

Treating chronic spontaneous urticaria in children



To the Editor:

The recent review of pediatric urticaria discussed the use of antihistamines for the treatment of urticaria.¹ This subject deserves additional details regarding the relative efficacy of these medications. Studies had previously demonstrated that the relative efficacy of hydroxyzine exceeded that of other antihistamines.² Because the active metabolite of hydroxyzine is cetirizine, those data also support the greater efficacy for cetirizine (Figure 1).³ Levocetirizine, the active optical R-enantiomer of racemic cetirizine, is equivalent to racemic cetirizine, containing an equimolar amount of the R-enantiomer.⁴

Also relevant is the dose-response of antihistamines. Increasing the dose of antihistamines to 4 times usual dosage is common practice. Levocetirizine, the active enantiomer of cetirizine, at doses of 5 to 20 mg (the molar equivalent of 20-40 mg racemic cetirizine), was compared with the same milligram doses of desloratadine, the active metabolite of loratadine. A progressive increase in the dose-response effect of levocetirizine, but not for desloratadine, was seen.⁵ On the basis of evidence, cetirizine (or its active enantiomer alone, levocetirizine) is likely to be the most effective antihistamine for chronic urticaria.

The recent review of urticaria¹ also included the rate of spontaneous resolution of chronic urticaria in adults but not for children. However, published data from 92 children found remissions of

19%, 54%, and 68% at 1, 3, and 5 years, respectively.⁶ Although omalizumab provides symptomatic improvement of chronic urticaria, symptoms return when the treatment is stopped. In contrast, cyclosporine provided prompt control of chronic urticaria with sustained remissions.⁷ Safety and efficacy in the pediatric study used the reliably absorbed microemulsion formulation of cyclosporine with therapeutic drug monitoring targeting serum concentrations of 100 to 200 ng/mL. With that strategy, prompt elimination of urticaria occurred and continued for most following rapid cessation of the cyclosporine.

Miles Weinberger, MD^{a,b}

^aUniversity of Iowa, Iowa City, Iowa

^bUniversity of California San Diego, Rady Children's Hospital, San Diego, Calif.

Conflicts of interest: The author declares no relevant conflicts of interest.

Received for publication April 7, 2018; accepted for publication May 1, 2018.

Corresponding author: Miles Weinberger, MD, 450 Sandalwood Court, Encinitas, CA 92024. E-mail: miles-weinberger@uiowa.edu.

REFERENCES

1. Ben-Shoshan M, Grattan CE. Management of pediatric urticaria with review of the literature on chronic spontaneous urticaria in children. *J Allergy Clin Immunol Pract* 2018;6:1152-61.
2. dos Santos RV, Magerl M, Mlynek A, Lima HC. Suppression of histamine- and allergen-induced skin reactions: comparison of first- and second-generation antihistamines. *Ann Allergy Asthma Immunol* 2009;102:495-9.
3. Gengo FM, Dabronzo J, Yurchak A, Love S, Miller JK. The relative antihistaminic and psychomotor effects of hydroxyzine and cetirizine. *Clin Pharmacol Ther* 1987;42:265-72.
4. Ino H, Hara K, Honma G, Doi Y, Fukase H. Comparison of levocetirizine pharmacokinetics after single doses of levocetirizine oral solution and cetirizine dry syrup in healthy Japanese male subjects. *J Drug Assess* 2014;3:38-42.
5. Staevska M, Popov TA, Kralimarkova T, Lazarova C, Kraeva S, Popova D, et al. The effectiveness of levocetirizine and desloratadine in up to 4 times conventional doses in difficult-to-treat urticaria. *J Allergy Clin Immunol* 2010;125:676-82.
6. Chanskulporn S, Pongpreuksa S, Sangacharoenkit P, Pacham P, Visitsunthorn N, Vichyanond P, et al. The natural history of chronic urticaria in childhood: a prospective study. *J Am Acad Dermatol* 2014;71:663-8.
7. Neverman L, Weinberger M. Treatment of chronic urticaria in children with antihistamines and cyclosporine. *J Allergy Clin Immunol Pract* 2014;2:434-8.

<https://doi.org/10.1016/j.jaip.2018.05.003>

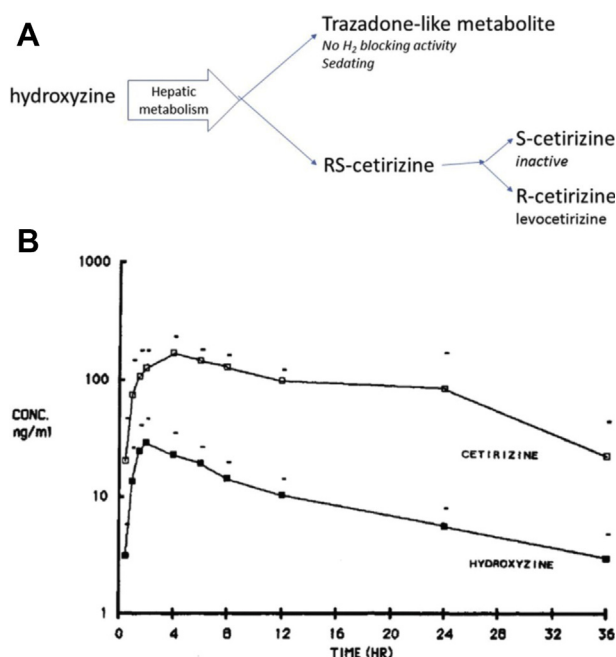


FIGURE 1. A, Metabolism of hydroxyzine to racemic cetirizine (RS-cetirizine) and a metabolite with sedation but no antihistaminic effect. Racemic cetirizine can be separated into the individual enantiomers, the inactive S-cetirizine and the active R-cetirizine. B, Mean cetirizine and hydroxyzine serum concentrations following administration of 25 mg hydroxyzine to 25 adult male volunteers (reproduced with permission from Gengo et al³). HR, hours.

Reply



To the Editor:

In his commentary, Weinberger¹ levied several critiques on our review² of the management of chronic urticaria (CU) in children, which we address below.

His first point relates to the premise that the relative efficacy of hydroxyzine exceeds that of other antihistamines. However, the referenced study assessed only the effect of hydroxyzine on allergen and histamine-induced skin prick test size³ rather than any effect on hives in the setting of CU, which might involve different pathogenic mechanisms. Numerous reviews and clinical trials support the use of second-generation rather than first-generation antihistamines due to similar efficacy but better safety profile.⁴ In clinical trials, including multicenter, double-blind, placebo-controlled studies, the safety and efficacy of cetirizine (a second-generation antihistamine) and hydroxyzine is similar and cetirizine has a greater safety margin over the older parent drug hydroxyzine.^{5,6} A systematic Cochrane review concluded that there is no difference in short-term treatment between