Desensitization to Trimethoprim-Sulfamethoxazole in Patients Infected with Human Immunodeficiency Virus

Sir—Gluckstein and Ruskin [1] recently described desensitization to trimethoprim-sulfamethoxazole (TMP-SMZ) in patients with AIDS who had previously been intolerant of the drug. We want to raise several points related to this procedure.

First, it is dangerous to give patients drugs to which they have exhibited hypersensitivity. This approach is appropriate only when an acute pathological condition cannot be treated with other drugs. Even in this situation, one must use steroids. Only if the reaction is IgE-mediated (e.g., allergy to penicillin) should desensitization be attempted. For prophylaxis for Pneumocystis carinii pneumonia (the indication described by Gluckstein and Ruskin), TMP-SMZ can be replaced by aerosolized pentamidine.

Second, eight desensitized patients in this protocol had already had serious anaphylactoid reactions to TMP-SMZ. In such cases, other serious reactions are especially likely to occur. In our experience [2], for example, four of 11 patients who developed serious exfoliative dermatitis in response to sulfa drug treatment had had a maculopapular reaction to sulfa drugs in the past.

Third, previous studies have documented a failure of desensitization in 25%–45% of cases [3, 4]. Furthermore, Carr et al. [5] demonstrated that 45% of HIV-infected patients who were hypersensitive to sulfa drugs had no reaction upon rechallenge, even without desensitization. Thus, any observed changes in drug tolerance are not necessarily attributable to desensitization.

Fourth, we are not even sure about the mechanism underlying sulfa drug hypersensitivity in HIV-infected patients. These allergies, unlike those mediated by IgE, are dose dependent and cannot be reproduced consistently. The desensitized patients in this protocol probably tolerated TMP-SMZ because of the lower dosage used for prophylaxis or because of the inconsistent occurrence of hypersensitivity reactions mediated mostly by mechanisms other than IgE.

In short, we believe that the kind of desensitization evaluated by Gluckstein and Ruskin is neither of proven efficacy nor free of risk.

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References

Reply

Sir—Quirino and colleagues express reservations about our report describing trimethoprim-sulfamethoxazole (TMP-SMZ) desensitization in patients with AIDS [1]. While we agree with their assertion that readministration of TMP-SMZ should not be undertaken casually in patients who have had adverse reactions to the drug, we believe the benefits of our approach outweigh its risks. TMP-SMZ is clearly more effective than alternative drugs in preventing Pneumocystis carinii pneumonia [2, 3]. Furthermore, we did not encounter serious adverse reactions to desensitization or subsequent TMP-SMZ prophylaxis among our 22 subjects, and no serious reactions were noted in another 21 patients who participated in earlier trials of desensitization [1]. Since submission of our manuscript, similar results have been described for TMP-SMZ desensitization in ≥100 hypersensitive patients with AIDS [4–8]. The cumulative results of these observational studies confirm that the benefits of TMP-SMZ desensitization do indeed exceed the potential risks of the procedure.

We disagree with the contention of Quirino et al. that corticosteroids must be used during TMP-SMZ desensitization in patients with AIDS. In the TMP-SMZ desensitization protocols published to date, there are no reports that document the value of corticosteroids. It is noteworthy in this regard that while adjunctive corticosteroid therapy for active P. carinii pneumonia may improve outcome, it does not appear to significantly reduce dose-limiting adverse reactions to TMP-SMZ [9].

Quirino and associates are concerned that a history of maculopapular rash after ingestion of TMP-SMZ predisposes patients who are subsequently treated with the drug to exfoliative dermatitis. However, none of our patients with prior TMP-SMZ–induced rash developed severe dermatitis during or after desensitization; in fact, eight of our patients who previously had anaphylactoid reactions

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