

Serum α_1 -Protease Inhibitor Levels in Patients with Chronic Idiopathic Urticaria

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A comparative study of serum α_1 -protease inhibitor levels in patients with chronic idiopathic urticaria and control subjects revealed that the values in the patients were significantly lower than those in the controls, especially in patients over 60 years. The results suggests that some protease which can be inhibited by α_1 -protease inhibitor may be involved in urticarial reactions in patients with chronic idiopathic urticaria. Key word: α_1 -antitrypsin.

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Because of a possible pathogenetic relationship between urticaria and the kallikrein system, serum protease inhibitor profiles have been examined, and the levels of serum α_1 -protease inhibitor (α_1 -PI) in patients with chronic idiopathic urticaria (CIU) have by several previous studies been indicated to be normal or elevated (1–3). The value of α_1 -PI varies depending upon age, and is usually higher in elderly persons (4). However, previous papers have not referred to this relationship between the value of α_1 -PI and age. Furthermore, studies should be performed using samples from patients who are clinically inactive at the time of study, because α_1 -PI is an acute phase reactant. Here, I have taken the age of the subjects into consideration when comparing the level of α_1 -PI between patients with CIU and healthy controls.

MATERIAL AND METHODS

All subjects were females ranging in age from 30 to 74 years. All of the 27 patients studied presented with chronic or recurrent urticaria of at least one month's duration. Despite thorough investigation, no allergic factors or relevant underlying disease could be identified in any of the cases. These patients were divided into two groups by age: under 59 years of age and above 60 years. The median ages were 47 years and 66 years, respectively. Thirty-three healthy hospital personnel and patients with non-immunological skin disease served as controls. The control subjects were also divided into two groups: under 59 years (median age of 47 years) and above 60 years (median age of 67 years).

All treatments were withdrawn for at least 3 days prior to study. None of the patients with CIU had any active lesions at the time of plasma collection. Serum levels of α_1 -PI were measured by automated immunoprecipitation, employing a Behring nephelometer analyzer (Behringwerke AG, Germany).

Some time after the initial study, a second measurement of α_1 -PI was carried out in 12 of 27 patients under treatment with antihistamine drugs. Three of the 12 patients had active lesions at the time of plasma collection.

Statistical analysis of the significance of the differences of the means was performed by Student's *t*-test.

RESULTS

The levels of α_1 -PI in patients with CIU were statistically significantly decreased compared with the controls (mean \pm SD, mg/dl, respectively 188 ± 22.0 , 211 ± 27.8 , $p < 0.01$) (Fig. 1). Furthermore, the difference in the serum levels of α_1 -PI between CIU patients and the controls was more pronounced in the aged group (≥ 60 years) than in the other group (< 60 years) (Table I). In most patients the values in the second measurement were higher than those in the first measurement ($182 \text{ mg/dl} \rightarrow 205 \text{ mg/dl}$). The difference between the initial assay and the second was conspicuous in 3

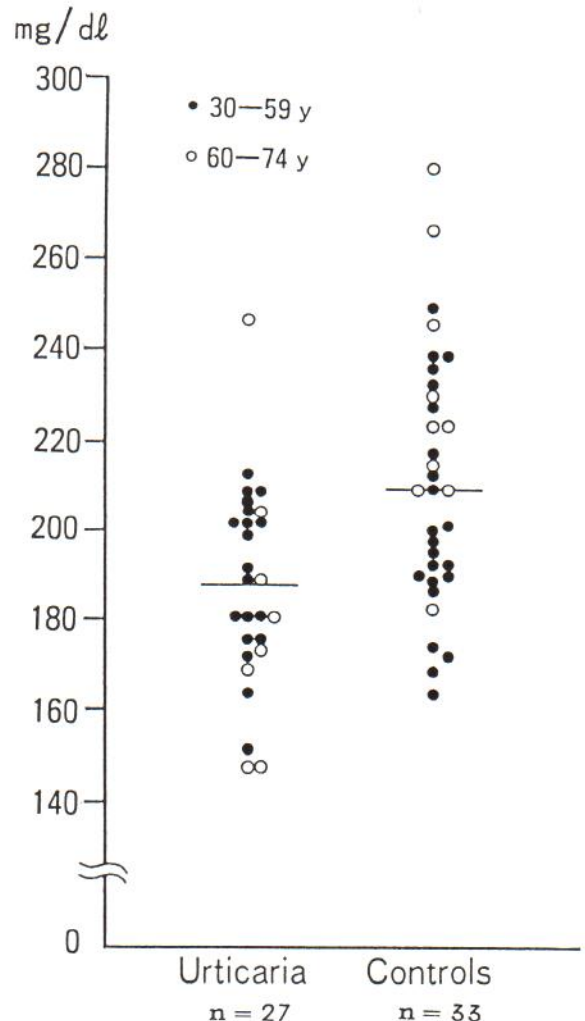


Fig. 1. The levels of serum α_1 -PI in patients with CIU were significantly lower than those of the controls. The difference was conspicuous in the group over 60 years. Horizontal bars represent means.

Table I. Serum α_1 -protease inhibitor levels in relation to age
 CIU: chronic idiopathic urticaria, α_1 -PI: α_1 -protease inhibitor.

	Age (years)	n	α_1 -PI (mg/dl)		
CIU	<60	19	190±16.9]	$p<0.05$
Controls		23	204±24.2		
CIU	≥60	8	183±30.4]	$p<0.01$
Controls		10	229±27.5		
			mean±SD		

patients with active lesions at the time of the second study (170 mg/dl → 218 mg/dl).

DISCUSSION

The levels of serum α_1 -antitrypsin in patients with CIU have been reported to be normal or elevated compared with control subjects (1–3), whereas the present study showed a significant decrease. At least to some extent, this discrepancy is probably due to the difference in the age of the subjects and the different degrees of urticaria in the patients at the time of study. That is, in the earlier series 1) subjects included the younger group (median age of about 30 years), 2) most patients had active lesions at the time of plasma collection. Patients with active lesions show higher levels of α_1 -PI than those who were clinically inactive at the time of study (2). This was proved also in our second assay. The marked increase of α_1 -PI levels seems to be caused by an acute phase reaction. However, the increase of α_1 -PI values in the second measurement in most patients in all likelihood indicates an approach to a normal level of α_1 -PI, even if it is temporary, which is probably due to the treatment.

During urticarial reactions serine proteases are released from mast cells together with histamine upon degranulation. Tryptase and chymase are the significant source of the proteases, being contained in the mast cells predominant in bowel submucosa and skin (5). Although the levels of tryptase in suction-blister fluid from patients with urticaria were increased, elevated tryptase levels were not found in the sera of

these patients (6). Furthermore, tryptase could not inactivate α_1 -PI (7). On the other hand, chymase can be inhibited by α_1 -PI and α_1 -antichymotrypsin (8). It may be hypothesized that the protease released from skin mast cells activated by certain pathways, for example chymase, could be reduced in the sera of patients with urticaria because of local depletion, which might lead to the depressed level of the circulating inhibitor of the protease. Significantly increased skin reactions to kallikrein in patients with CIU compared with healthy controls have already been confirmed (9, 10), and these are likely support our findings. The result of the present study indicates that the protease related to α_1 -PI may play a part in the pathogenesis of CIU, particularly in elderly patients.

REFERENCES

- Chodirker WB, Bauman W, Komar RR. Immunological parameters and α_1 -antitrypsin in chronic urticaria. *Clin Allergy* 1979; 9: 201–210.
- Eftekhari N, Milford Ward A, Allen R, Greaves MW. Protease inhibitor profiles in plasma of patients with chronic urticaria. *Br J Dermatol* 1980; 103: 33–39.
- Doeglas HMG, Bleumink E. Plasma protease inhibitors in chronic urticaria. In: Greaves MW, Champion RH, eds. *The urticarias*. London: Churchill Livingstone, 1984: 59–69.
- Nemoto I. Measurement of α_1 -antitrypsin and its normal value. *Jap J Med Tech* 1978; 28: 170–173.
- Schwartz LB. Mast cells and their role in urticaria. *J Am Acad Dermatol* 1991; 25: 190–204.
- Deleuran B, Kristensen M, Grønhøj Larsen C, Matsson P, Enander I, Andersson A, et al. Increased tryptase levels in suction-blister fluid from patients with urticaria. *Br J Dermatol* 1991; 125: 14–17.
- Alter SC, Kramps JA, Janoff A, Schwartz LB. Interactions of human mast cell tryptase with biological protease inhibitors. *Arch Biochem Biophys* 1990; 276: 26–31.
- Schechter NM, Sprows JL, Schoenberger OL, Lazarus GS, Cooperman BS, Rubin H. Reaction of human skin chymotrypsin-like proteinase chymase with plasma proteinase inhibitors. *J Biol Chem* 1989; 264: 21308–21315.
- Juhlin L, Michaelsson G. Cutaneous reactions to kallikrein, bradykinin and histamine in healthy subjects and in patients with urticaria. *Acta Derm Venereol (Stockh)* 1969; 49: 26–36.
- Imai S. Cutaneous reactions to kallikrein and histamine in patients with urticaria. *Arch Dermatol Res* 1989; 281: 437–439.