

Hymenoptera venom anaphylaxis: may decreased levels of angiotensin peptides play a role?

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Introduction

The renin–angiotensin system (RAS) plays an important role in the control of blood pressure, fluid and electrolyte balance. Angiotensin II (ANG II), the effector peptide of the RAS, is a potent vasoconstrictor. Besides that, it influences the activity of the central and peripheral sympathetic nervous system and stimulates the secretion of aldosterone from the adrenal gland.

People with hypersensitivity to bee or wasp venom can develop life-threatening anaphylactic reactions after a single sting [1]. In severe cases, the symptoms comprise cardiovascular changes with hypotension and shock. While an IgE-mediated reaction has been established as a relevant pathomechanism in most cases of hymenoptera venom allergy, there is no convincing correlation between the degree of immunological sensitization or skin test reactivity and the severity of clinical symptoms [2]. Therefore we asked the question whether a non-immunological parameter, relevant to blood pressure control, might also be altered in these patients. This paradigm prompted us to investigate the plasma levels of ANG I and ANG II in patients with hymenoptera venom allergy and control individuals. Likewise, we were interested to see whether leucocytes from allergic individuals contain angiotensin peptides.

Subjects and methods

The control group consisted of four male and six female volunteers (mean age 32 yr) without any indication of cardiovascular disorders. Subjects, 10 males and six females (mean age 36 yr), without evidence for cardiovascular diseases, had experienced anaphylactic reactions after a bee or wasp sting. For statistical evaluation, Student's *t*-test was used.

Blood was collected from the cubital vein. For the determination of angiotensin peptides in plasma, blood samples were collected in the presence of the peptidase inhibitors EDTA and *o*-phenanthroline and plasma was prepared by centrifugation. Leucocytes were precipitated

from heparinized blood with a 6% dextran solution. Peptides were extracted from plasma and leucocytes with a mixture of acetone, 1 N HCl and water (40:1:10; v/v) as reported previously [3]. Extracts were dried in a vacuum centrifuge. The dried samples were dissolved in Tris–HCl buffer pH 7.2 and ANG I and ANG II measured radioimmunologically [4].

Results

The plasma concentrations of ANG I and ANG II were significantly reduced in patients with bee or wasp venom allergy compared to non-allergic controls (Table 1). Both peptides were characterized on HPLC as (Ile⁵)–ANG I and (Ile⁵)–ANG II. In basophil leucocytes, 24.36 ± 6.65 fmol/mg protein of ANG I and 13.97 ± 2.22 fmol/mg protein of ANG II were present (mean $\pm$ s.e.m. *n* = 5). HPLC characterization demonstrated (Ile⁵)–ANG I and (Ile⁵)–ANG II.

Table 1. Concentrations of ANG I and ANG II in plasma of subjects with a bee/wasp venom allergy and control individuals

Controls (<i>n</i> = 10)	30.34 ± 3.83	9.37 ± 1.05
Subjects (<i>n</i> = 16)	$14.04 \pm 1.06^{**}$	$4.75 \pm 0.27^{*}$

Subjects with bee or wasp venom allergy showed significantly reduced levels of ANG I and ANG II.

Values are expressed as means $\pm$ s.e.m. in fmol peptide per ml plasma. * *P* < 0.02; ** *P* < 0.01.

Discussion

The significant differences of ANG I and ANG II levels in plasma between control individuals and patients with hymenoptera venom allergy led us to speculate about a possible disturbance of the RAS as an additional factor in the pathogenesis of anaphylactic reactions after bee or wasp stings. Basophil leucocytes contain ANG I and ANG II. Besides histamine and other mediators, ANG II might be released from these cells and act on different target tissues. Patients with severe anaphylactic reactions to hymenoptera venom may have a dysregulation in the complex interaction between the RAS and basophil or

mast cell-mediated events. The measurement of ANG II in plasma could give additional information of possible importance with regard to the severity of clinical symptoms of hymenoptera venom anaphylaxis.

References

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