Successful Desensitization of Two Patients Who Previously Developed Stevens-Johnson Syndrome While Receiving Trimethoprim-Sulfamethoxazole

The prevalence of hypersensitivity reactions to trimethoprim-sulfamethoxazole (TMP-SMZ) in HIV-infected patients, variably reported between 27% and 64% [1], is many fold greater than in the general population. A number of desensitization protocols have been successfully used to enable previously hypersensitive patients to receive prophylaxis and therapy with this drug combination [2, 3]. However, the protocols published to date have specifically excluded patients with severe hypersensitivity reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis for fear of provoking such reactions during the desensitization process. We report the successful desensitization, using the oral route, of two patients who had previously developed Stevens-Johnson syndrome while being treated with TMP-SMZ.

A 34-year-old HIV-infected man developed Pneumocystis carinii pneumonia (PCP) in 1994. Treatment with oral TMP-SMZ was begun, and the patient initially tolerated this treatment well. After 10 days of therapy he developed a widespread macular rash, ulceration of the buccal mucosa, conjunctivitis, sweats, fever, confusion, and anorexia. The drug was discontinued, but he remained unwell for three weeks. He received nebulized pentamidine, which exacerbated his asthma, and he developed pruritus while he was receiving dapsone prophylaxis; nonetheless, he was able to tolerate this drug.

Despite dapsone prophylaxis, he developed recurrent PCP in June 1996. He was treated with a combination of oral clindamycin and primaquine but developed a rash and diarrhea; culture of diarrheal specimens was positive for Clostridium difficile toxin. Treatment with atovaquone was completed successfully. Because he had recurrent PCP despite prophylaxis with dapsone and could not tolerate several of the alternative agents for treating this condition, cautious desensitization was attempted. An 8-day protocol was used (M. A. Conant, personal communication); this protocol began with a 1-mL dose of 1:1,000,000 dilution of TMP-SMZ syrup for 10-fold, and the patient again took 1-, 2-, 4-, and 8-mL doses. This pattern continued until day 8, when the final dose of syrup was replaced with a double-strength tablet of TMP-SMZ. Desensitization proceeded uneventfully, and the patient currently remains well and continues to receive prophylaxis with TMP-SMZ.

A 33-year-old man was found to be infected with HIV in 1990. In 1994, PCP developed. After 1 week of oral treatment with high-dose TMP-SMZ, he developed a widespread macular rash with severe mouth ulceration, fever, and nausea. Subsequently, therapy with dapsone and nebulized pentamidine was poorly tolerated, and he had two further episodes of PCP. By using the above-described protocol, he was also desensitized successfully. He continued to receive a prophylactic dose of TMP-SMZ until shortly before his death, which occurred 4 months later and was not related to PCP.

These patients were desensitized despite their previously severe hypersensitivity reactions because alternative prophylactic medication had not been tolerated or had been ineffective. Although desensitization may provoke a recurrent reaction, in both of these cases it proceeded smoothly. The mechanism of hypersensitivity reactions to TMP-SMZ in HIV-infected patients has not been fully elucidated, although it is clear that these reactions are not usually IgE mediated. The reactions probably result from a combination of enhanced CD8⁺ lymphocyte hypersensitivity to drugs and changes in drug metabolism, both secondary to HIV infection [4].

Our experience suggests that a history of Stevens-Johnson syndrome due to TMP-SMZ is not necessarily an absolute contraindication to desensitization. In highly selected cases, cautious desensitization to TMP-SMZ is possible but clearly must be performed under close supervision.

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References