

Brief communications

Terfenadine ineffective in the prophylaxis of exercise-induced pruritus

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We studied a case of a 41-year-old man who suffered from pruritus while he was running. This pruritus was diagnosed as a mild form of cholinergic urticaria.

The exact mechanism of cholinergic urticaria is unknown, but it is believed to be initiated by an increase in body temperature (by 0.7° to 1° C), which triggers a cholinergic response and subsequent release of histamine from mast cells.¹ The focus on histamine as an important mediator followed studies of increases in the concentrations of histamine in patients with cholinergic urticaria,² in some cases, from eightfold to 25-fold, 15 to 30 minutes after exercise.^{3, 4} The degree of response does not, however, appear to be closely related to the concentration of histamine.⁴

When cholinergic urticaria is induced by exercise, an initial response is usually observed after 6 minutes (pruritus and mild urticaria). At 12 minutes, urticaria develops, and the maximal response that may include angioedema is observed at 25 minutes.³ Recovery, in individuals not suffering angioedema, normally takes 2 to 4 hours, and resolution of symptoms subsequent to anaphylaxis may take as long as 48 hours.

Given the involvement of histamine as a mediator and the recent availability of nonsedating H₁-receptor antagonists, such as terfenadine, we postulated that exercise-induced pruritus may respond to these agents. The sedating properties of the histamine-receptor antagonists, such as hydroxyzine and ketotifen, make them less appealing for use during exercise.

We performed a trial of the use of terfenadine as prophylaxis against the occurrence of pruritus. This study was done in a prospective, randomized, double-blind, and placebo-controlled fashion in a 41-year-old man who invariably suffered symptoms starting about 5 minutes into a run. An unmarked capsule containing either 60 mg of terfenadine or lactose was adminis-

Abbreviations used

CI: Confidence interval

VAS: Visual analogue score

TABLE I. The distance measured (in millimeters) from the "no itching" end of the VAS after treatment with terfenadine and placebo

Terfenadine (mm)*	Placebo (mm)†
72	74
79	66
71	83
69	71
66	79

*Mean, 71.4 mm; SEM, 2.15; 95% CI, 65.45 to 77.35.

†Mean, 74.6 mm; SEM, 2.95; 95% CI, 66.41 to 82.8 ($p = 0.2$; $\alpha = 0.05$; $\beta = 0.13$).

tered 2 hours (time to maximum blood concentration) before a run on 10 separate occasions.

Immediately after the run, the subject was instructed to indicate on a VAS the position that best represented the degree of pruritus. The VAS was a 10 cm line, without graduations, the ends of which were labeled "no itching" and "maximum degree of itching (Fig. 1)." The results were analyzed by measuring the position of the markings (in millimeters) from the "no itching" end of the scale (Table I).

The results were analyzed with a two-way Student's unpaired t test. There was no statistical difference ($p = 0.2$) between the terfenadine-treated (mean, 71.4 mm; 95% CI, 65.45 to 77.35) and placebo-treated (mean, 74.6 mm; 95% CI, 66.41 to 82.8) groups. A power analysis of the results ($\alpha = 0.05$) revealed that the study was capable of detecting a difference between the terfenadine and placebo treatments of as little as 9%. There were no side effects reported with either placebo or terfenadine treatment, and no demonstrable decrement in running performance.

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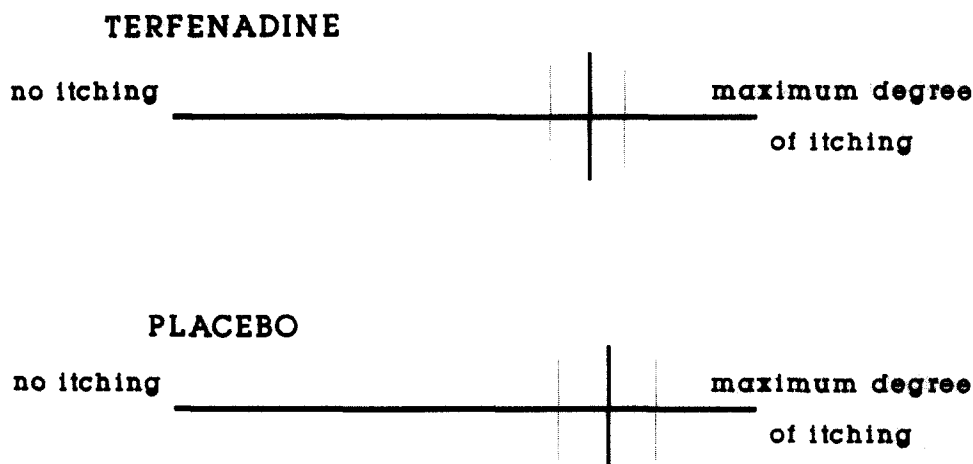


FIG. 1. VAS.

This small, but comprehensive, trial of one case illustrates the ineffectiveness of terfenadine in preventing even mild forms of cholinergic urticaria. A previous single-case study, not set up in a trial fashion, described the ineffective use of terfenadine and hydroxyzine in the treatment of a severe cholinergic urticaria.⁵ Other studies with hydroxyzine have been conflicting.⁴ The lack of effect displayed by terfenadine treatment may cast some doubt on the exact role of histamine in the etiology of this condition. It is clear that additional controlled studies are required to clarify probable mediators and the most effective treatment.

REFERENCES

1. Wilke WS. Exercise-induced allergic syndrome on the increase. *Cleve Clin J Med* 1989;56:665-6.
2. Leung AKC, Hegde HR. Exercise-induced angioedema and asthma. *Am J Sports Med* 1989;17:442-3.
3. Lawrence CM, Jorizzo JL, Kobza-Black A, Coutts A, Greaves MW. Cholinergic urticaria with associated angio-oedema. *Br J Dermatol* 1981;105:543-50.
4. Kaplan AP, Natbony SF, Tawil AP, Fruchter L, Foster M. Exercise-induced anaphylaxis as a manifestation of cholinergic urticaria. *J ALLERGY CLIN IMMUNOL* 1981;68:319-24.
5. McClean SP, Arreaza EE, Lett-Brown MA, Grant JA. Refractory cholinergic urticaria successfully treated with ketotifen. *J ALLERGY CLIN IMMUNOL* 1989;83:738-41.

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