

expression has played only a peripheral role in research pertaining to common inflammatory skin disease. Elucidating and defining the danger in different inflammatory skin diseases may open new therapeutic avenues upstream of cytokine neutralization. Perhaps it is time for danger signalling to take centre stage.

Conflicts of interest

None declared.

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Night-time sedating H1 antihistamine increases daytime somnolence but not treatment efficacy in chronic spontaneous urticaria: a randomized controlled study

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The within-patient crossover study by Staevska et al.¹ looks at the response of patients with relatively severe, chronic spontaneous urticaria, many of whom had a history of associated

dermographism, delayed pressure urticaria and angio-oedema, who remained symptomatic despite treatment with low-dose prednisolone and H1 antihistamines to higher-than-licensed doses of a second-generation antihistamine, levocetirizine, with or without the addition of a first-generation H1 antihistamine, hydroxyzine, which is known to have sedating properties.

Apart from showing a similar beneficial response of both randomized treatments with respect to daily urticarial activity and 5-day quality of life scores compared with baseline (following an inpatient randomized crossover study of levocetirizine and hydroxyzine at high doses), patients in the study arm randomized to receive additional hydroxyzine had a slightly higher median score for daytime somnolence/sedation, as assessed by a visual analogue scale [five of 100 rather than zero of 100, which reached statistical significance ($P < 0.05$)]. The authors present this as evidence of the detrimental sedative effects of hydroxyzine owing to its prolonged effects on the central nervous system, which result in 'hang-over' effects the next day. The authors conclude that it is better not to offer a sedating antihistamine at night for the treatment of chronic spontaneous urticaria because of the potential detrimental effects of residual daytime sedation on school performance and study, impaired productivity at work and, possibly more importantly, driving motor vehicles, although the study results do not specifically address any of these issues.

Perhaps of greater interest is that daily urticarial activity scores, quality of life and night-time sleep disturbance were, with a high level of probability in both treatment arms, substantially reduced, demonstrating that improved control of chronic urticaria symptoms leads to better sleep quality. In comparison with baseline, daytime somnolence was also reduced with levocetirizine monotherapy. Evidence for reduced somnolence in patients with chronic urticaria responding to levocetirizine has also been presented in an earlier study, indicating that patients with active chronic urticaria feel better after a good night's sleep, when their symptoms have been controlled.²

The authors acknowledge that the short duration of the study (5 days in each treatment arm) is shorter than many similar studies of urticaria, and that they did not perform objective assessments of alertness and productivity. There is evidence that the detrimental effect of hydroxyzine on driving performance is reduced after 8 days of continuous treatment,³ so it is possible that the small increase in subjective daytime somnolence in the hydroxyzine study arm observed at 5 days would have become even less with a longer study duration. Furthermore, in clinical practice, a regular 50-mg night-time dose of hydroxyzine would be relatively high for many patients with chronic urticaria and proportionately higher than 5 mg of levocetirizine if a therapeutic equivalence of 30 mg of hydroxyzine is accepted.

Nevertheless, this is the first published controlled study to examine and challenge the dogma that taking a sedating (first-generation) H1 antihistamine at night in addition to a

nonsedating H1 antihistamine at its licensed dose during the day provides a better night's sleep for patients with chronic urticaria than not taking a sedating antihistamine; this is in keeping with the recommendation of the 2009 European consensus guideline on the management of chronic urticaria, which recommends that sedating antihistamines should not be used unless there is a special indication.⁴

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