
Correspondence

DIPHENHYDRAMINE VS DESLORATADINE COMPARISONS MUST CONSIDER RISK-BENEFIT RATIO

To the Editor:

The recent study by Raphael et al¹ that compared 1 week's treatment with diphenhydramine hydrochloride, 50 mg, 3 times daily vs desloratadine, 5 mg, once daily and placebo in patients with seasonal allergic rhinitis (AR) raises important points that warrant comment. First, the findings reported for desloratadine are in contrast to its documented efficacy vs placebo in the treatment of nasal and nonnasal symptoms of seasonal (fall/spring) AR for 2 and 4 weeks and perennial AR for up to 4 weeks, as reported in multiple studies.²

Second, the underlying rationale for the study is unclear. Although the efficacy of first-generation agents has been acknowledged, second-generation compounds have long replaced them as preferred treatment for AR. National and international guidelines note that a more favorable risk-benefit ratio and enhanced pharmacokinetics make second-generation drugs preferable to first-generation drugs.^{3,4} Neither of these issues was considered in the study by Raphael et al.¹ The risk-benefit ratio for diphenhydramine is poor owing to the high incidence of sedation and cholinergic adverse effects, as confirmed by this study. Although sedation was reported in 22.1% of patients, this likely represents an underestimation because participants may experience significant objective cognitive impairment without reporting sedation. The decrease in reported somnolence to approximately 15% later in the week could represent patients "getting used to" feeling sedated but still remaining objectively impaired.

Cognitive impairment due to sedating antihistamines is a serious issue with important occupational correlates. Sedating antihistamines can impair learning and academic performance in schoolchildren.⁵ As noted in the Joint Task Force guidelines,³ first-generation antihistamines cause driving impairment and may contribute to automobile accidents. Everyday activities requiring mental alertness, such as driving and operating machinery, can be impaired by diphenhydramine.^{6,7} The Federal Aviation Authority forbids medical certification of pilots taking sedating antihistamines, whereas nonsedating antihistamines, including desloratadine, are permissible.⁸ Sedation is a subjective feeling of drowsiness, whereas impairment is an objective measure. Studies^{9,10} have shown that patients taking diphenhydramine may not complain of sedation but have significant impairment when measured.

Desloratadine has a subjective/objective impairment profile similar to placebo, and direct comparisons using

relevant measures have shown that desloratadine causes significantly less impairment of performance and vigilance in patients with seasonal AR.¹¹ It is unclear from the study by Raphael et al¹ whether relevant warnings/screenings regarding cognitive impairment were part of patient management. Given that the maximum dose of diphenhydramine (150 mg/d) was used, it seems appropriate for the study sponsor to have included such safety screening in a prospective trial.

When judging the relative clinical value of antihistamines, one must take account of clinical safety and efficacy because both factors determine optimal patient care. Apportioning greater relative importance to short-term statistical benefits in terms of symptom scores while minimizing the sizable impact of cognitive impairment seems to be a retrograde step and runs counter to the current standard of care.

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EMERGENCY DEPARTMENT TREATMENT OF ANAPHYLAXIS: IS EPINEPHRINE ALWAYS INDICATED?

To the Editor:

Injectable epinephrine is the treatment of choice for anaphylaxis. My experience with anaphylaxis suggests that epinephrine may not always be needed in the emergency department (ED) treatment of anaphylaxis.

Recent symposia and practice parameters state that injectable epinephrine is the treatment of choice for anaphylaxis and antihistamines are slow in onset and are second-line drugs in anaphylaxis treatment.^{1,2} Certainly, epinephrine is the treatment of choice in anaphylaxis that occurs outside the hospital. However, there is some debate between ED physicians and allergists regarding whether epinephrine is the drug of choice for treating anaphylaxis in patients who present to an ED without respiratory compromise, reduced blood pressure, or symptoms of end organ dysfunction.

In July 2005, approximately 15 minutes after taking 2 naproxen tablets (200 mg), I experienced intense itching in my groin followed by generalized pruritus, erythema, and swelling of my hands, feet, and tongue. On arrival at a local ED, my pulse rate was 120/min, blood pressure was 160/110 mm Hg, and oxygen saturation was normal. On physical examination, I had generalized erythema and edema of my hands, feet, tongue, and uvula. The emergency physician, who was understandably reluctant to administer epinephrine in view of my age, tachycardia, and hypertension, administered intravenous diphenhydramine (50 mg), cimetidine (300 mg), and methylprednisolone sodium succinate (80 mg). Within 2 minutes, the erythema, edema, and pruritus of my hands, feet, and tongue began to resolve. Fifteen minutes later, my pulse rate was 80/min and my blood pressure was 110/60 mm Hg. Four hours later, I was asymptomatic and was discharged.

The point of this letter is that maybe not every anaphylactic patient who presents to an ED with no respiratory or cardiovascular compromise requires epinephrine, especially if he or she has tachycardia or hypertension. In a medical record review of 678 patients who presented with food allergy to 21 EDs, only 16% received epinephrine.³ In another study of 617 patients with insect sting allergy, only 12% received epinephrine.⁴ In both these studies, more than 95% of the patients were discharged, implying that epinephrine was not needed in many cases.

After this encounter, I am not sure that the underuse of epinephrine by ED physicians is as bad as allergists perceive. I was impressed with the rapid onset of action of intravenous antihistamines. The dogma that antihistamines are “slow in onset and are second-line” drugs in anaphylaxis may only apply to oral antihistamines. Clinical trials in ED patients with anaphylaxis that compare intramuscular epinephrine

with intravenous antihistamines might be worthwhile in normotensive or hypertensive patients with no respiratory compromise or no signs of end organ dysfunction.

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RAGWEED POLLEN TRAVELS LONG DISTANCE

To The Editor:

The article by Cecchi et al¹ provides new information on the mechanisms by which ragweed pollen, traveling across Europe, can cause allergy in Italy, where the plant is not indigenous. The authors remark that whereas Lombardia² and Friuli Venezia-Giulia are the most affected regions in Italy, no data are available from other more central Italian regions about the prevalence of ragweed sensitization in atopic individuals. Our outpatient allergy clinic is located in Bologna (approximately 100 km east of Pistoia and Florence), and most of the patients referred are locals. Approximately 7 months ago we introduced an extract of *Ambrosia artemisiifolia* into the panel of airborne allergens to be tested in individuals with a clinical history of respiratory symptoms (rhinitis with or without asthma). Of 1,048 patients (406 males and 642 females) who have since undergone skin prick testing, 360 were negative for all airborne allergens. Five hundred patients (211 males and 289 females) had positive reactions (wheal of at least 3 mm) to at least 1 allergen, of which 188 (37%) have been found to be positive for *A artemisiifolia*; the 2 sexes were similarly represented (90 males and 98 females), with prevalences of 43% and 34%, respectively ($\chi^2 = \text{NS}$). Their median age was 36 years (range, 7–73 years), and all the patients, except 1 male, were sensitized to at least 1 other airborne allergen. In particular, 144 patients (76%) also had positive skin test reactions to other Compositae, ie, *Artemisia vulgaris* or *Artemisia absinthium* (mugwort). In conclusion, more than one third of our atopic patients are sensitized to ragweed. Whether the sensitization to ragweed is primarily induced by the ragweed pollen itself or is due to cross-reactivity with the indigenous

Compositae (mugwort) remains to be established. Indeed, recent studies³ have shown that although ragweed and mugwort belong to the same plant family and share some cross-reactive allergens, their major allergens (protein of the family of pectate lyases and glycoprotein rich in hydroxyproline residues, respectively) are unrelated proteins.

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