

Urticaria in Thai Children

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Urticaria, with or without angioedema, is a common disorder which affects up to 20% of the population at some time or other.¹ Survey of 1,256 Mahidol University students in Thailand revealed that 58.2% of them had a history of urticaria.² The acute form of the disease is common in young patients of either sex and it is usually mediated by IgE-dependent mast cell activation. It occurs primarily in atopic individuals and often has a definable etiology. Chronic urticaria is less common, and has no predilection for atopic individuals. It is usually found in middle-aged women. It presents more difficulty in diagnosis, and we usually fail to find the cause in the majority of individuals affected.^{3,4}

Since no study of urticaria has been described in Thai children to date, we conducted a prospective study to elucidate its general occurrence.

SUBJECTS AND METHODS

For this study, 142 children under 12 years of age with a diagnosis of urticaria, with or without angioedema were studied. They had been referred to the Allergy Clinic, Department of

SUMMARY In this study, 142 patients under 12 years of age with the diagnosis of urticaria accompanied or not by angioedema were examined. In all 72.6% of the patients were under 6 years of age. Boys and girls were equally affected, 13.4% of the cases had chronic urticaria, 56.3% had a previous history of urticaria, 88.0% had generalized urticaria, and about half of the cases had associated angioedema. The causes of the urticaria were identified or suspected in 32.4% of the cases. Drugs, foods, insect bites and stings, infections and cold were the most common or associated precipitating agents in that order. Histories revealed 27.5% of the cases had records of other allergic diseases, and 76.1% had allergic diseases in the family. Dermographisms were found in 16.2% of the cases, and 22.5% of cases had eosinophilia. The means of IgE levels in both acute and chronic urticaria were within normal limits, and there was no statistically significant difference between the two groups. Skin testing was of little practical value in evaluating the etiology of the urticaria. Clinical trials of drugs for symptomatic treatment revealed that clemastine, ketotifen and hydroxyzine gave approximately equally high response rates. All these three medications gave significantly greater response rates than chlorpheniramine.

Pediatrics, Faculty of Medicine, Siriraj Hospital in the period of 1982-1984. Comprehensive histories, physical examinations, and diagnostic tests were performed. History details included age, duration of illness, history of previous urticarial episodes, factors which might be etiologic causes and associated allergic diseases in the patients and in the family. Laboratory tests included complete blood counts, absolute eosinophil, and stool examinations for ova and parasites.

A test for dermographism was evaluated by development of wheal after stroking with moderate pressure on the volar surface of the forearm.

Serum IgE was determined by the ELISA method. Some patients received allergy skin tests by the prick method with 34 common antigens including inhalants, household materials and foods.

To evaluate the efficacy for symptomatic relief of urticaria of different types of antihistamines, the patients were randomized into 4 groups by sex ratio, age distribution and duration of urticaria to receive one of

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four medications. These were chlorpheniramine, hydroxyzine, clemastine and ketotifen. The doses were chlorpheniramine maleate 0.35 mg/kg/day, hydroxyzine hydrochloride 1 mg/kg/day, clemastine 0.05 mg/kg/day, and

ketotifen 0.04 mg/kg/day. The medication was given by mouth in divided doses twice daily. The patients were then followed up every week. If the lesions completely disappeared within 7 days, the treatment was considered to

be effective and the date of disappearance of the lesions after treatment was recorded. If the lesions persisted beyond 7 days, the treatment was considered a failure. The rate of improvement of each drug was compared by statistical analysis.

Table 1 Age and Sex

| Patients | Cases | Percent |
|-----------|-------|---------|
| Number | 142 | 100 |
| Age (yrs) | | |
| < 1 | 17 | 12.0 |
| 1-6 | 86 | 60.6 |
| > 7 | 39 | 27.4 |
| Sex | | |
| Male | 69 | 48.6 |
| Female | 73 | 51.4 |

Table 2 Possible causes of urticaria

| | Cases | Percent |
|------------|-------|---------|
| Yes | 46 | 32.4 |
| No | 96 | 67.6 |
| Causes | | |
| Drugs | 24 | 16.9 |
| Foods | 14 | 9.9 |
| Insects | 3 | 2.1 |
| Infections | 3 | 2.1 |
| Cold | 2 | 1.4 |

Table 3 Associated allergic diseases in the patients

| | Cases | Percent |
|----------------------------------|-------|---------|
| No associated allergy | 103 | 72.5 |
| Associated with other allergies* | 39 | 27.5 |
| Asthma | 12 | 8.5 |
| Allergic rhinitis | 8 | 5.6 |
| Food allergy | 13 | 9.2 |
| Drug allergy | 12 | 8.5 |
| Atopic dermatitis | 5 | 3.5 |

*Some patients had more than one associated allergic disease.

Table 4 History of allergic diseases in the family.

| | Cases | Percent |
|-----------------------------|-------|---------|
| Negative | 34 | 23.9 |
| Positive | 108 | 76.1 |
| Positive family history of* | | |
| Urticaria | 61 | 43.0 |
| Allergic rhinitis | 49 | 34.5 |
| Asthma | 42 | 29.6 |
| Drug allergy | 16 | 11.3 |
| Atopic dermatitis | 8 | 5.6 |
| Food allergy | 6 | 4.2 |

*Some patients had a history of more than one allergic disease in the family.

Table 5 Investigations

| | Percent |
|---------------------------------|---------|
| Dermographism | 16.2 |
| WBC > 10,000/mm ³ | 69.9 |
| Peripheral eosinophils | |
| < 500/mm ³ | 77.5 |
| > 500/mm ³ | 22.5 |
| Positive parasitic ova in stool | 10.6 |

Table 6 Skin tests (Prick test with 34 antigens)

| | 20 Cases |
|--------------------------|----------|
| Total cases | 20 Cases |
| Negative to all antigens | 55 % |
| Positive to* | |
| Households | 30 % |
| Epidermals | 10 % |
| Weeds | 10 % |
| Grasses | 5 % |
| Trees | 5 % |
| Molds | 5 % |
| Foods | 5 % |

*Some patients had positive skin tests for more than one antigen.

RESULTS

The results of the study are shown in Tables 1-6.

Serum IgE was determined in 105 cases. Analysis was made to delineate any difference between patients with acute and those with chronic urticaria. However, we found that the means of IgE in the groups of acute and chronic urticaria were 281.1 IU/ml and 198.9 IU/ml, respectively, which were within the normal range. There was no statistical significant difference.

The children were allocated to

one form of symptomatic treatment. Details of the randomization sex ratio, age distribution and duration of urticaria are shown in Table 7. Details of the results are shown in Table 8. The response rate to the 4 drugs appeared to be independent of past history, IgE levels, or skin test results.

DISCUSSION

Urticaria is a manifestation of mediators released from cutaneous mast cells, which can be activated by several mechanisms. Although urticaria is common in adulthood, infants and

children are also affected. The age of our patients was limited to less than 12 years, with 72.6% under 6 years of age and 12% infants. Females accounted for 51.4% of the patients, so that no sex predilection was found. This figure is approximately the same as that of Champion *et al*³ who found that 54% of 438 cases with urticaria were females. Of our patients, 86.6% had the acute type of urticaria (duration less than 6 weeks).

The majority of our patients had generalized urticaria. Half of the cases were associated with angioedema. This

Table 7 Randomized groups of patients in trials with 4 different drugs

| | Cases | | | |
|-------------------------|------------------|-------------|------------|-----------|
| | Chlorpheniramine | Hydroxyzine | Clemastine | Ketotifen |
| Total | 38 | 35 | 32 | 37 |
| Age (yrs): < 1 | 6 | 5 | 2 | 4 |
| 2-6 | 22 | 22 | 20 | 22 |
| 7-12 | 10 | 8 | 10 | 11 |
| Mean | 4.5 | 4.5 | 5.0 | 4.6 |
| Sex : Male | 22 | 14 | 10 | 23 |
| Female | 16 | 21 | 22 | 14 |
| Duration of urticaria : | | | | |
| < 1 week | 25 | 19 | 18 | 14 |
| 1-2 weeks | 7 | 5 | 8 | 8 |
| 2-6 weeks | 3 | 8 | 3 | 5 |
| >6 weeks | 3 | 3 | 3 | 10 |

Table 8 Results of treatment

| Drugs | No. of Patients | No improvement % | Improvement % | Time required for improvement | |
|------------------|-----------------|------------------|---------------|-------------------------------|------------|
| | | | | <3 days % | 3-7 days % |
| Chlorpheniramine | 38 | 26.3 | 73.7 | 60.5 | 13.2 |
| Hydroxyzine | 35 | 14.3 | 85.7 | 54.3 | 31.4 |
| Clemastine | 32 | 8.1 | 91.9 | 62.2 | 29.7 |
| Ketotifen | 37 | 6.3 | 93.7 | 75.0 | 18.7 |

figure is similar to that in a previous report which considered urticaria and angioedema together. There, approximately 40% of the patients had urticaria without associated angioedema, 49% had urticaria and angioedema and 11% had angioedema only.³

In the present study, the etiologic factors of urticaria were identified or suspected in 32.4% of the cases. Previous studies have reported variable success in establishing the etiology of urticaria ranging from 21%³ to 100%.⁸ The reasons for the variation are potentially many but are mostly related to the criteria used for establishing an etiology and to the population studied. The most frequently encountered diagnosis in our series was drugs. The penicillins group, sulfonamides, and aspirin were found to be the most common causes in that order. Food was found to be second rank of etiologic factors of our patients. Of these, sea foods, fish, raw or preserved foods, egg, and some cases of food additives were suspicious.

Insect bites and hymenoptera stings can cause urticaria.⁵ One case of insect bite and 2 cases of hymenoptera stings were the preceding events in our patients. Various infections have been reported to be the etiologic factors of urticaria including parasitic infestations,⁷ streptococcal infections,⁹ mycoplasma infections,¹⁰ type B virus hepatitis⁴ and fungal infections.¹¹ Focal bacterial infections such as sinus, dental, tonsillar, chest, gastro-intestinal and genitourinary infections have also been noted as cause of urticaria.⁶ One of our patients developed urticaria after generalized pyoderma. Fifteen of our cases were found to have ova of parasites in stools. These were *Ascaris lumbricoides* ova and *Giardia lamblia* cyst. In two of our cases, urticaria was probably caused by ascaris infestations since urticaria persisted after antihistamine therapy

but disappeared after anthelmintic administration. In the remainder of the cases, parasitic ova were probably coincidental. We could not correlate urticaria with dental caries in our patients, since the majority of our children had this problem. We did not study HBsAg since there was no history or physical examination suggestive of hepatitis in our cases.

Association with other allergic diseases was found in 27.5% of our cases. This figure is less than the association with other allergic diseases in Thai asthmatic children (64%).¹²

Our patients had a history of allergic diseases in the family in 76.1% of the individuals and urticaria in the family in 43.0%. Genetic factors are found to be important in certain types of urticaria or angioedema including hereditary angioedema, familial cold urticaria, vibratory angioedema, hereditary familial syndrome of urticaria, deafness and amyloidosis, and erythropoietic protoporphyria. In addition, the occurrence of some forms of urticaria, especially the acute ones, is probably increased in patients with an atopic genetic background.¹⁶

Dermographism was found in 16.2% of our cases. This condition occurs in 1.5-23% of the general population and may be elicited in patients with chronic urticaria.¹⁰ However, there is some debate concerning the incidence of this association, which seems to be no greater than that in the normal population. The reason is that skin which has been the site of a recent urticarial wheal will not show any increased tendency to wheal on trauma in chronic urticaria. However, in some acute urticarias this phenomenon has been noted.^{1,3} Some authors believe that dermographism is a condition quite distinct from chronic urticaria.¹⁰ In our cases there was no history sugges-

tive of solar, cholinergic, psychogenic urticaria or evidence of vasculitis.

Serum IgE was determined in 105 cases in our study. The means of serum IgE levels were within normal limits, and there was no difference between acute and chronic cases. This finding confirmed that of Julin *et al*¹⁴ who found that serum IgE values were generally normal in a group with chronic urticaria. It therefore seems that very little practical value would arise in clinical practice from determination of the IgE levels in urticaria.

Skin tests are of limited value, but may be beneficial in cases of suspected inhalant or food. The majority of our cases that showed positive skin tests had association with respiratory allergic diseases, and the positive tests were not correlated well with suspected cause of urticaria. We have found little reason to encourage routine skin testing in all patients with urticaria. Exceptions include those patients with a history suggestive of urticaria after exposure to antigen; skin tests may confirm such suspected antigens.

For treatment of urticaria, identification and removal of the cause is the ideal. If this is not possible then reduction of various triggering factors should be attempted. Traditional antihistamines of the H₁ type are the mainstay in symptomatic management of urticaria. It is difficult to compare the efficacy of antihistamines in the treatment of urticaria, since there are many factors involved. These include etiology, duration of lesion, severity of disease, etc. However, in this study we tried to eliminate bias by randomizing the patients according to sex, age, and duration of urticaria into 4 groups which received different medications. The response rate to chlorpheniramine was 73.7%, to hydroxyzine 85.7%, to clemastine 91.9%, and to ketotifen 93.7%.

At the present time, hydroxyzine hydrochloride is being increasingly used in the treatment of urticaria.^{5,6} Previous studies have shown that hydroxyzine is more effective than traditional antihistamines in inhibiting wheal-flare skin reactions,¹⁵ suppressing histamine-induced pruritus¹⁶ and dermatographia.¹⁷ Our results have shown that clemastine and ketotifen give approximately equally high response rates in treatment of urticaria and this confirms the study of Esau *et al.*¹⁸ They found that ketotifen had antihistaminic action in man equivalent in potency to clemastine in attenuation of cutaneous reactions to histamine and allergen challenge. Furthermore, our results showed that ketotifen and clemastine were effective without statistical difference from hydroxyzine ($p > 0.05$). All these three medications showed significantly greater response rates than chlorpheniramine ($p < 0.05$).

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