reduction of these treatments by half without some explanation.

Another concern is reference 6, a letter that was published in Lancet, which is quoted as evidence that S-albuterol is potentially dangerous. Before we discard a drug that is cheap, safe, and effective, we should use articles that have been peer-reviewed and the data in which are reproducible.

In regard to the patients in the study, it appears that asthma patients were overrepresented when racemic albuterol was used (28% vs 18%, respectively). Also, these patients had a lower FEV\(_1\) at hospital admission (44.6% predicted vs 48.6% predicted, respectively), suggesting that they were sicker and required more interventions.

Furthermore, despite receiving albuterol on hospital discharge, the authors cite a reduction in 30-day readmission rates for the levalbuterol group. Are the authors suggesting that the effects of the drug last for 30 days? Notably, none of the asthmatic patients in the racemic albuterol group required readmission.

In this article may question the dosing of albuterol every 4 h. Perhaps dosing every 8 h, in some patients, would be just as effective. And perhaps the best treatment is bronchodilator use only when a patient is symptomatic as a result of bronchospasm.

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Référence


Levalbuterol Is Not More Cost-Effective Than Albuterol for COPD

To the Editor:

In a recent issue of CHEST, Truitt et al (January 2003)1 claimed that their retrospective chart review demonstrated that “levalbuterol afforded clinical and pharmacoeconomic advantages over racemic albuterol” in the treatment of hospitalized patients with COPD and asthma. The primary end point of the study was the total number of nebulizer treatments required. However, the target care path that was in operation during the historical cohort required albuterol to be administered every 4 h (six treatments per day), while in the current cohort levalbuterol was administered every 8 h (three treatments per day). Thus, the statistically significant difference in the primary end point was a result of differences in the care plans. There were no statistically significant differences in the number of extra treatments required by either cohort. Surprisingly, the reviewers missed this fatal flaw in the study design.

The combination of more treatments, by design, and an artificially higher cost basis for albuterol resulted in a spurious statistical difference for the total cost of nebulizer therapy. They used the “average wholesale price” (AWP), but no hospital pharmacy ever pays the AWP. For many hospitals, the acquisition cost of racemic albuterol is around $0.32 per 2.5-mg dose compared to $1.82 per 1.25 mg for an equivalent dose of levalbuterol (ie, a 5.7-fold difference). In contrast, the AWP for the two products are $1.21 and $2.08, respectively (a 1.7-fold difference).2

No conclusions can be drawn about clinical advantages since the treatments were not administered in a double-blind randomized manner. Moreover, in patients with COPD (about 80% of the patients), FEV1 did not significantly increase from hospitalization to discharge. Therefore, the authors inferred that important pharmacoeconomic end points were different when they were not statistically different. For example, the authors state that those treated with levalbuterol “had shorter lengths of hospital stay” and “decreased costs for hospitalization,” but the p values for these end points for patients with COPD were 0.07 and 0.11, respectively.

We conclude that the differences between albuterol and levalbuterol in this study were a result of differences in the number of treatments required by the care plan, invalid cost calculations, and the emphasizing of numerical differences that were not statistically significant by conventional criteria.

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