

Increased urinary excretion of 1.4-methyl-imidazoleacetic acid in patients with atopic dermatitis

R. LINDSKOV,^{1,2} A. WÆRSTED,¹ O. BAADSGAARD² & I. SØNDERGAARD³

¹Dept. of Dermatology, the Finsen Institute, Copenhagen, ²Dept. of Dermatology, Gentofte Hospital, and ³Medical Dept. TA, Division of Allergology and Laboratory for Medical Allergology, Rigshospitalet, University of Copenhagen, Denmark

To investigate whether the overall histamine turnover is increased in patients with atopic dermatitis, without respiratory disease, the urinary excretion of the main histamine metabolite 1.4-methyl-imidazoleacetic acid (MIAA) was examined in 23 patients and in 23 age- and sex-matched non-atopic controls. The patients excreted significantly more MIAA than the controls. One third of the patients however, showed MIAA excretion within or below normal range. The MIAA excretion was neither correlated to the severity of the eczema nor to the total serum IgE. It was concluded that histamine does not play a significant role in the pathophysiology of atopic dermatitis, and that the great variation in MIAA excretion, and hence the histamine turnover, reflected the spectrum of histamine releasability in the patients.

Key words: atopic dermatitis; histamine; methyl-imidazoleacetic acid; IgE

Accepted for publication 24 May 1988

Histamine levels have been shown to be elevated in the affected skin of patients with atopic dermatitis (AD) (6). Plasma histamine levels were increased in two studies (13) and normal in one study (12) concerning AD patients. Atopics show a reduced threshold to stimuli in the maximal histamine release from leucocytes both after anti-IgE and non-specific stimulation (1, 3, 7, 12).

To investigate whether the overall histamine turnover is increased in patients with AD we examined the urinary excretion of the main histamine metabolite 1.4-methyl-imidazoleacetic acid (MIAA) in 23 patients with AD.

MATERIAL AND METHODS

The investigation comprised six men and 17 women, median age 19 years (range 4-43), with moderate to severe AD, as defined by Hanifen & Rajka (5). None of the patients had had symptoms of asthma or rhinitis within 3 months

prior to the investigation. Median serum IgE level was 942 units/ml (range 11-9400). At the time of investigation the patients received medium strength topical steroids for their eczema. The eczema severity was assessed using a 4-graded global score: slight = 1, moderate = 2, severe = 3, very severe = 4. Age- and sex-matched healthy non-atopic individuals were used as controls.

A 24-h urine sample was collected from each subject. Volumes were measured and 10 ml aliquots were taken and stored at -20°C until analysis. Quantitative determination of MIAA in urine specimens was performed by reversed phase ion-pair high-performance liquid chromatography (HPLC) as described by Søndergaard (14). To minimize the intake of histamine the patients followed our laboratory's standard low histamine diet during the urine collection (14).

The Mann-Whitney's rank sum test and linear regression with the least squares' method were used to analyse the data.

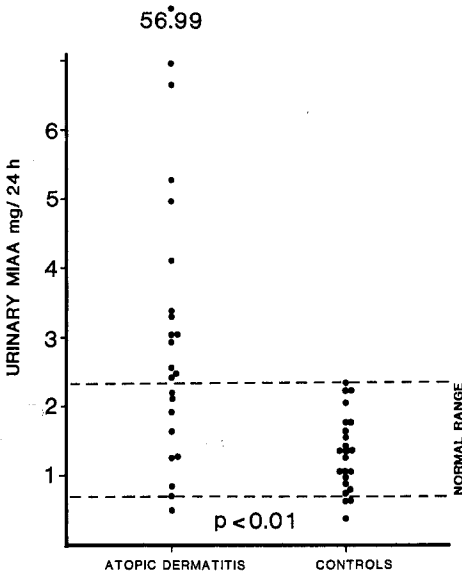


Fig. 1. Urinary excretion of MIAA in 23 patients with AD and in 23 non-atopic controls.

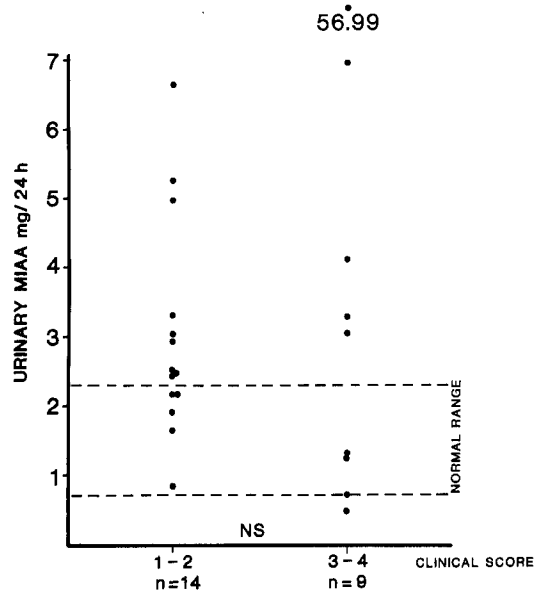


Fig. 2. Urinary excretion of MIAA in patients with moderate eczema (scores 1-2) and in patients with severe eczema (scores 3-4).

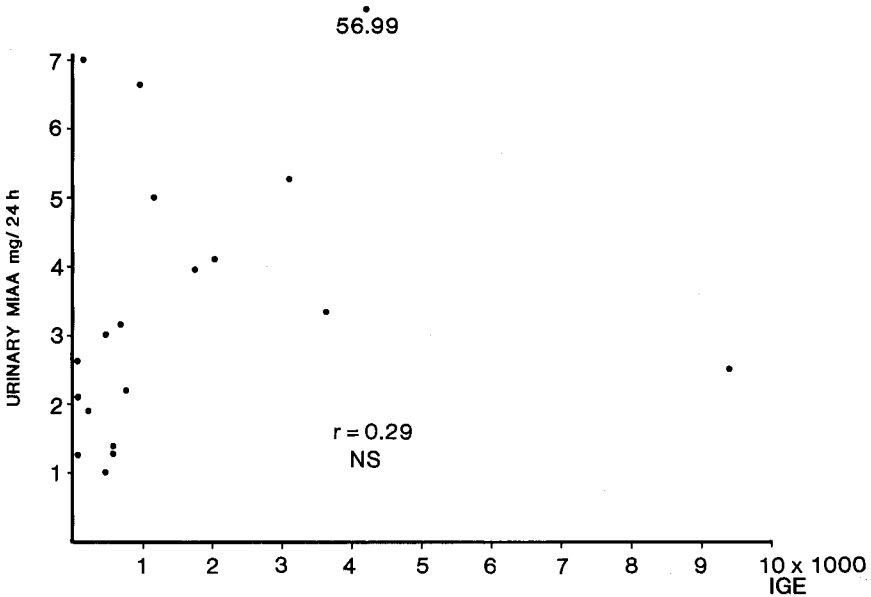


Fig. 3. Correlation between urinary excretion of MIAA and total serum IgE.

RESULTS

Median urinary excretion of MIAA was 2.52 mg/24 h (range 0.49–56.99) in the 23 patients compared with 1.37 mg/24 h (range 0.39–2.34) in the controls. The difference was significant ($P < 0.01$) (Fig. 1). However, nine patients (39%) had urinary excretion of MIAA within or below normal range. The median MIAA excretion in 14 patients with slight to moderate eczema (scores 1 and 2) was 2.50 mg/24 h (range 0.84–6.66), while the median MIAA excretion in nine patients with severe eczema (scores 3 and 4) was 3.03 mg/24 h (range 0.49–56.99). The difference in MIAA excretion between these two groups was not significant (Fig. 2). There was no correlation between total serum IgE and urinary excretion of MIAA (Fig. 3).

DISCUSSION

In the present study we have shown that, compared with a control group of non-atopics, a proportion of patients with AD excrete increased amounts of the main histamine metabolite MIAA in urine. This result is apparently in contrast to that of Overgaard-Pedersen et al. (9), who found that patients with AD did not excrete more histamine in the urine than non-atopic controls. However, urinary histamine may not be a reliable indicator of the histamine metabolism (4), while determination of the amount of MIAA in a 24-h urine should be a good indicator of the overall histamine turnover (8). All patients were treated with a medium strength topical steroid. This may have caused reduction of the histamine release from basophilic leucocytes (2), implying that the MIAA excretion might have been even higher without steroid treatment. We found no correlation between MIAA excretion and eczema severity. Moreover, approximately one third of the patients showed MIAA excretion within or below normal range. Butler et al. (3) and Lebel et al. (7) have defined high and low histamine releaser subgroups of patients with AD. Histamine releasability was not correlated to the activity of the eczema (3). The MIAA excre-

tion, in the present investigation, did not correlate to the serum IgE levels. This result is in line with the reported poor correlation between histamine releasability and serum IgE levels (3).

In conclusion, the results of the present study do not support the view that histamine plays a significant role in the pathophysiology of AD. To further classify the role of histamine in AD, longitudinal studies of the MIAA excretion are desirable.

REFERENCES

- Allen, D. H., Mathison, D. A., Wagner, P. D., Arroyave, C. M., Plow, E. & Tan, E. M.: Mediator release during methacholine-induced bronchoconstriction in asthmatic patients. *Allergy Clin. Immunol.* 61, 140, 1978.
- Bergstrand, H., Björnsson, A., Lundquist, B., Nilsson, A. & Brattsand, R.: Inhibitory effect of glucocorticosteroids on anti-IgE-induced histamine release from human basophilic leucocytes: Evidence for a dual mechanism of action. *Allergy* 39, 217–230, 1984.
- Butler, J. M., Chan, S. C., Stevens, S. & Hanifen, J. M.: Increased leucocyte histamine release with elevated cyclic AMP-phosphodiesterase activity in atopic dermatitis. *J. Allergy Clin. Immunol.* 71, 490–497, 1983.
- Demis, J.: The mastocytosis syndrome: Clinical and biological studies. *Ann. Intern. Med.* 59, 194–206, 1963.
- Hanifen, J. M. & Rajka, G.: Diagnostic features of atopic dermatitis. *Acta Derm. Venereol. Suppl.* 92, 44–47, 1980.
- Johnson, H. H., DeOreo, G. A., Lascheid, W. P. & Mitchell, F.: Skin histamine levels in chronic atopic dermatitis. *J. Invest. Dermatol.* 34, 237–238, 1960.
- Lebel, B., Venencie, P. Y., Saurat, J. H., Soubrane, C. & Paupe, J. P.: Anti-IgE induced histamine release from basophils in children with atopic dermatitis. *Acta Derm. Venereol. Suppl.* 92, 57–59, 1980.
- Lindell, S. E. & Westling, H.: Histamine metabolism in man. In: *Handbook of experimental pharmacology*, 1811, pp. 734–788, Springer, Berlin, 1966.
- Overgaard Petersen, H., Thormann, T. & Zachariae, H.: Urinary histamine in severe atopic dermatitis. *Arch. Dermatol. Res.* 264, 193–195, 1979.
- Ring, J.: Plasma histamine concentrations in atopic eczema. *Clin. Allergy* 13, 545–552, 1983.
- Ring, J., Allen, D. H., Mathison, D. A. & Spiegelberg, H. L.: In vitro releasability of histamine and serotonin: Studies of atopic dermatitis. *J. Clin. Lab. Immunol.* 3, 85–91, 1980.
- Ruzicka, T. & Glück, S.: Cutaneous histamine and histamine releasability from the skin in atopic dermatitis and hyper-IgE-syndrome. *Arch. Dermatol. Res.* 275, 41–44, 1983.
- Sampson, H. A. & Jolie, P. L.: Increased plasma histamine in the present investigation, did not correlate to the serum IgE levels. This result is in line with the reported poor correlation between histamine releasability and serum IgE levels (3).

mine concentrations after food challenges in children with atopic dermatitis. *N. Engl. J. Med.* 311, 372-376, 1984.

14. Søndergaard, I.: Quantitative determination of 1.4-methyl-imidazoleacetic acid in urine by high performance liquid chromatography. *Allergy* 37, 581-586, 1982.

Address

Rune Lindskov

Stokholmsvej 41 B

DK-3060 Espergærde

Denmark

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.