

Correspondence

Low-dose cyclosporine is a good option for severe chronic urticaria

To the Editor:

In his review,¹ Dr Alan Kaplan, a leading figure in the area of chronic urticaria (CU), shares his experience in the management of this disabling disorder. Indeed, the time has come for some of the previously accepted myths to remain in the history books. Myths such as "CU is caused by food additives or is exacerbated by pseudoallergens contained in food" should no longer be considered.

When higher doses of antihistamines are required for severe CU and sedation (even if mild) appears, then quality of life becomes the main issue of how to continue therapy. We dispute the statement that "first-generation antihistamines are discontinued because of their sedative effects in only 2% of patients with CU." In our experience and that of others, 10% to 15% of patients with severe CU are unable to continue taking high doses of antihistamines and maintain daily activities.² In addition, 40% of patients with extremely severe CU who could tolerate high doses of sedative antihistamines remain nonresponders and therefore require a more aggressive therapy.³

The other point that we would like to discuss is the statement that "any sedation that might be seen is not comparable with the side effects of corticosteroids or cyclosporine." The side effects of corticosteroids, especially when repetitively used, are not at all comparable with those of low doses of cyclosporine. After treating more than 100 patients with severe CU with 2 to 3 mg/kg cyclosporine, we observed that in 40% of our patients, CU disappears, whereas in 30% we observed a partial improvement. A similar experience was reported during the last decade in 12 original studies, 3 that were double-blind controlled studies.⁴

When side effects of cyclosporine are taken into account, one should consider its initial dose. In 5 of 12 reported studies, the dose of cyclosporine was between 4 and 5 mg/kg, whereas a low dose (2-3 mg/kg) was given in the other 7 studies, including ours.⁵ For higher doses, side effects, such as hypertension, peripheral neuropathy, and increased serum creatinine values, were reported in 20% to 30% of cases. In most cases they were transient or improved after dosage decrease, and discontinuation of therapy was rare. However, when cyclosporine was given at 2 to 3 mg/kg, most studies reported a very low incidence of side effects (mostly gastrointestinal or peripheral neuropathy) and almost no cases of therapy discontinuation.

Some of our patients with very severe CU are kept on very low doses of cyclosporine (1.5-2.0 mg/kg) for 5 to 7 years continuously, being unable to stop therapy. The fear of malignancy caused by long-term cyclosporine therapy is adopted from its higher frequency in patients who have undergone transplantation. These are usually treated with higher doses of cyclosporine in combination with rapamycin or mycophenolate. We did not observe any malignancy in any of our patients (although it was a small group). Thus we believe that cyclosporine is a safe drug to be considered earlier when urticaria is very severe so that the patients achieve a better quality of life.

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Reply

To the Editor:

I thank Drs Toubi and Kessel¹ for their comments regarding the treatment of chronic urticaria after my recent Clinical pearl article in the Journal.² We agree that cyclosporine is one of the best alternatives for refractory chronic urticaria and emphasized that in the article. We typically use 200 to 300 mg for our adult population, and our more than 75% success rate is close to their observation that 40% of patients remitted and 30% improved significantly. A 200-mg dose usually is successful, but a 250- to 300-mg dose is sometimes needed and can approach 4 mg/kg. We taper by 50 mg per month once an obvious effect is seen. Nevertheless, of 50 patients treated in this fashion, 5 required temporary dose reduction or elimination because of increasing blood urea nitrogen and creatinine values, and 3 others gradually become hypertensive. We treated 2 of the latter group with 50 to 100 mg of losartan with normalization of blood pressure because no other drug has ever controlled their symptoms of urticaria and angioedema, and they were able to continue the cyclosporine. Such patients would be excellent candidates for a trial of omalizumab.³ I agree that the risk of prolonged steroid use far exceeds that of cyclosporine; however, I believe that any hypertension or renal dysfunction is a more serious event than the sedation seen with antihistamines. The literature does suggest that 10% to 15% of patients discontinue first-generation antihistamines because of sedation, but our experience of 2% with a huge denominator is, in my opinion, an example of what can be done if the dose is given 4 times daily and not discontinued until at least 1 week has passed with sedation still persisting. In that fashion responders are maximized, and those who fail can move on to other modalities. Our referral center has evaluated too many patients treated with steroids before antihistamine responsiveness has been determined properly, and we would not wish to use cyclosporine in someone who might respond to hydroxyzine, particularly because our experience at 2 mg/kg is not nearly as good as that at 3 mg/kg for initial therapy.

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