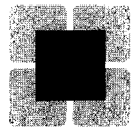

Treatment of chronic idiopathic urticaria with astemizole

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■ Astemizole is a new, long-acting H_1 receptor antagonist that has proven effective in controlling the signs and symptoms of chronic idiopathic urticaria, without the sedative and anticholinergic side effects that typify use of many antihistamines. In an eight-week open study of 20 patients, astemizole significantly decreased the signs and symptoms of urticaria, as well as the severity of urticaria by anatomic location. Five patients reported complete clearing. Modest weight gain while on chronic therapy appears to be a significant side effect.

□INDEX TERM: URTICARIA, DRUG THERAPY □CLEVE CLIN J MED 1989; 56:263–266

CHRONIC idiopathic urticaria is notoriously difficult to treat. Therapy using a variety of antihistamines often affords minimal relief. Since antihistamine dosing to control the urticaria can lead to incapacitating sedation or anticholinergic symptoms, physicians may resort to systemic corticosteroids to achieve symptomatic relief.

Astemizole, a new, long-acting H_1 receptor antagonist, has no chemical relationship to other known drugs.[1] Preliminary studies[2–7] reveal astemizole to be devoid of central, sedative, and/or peripheral anticholinergic effects while controlling the symptoms of chronic idiopathic urticaria. This absence of typical antihistamine side effects makes astemizole an attractive option for drug treatment of this disorder.

Twenty patients were entered in an open clinical trial to assess the efficacy of astemizole in reducing symptoms of chronic idiopathic urticaria and whether symptom reduction was associated with absence of classic antihistamine side effects.

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MATERIALS AND METHODS

The study included men and women aged 18 years and older who had urticaria not related to a known underlying disease and recurring at least two to three times a week for more than three months. Study inclusion required urticaria symptoms of at least moderate severity, defined as bothersome but tolerable and not interfering with daily activity.

All antihistamines, aspirin, or corticosteroids (systemic or topical) were discontinued for all patients for three days prior to initiation of therapy and for the duration of the study.

Patients took three astemizole tablets (10 mg) on the first day, two astemizole tablets (10 mg) on the second day, and one astemizole tablet (10 mg) daily for the next 54 days. The tablets were taken all at once before bedtime, at least two hours after a meal.

Evaluation on day 1 of the study included an SMA-16, complete blood count with differential, serum preg-

TABLE 1
SUBJECTIVE ASSESSMENTS OF URTICARIA SEVERITY BY ANATOMIC LOCATION OVER TIME*

	After Washout			Week Four			Week Eight		
	N	Mean	Median	N	Mean	Median	N	Mean	Median	P
Head	20	1.6	2.0	19	0.6	1.0	17	0.5	0	<.01
Trunk	20	2.2	2.0	19	0.8	1.0	8	1.0	0	.02
Arms	20	2.0	2.0	19	0.9	1.0	16	0	0	<.01
Hands	20	1.4	1.0	19	0.6	0	2	1.0	1.0	.26
Legs	20	2.2	2.0	19	1.0	1.0	5	1.6	2.0	.32
Feet	20	1.0	1.0	19	0.4	0	15	0	0	<.01

TABLE 2
GLOBAL ASSESSMENT OF URTICARIA SEVERITY OVER TIME*

	After Washout			Week Two			Week Four		
N	Mean	Median	N	Mean	Median	N	Mean	Median	P
20	1.7	1.8	19	0.8	0.8	19	0.7	0.5	<.01

*Determined by Friedman's two-way analysis of variance
Rating code: *0* = absent (no urticaria), *1* = mild (noticed only a slight problem with urticaria), *2* = moderate (have been aware of bothersome urticaria from time to time), *3* = severe (urticaria has been bothersome all the time but did not disrupt daily activities), and *4* = very severe (urticaria was very bothersome and disrupted daily activities)

nancy test (as applicable), clinical assessment, baseline plasma sampling, and photograph. At follow-up visits two and four weeks later, astemizole plasma samples were obtained and clinical assessment was done. At the final visit, eight weeks later, the same laboratory tests as performed on day 1 were repeated. A clinical assessment was also done, and a photograph was taken.

All patients kept a daily diary to record frequency and severity of urticaria. The severity of the worst daily attack was graded on a scale of 0 to 10 by the patient.

RESULTS

Seventeen of the 20 patients completed the study. One patient was excluded because of a protocol violation at week 2. A second patient quit the study at week 4 because the drug was ineffective; this patient had been on long-term dexamethasone (0.75 mg/d) prior to the study. A third patient left the study at week 7, complaining of "water" weight gain and bloated feeling. Her urticaria, in her own view, had decreased.

The severity of urticaria by anatomic location and by signs and symptoms was determined before and after the washout period. There was no statistical difference between pre-washout and post-washout severity of urticaria for these variables (assuming a level of significance at $P<.05$).

Subjective assessment of severity of urticaria over time by anatomic location revealed a statistically significant improvement for the head, trunk, arms, and feet (*Table 1*). A global assessment also revealed significant improvement (*Table 2*). A subjective assessment of the signs and symptoms of urticaria over time indicated statistical improvement except for angioedema and excoriations (*Table 3*).

Five of the patients reported complete clearing at study's end.

There were nine recorded adverse reactions. One patient complained of unusual dreams, another reported blurred vision, a third said she missed her menstrual period once, a fourth complained of weight gain, and a fifth reported sore nipples. A sixth patient complained of nausea and change of hair color, as well as increased thirst and appetite. There was not a single report of sedation or anticholinergic effects; however, there was a statistically significant weight gain for the group finishing the study (*Table 4*).

DISCUSSION

The symptoms of chronic idiopathic urticaria can be controlled with a variety of antihistamines. A major drawback to this form of therapy has been the dose-limiting sedative and anticholinergic effects that many H_1 receptor antagonists produce.[8]

The effects of astemizole differ from those of H_1 antihistamines in that there are negligible central nervous system depressant or anticholinergic effects.[1] Not surprisingly, it does not readily cross the blood-brain barrier.[8] Once bound to H_1 histamine receptors, astemizole

TABLE 3
SUBJECTIVE ASSESSMENT OF URTICARIA SEVERITY OF SIGNS AND SYMPTOMS OVER TIME*

	After Washout			Week Four			Week Eight		
	N	Mean	Median	N	Mean	Median	N	Mean	Median	P
Wheals	20	6.8	7.5	19	2.4	2.0	17	1.8	2.0	<.01
Pruritus	20	6.9	8.0	19	1.7	1.0	17	1.1	1.0	<.01
Erythema	20	6.8	7.0	19	3.0	2.0	17	2.1	2.1	<.01
Edema	20	3.6	3.5	19	0.4	0	17	0.5	0	<.01
Angioedema	20	1.2	0	19	0.5	0	17	0.4	0	.43
Excoria	20	0.5	0	19	0	0	17	0	0	.99

*Determined by Friedman's two-way analysis of variance
Rating code range: *1* = none to *10* = severe

TABLE 4
WEIGHT GAIN (IN POUNDS)*

	N	Mean	SD	Range	P
Begin	20	169.2	36.4	124–275	
End	16†	178.2	40.4	128–280	
Δ	16				.02

*Determined, in part, by paired *t* test
†The final number of patients recorded is 16 because of the inadvertent failure to record a final weight for one patient

is extremely slow to dissociate.[1] Elimination of the metabolized drug is slow, with a half-life between 18 and 20 days reported for patients on long-term dosing of 10 mg/d.[1] These characteristics allow single daily dosing. Food intake decreases drug bioavailability,[1] which necessitates ingesting the drug on an empty stomach.

Our results concur with those of previous studies assessing the positive effect of astemizole on controlling the signs and symptoms of chronic idiopathic urticaria.[3–7] The notable lack of central nervous system depression and anticholinergic effects has also been reported.[2–4,6,8] Although it was not a major complaint of our patients, there was a statistically significant increase in weight for those who completed the study. Weight gain while on astemizole has been noted.[3,4]

In a recent clinical trial[3] of astemizole in the treatment of chronic idiopathic urticaria, patients on chronic systemic corticosteroids were allowed to continue their use during the study. Our protocol required discontinuation of corticosteroids (topical and systemic) prior to and during the study. The single patient dropped from our study as a result of poor drug efficacy had been taking dexamethasone for several years. He recently has combined astemizole with low-dose dexamethasone, which has allowed him to decrease his steroid dose by 50% (to 0.375 mg/d). We will attempt to taper his dose further. In this way, astemizole may allow patients with chronic urticaria to decrease or discontinue use of systemic steroids.

The use of an open clinical trial without controls can be viewed as a drawback when assessing our data. It cannot be denied that some patients might have experienced a lessening of their urticarial signs and symptoms, had there been no treatment. However, two of our patients suffered from severe urticaria with associated angioedema resulting in emergency-room visits and periodic dosing with systemic corticosteroids. All of these patients regarded astemizole as the best noncorticosteroid therapy they had used.

SUMMARY

Astemizole appears to be effective in the treatment of chronic idiopathic urticaria. Side effects are minimal, without a single complaint of sedation in the 17 patients who completed our study. The major drawback associated with astemizole use appears to be weight gain. Astemizole may allow for a decrease or discontinuation of systemic corticosteroids in patients who require chronic steroid therapy for control of urticaria; conclusive statements would require further study.

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