

Evidence-based considerations regarding the US and international guidelines for chronic urticaria



To the Editor:

In comparing the US and international guidelines for chronic urticaria,¹ some evidence-based information appears not to have been adequately considered. Specifically, the differences in the antihistaminic effect of various antihistamines were not considered in either US or international guidelines. All antihistamines are not equal in suppressing histamine-induced lesions. Both past and more recent studies have demonstrated that the relative efficacy for preventing histamine-induced effect can differ substantially for the various first- and second-generation antihistamines.²⁻⁴ Moreover, the consideration for hydroxyzine as a potential “dose advancement” in the US guidelines (Table II of the article) does not consider that the antihistamine effect of hydroxyzine is from its active metabolite, cetirizine.⁵ Adding hydroxyzine is therefore equivalent to just adding more cetirizine. Cetirizine is a second-generation antihistamine generally recognized, along with its active enantiomer levocetirizine, as the most effective antihistamines of that class. Of additional importance, increasing the dosage of cetirizine increases the effect, which does not necessarily occur to the same extent with all antihistamines.⁶ The unique contribution of cyproheptadine in the treatment of cold urticaria should also be recognized.⁷

Neither the US nor the international perspective¹ considers the potential for cyclosporine to induce sustained medication-free remission.^{8,9} That has not been associated with omalizumab or other treatments. Moreover, although cyclosporine has been demonstrated to be effective in controlled clinical trials,⁸ that is not true for other immunosuppressants considered in the US guidelines.¹⁰

Primary care physicians would be best advised to treat chronic spontaneous urticaria beginning with cetirizine or levocetirizine and gradually increasing the dose, if needed, to 4 times the starting dose. Cyproheptadine appears to be the initial drug of choice for cold urticaria. If urticaria is not controlled, referral to an allergist familiar with the literature and experienced in treating urticarias should be considered.

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Reply



To the Editor:

We thank Weinberger for his comments¹ suggesting that several points regarding chronic idiopathic urticaria (CIU) treatment were not adequately considered in either the US or international evidence-based guidelines.² Before specifically addressing his comments, we would like to first emphasize that the task of this review was to compare the similarities and differences between the existing US and international guidelines and not to investigate or critique the quality of these documents. However, in our review, both documents devoted a considerable amount of time describing the evidence-based style methodologies used in their development, with the most recent international guideline adhering to a strict Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.²

Weinberger recommends cetirizine, a metabolite of hydroxyzine, or levocetirizine as initial preferred monotherapy for CIU; however, this is not a guideline-based recommendation because other second-generation H1 antagonists may be equally effective and there are insufficient head-on-head comparison studies supporting this recommendation.^{3,4} Furthermore, the assertions made by Weinberger regarding H1-antagonist potency are based on either dated references or using skin prick testing as a measurement of potency, which has not been demonstrated to be an adequate means for comparing the clinical efficacy of H1 antagonists.⁵⁻⁸ Therefore, both guidelines concluded that based on the available evidence and lack of head-to-head trials for H1 antagonists, no recommendations can be made regarding differences in potency or effectiveness of these agents.^{3,9} Notwithstanding, we recognize that one's clinical experience may differ from recommendations made by evidence-based guidelines regarding the use of one specific treatment over another from the same medication class such as second-generation H1 antagonists. However, a clear difference between the 2 guidelines was that the international guideline strongly recommended using second-generation H1 antagonists preferentially over first-generation H1 antagonists because of risk and benefit analyses as first-generation H1

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