

Blood rheological profiles in patients with chronic urticaria

A. Kasperska-Zajac · L. Slowinska · T. Jasinska

Received: 13 January 2010 / Revised: 17 February 2010 / Accepted: 22 February 2010
© Springer-Verlag 2010

Abstract Psychological factors, such as stress, anxiety, depression, as well as immuno-inflammatory processes may influence blood rheology. On the other hand, these factors may be involved in triggering, aggravating or maintenance of urticaria symptoms. The present study was designed to compare blood rheological properties of patients with chronic urticaria with positive response to autologous serum skin test (ASST) and negative response to ASST. The study comprised 15 female patients with chronic urticaria showing positive response to ASST, 14 female patients with chronic urticaria showing negative response to ASST and 15 healthy subjects. Rheological properties of erythrocytes, such as deformability and aggregation, were measured. Overall blood viscosity measurements were performed with the use of cone-plate Brookfield's viscometer, and plasma viscosity measurement employed capillary Ubbelohd's viscometer. The hemorheological parameters did not differ significantly between the groups. It seems that blood rheological properties do not alter in patients with chronic urticaria, irrespective of their response to ASST.

Keywords Urticaria · Blood rheology · Immuno-inflammatory processes

Introduction

Blood rheological properties, including red blood cell (RBCs) deformability and aggregation, and blood viscosity are markedly influenced by changes in the surrounding milieu triggered by inflammatory processes, metabolic abnormalities, and psychological state [2]. RBC aggregation is primarily determined by plasma protein composition and surface properties of RBCs, with increased plasma concentrations of acute phase reactants in inflammatory disorders—a common cause of increased RBC aggregation [1]. Changes in RBCs deformability may be induced by abnormal local tissue metabolism, oxidant stress and activated leukocytes [1]. Some chronic immuno-inflammatory disorders are associated with the changes in blood rheology [6, 12]. Emotional state, including mental stress as well as inflammatory response, may also affect blood rheology [5, 11]. It is known that mental stress [3, 9, 14] and inflammation [4, 10] are associated with chronic urticaria.

To the best of our knowledge there is only one study regarding blood rheology in urticaria patients [8]. For better understanding of the pathophysiologic changes associated with urticaria, we examined blood rheologic parameters in chronic urticaria patients. In the present study whole blood and plasma viscosity, RBCs aggregability and deformability have been compared between chronic urticaria patients with positive response to autologous serum skin test (ASST) and chronic urticaria patients with negative response to ASST. The objective was to determine whether two different rheological patterns occur in such patients.

A. Kasperska-Zajac (✉)
Clinical Department of Internal Diseases,
Allergology and Clinical Immunology,
Medical University of Silesia, ul. Ceglana 35,
40-952 Katowice, Poland
e-mail: kasperska@plusnet.pl

L. Slowinska
Department of Biophysics, Faculty of Medicine in Zabrze,
Medical University of Silesia, Katowice, Poland

T. Jasinska
Department of Dermatology,
Regional Specialised Hospital No. 4, Bytom, Poland

Table 1 Clinical characteristics of the two groups

Variable	Negative-ASST/ CU group (<i>n</i> = 14)	Positive-ASST/ CU group (<i>n</i> = 15)
Age (years)	36.2 ± 6.5	38 ± 4.6
Body mass index (kg/m ²)	23.3 ± 1.0	24 ± 1.5
Disease duration (months)	10.6 ± 6.3	14.6 ± 4.6

Values are mean ± SD

Materials and methods

Subjects

Twenty-nine female symptomatic patients suffering only from spontaneous chronic urticaria were divided into two groups depending on ASST results. Fourteen chronic urticaria patients showed negative response to ASST (negative-ASST/CU group) and 15 patients had positive reactivity on ASST (positive-ASST/CU group) and all other identified causes of urticaria had been excluded after extensive investigations. Each patient underwent the following tests: full blood count, erythrocyte sedimentation rate, C-reactive protein, serum glucose, complete urine examination, liver function tests, creatinine, hepatitis serology, rheumatoid factor (Waller Rose test), antistreptolysin-o (ASO), immunoglobulins (IgE, IgA, IgM, IgG), complement (C3 and C4), antinuclear (ANA) and antithyroid microsomal antibody, thyroid function tests (TSH and free thyroxine-FT₄), stool examination for parasites, chest X-ray and abdominal ultrasonography. The oral provocation challenge tests with dyes, food additives and aspirin were performed when indicated by the patient's history. In all patients, investigations for focus of infection in various locations were performed. If there were gastrointestinal symptoms or specific IgG and IgM antibodies for *H. pylori* in serum (ELISA test), gastroscopy with mucosal biopsy and a rapid urease test were performed to verify the presence of *H. pylori* infection. Physical urticaria was excluded by history and/or diagnostic tests.

The clinical characteristics of the urticaria patients are shown in Table 1. The disease was characterized by hives occurring daily, or throughout most days of the week during more than 6 weeks. All the patients had clinical manifestation of urticaria upon serum sampling; anti-histamine treatment was discontinued at least 3 days before the study. They had not been treated with any other medication including systemic steroids for more than 12 weeks preceding the study.

The disease intensity was measured by assessment of wheals and pruritus on a (0–3 scale sum of score: 0–6)

proposed by Zuberbier et al. [15]. Briefly, the number of the wheals and severity of pruritus were scored as follows: number of wheals— 0 = no wheals, 1 = mild wheals (<20 wheals/24 h), 2 = moderate wheals (21–50 wheals/24 h), 3 = intense wheals (>50 wheals/24 h, or large confluent areas of wheals); pruritus, 0 = none, 1 = mild, 2 = moderate, 3 = intense. Our patients' scoring ranged between 3 and 6. Such scoring was maintained during 2 days preceding blood sampling and on the examination day.

The control group consisted of 15, non-smoking healthy women, which were matched with CU patients for age and body mass index. Individuals were not accepted into the study, if they suffered from concomitant disorders, including those which would affect blood rheology, i.e. obesity, hypertension or diabetes. All participants gave their written, informed consent and the study was approved by the University Ethics Committee.

Blood collection

Blood samples were obtained in the morning (7.00–8.00 a.m.; in the fasting state) after rest at slight or no stasis from the antecubital vein and anticoagulated with K3EDTA for rheological tests. The samples were taken during the early to mid-follicular phase of the menstrual cycle.

Methods

Blood viscosity (BV) measurements were performed with the use of cone-plate Brookfield's viscometer at a shear rate of 150 s⁻¹ and plasma viscosity (PV) with capillary Ubbelohde's viscometer.

Erythrocyte deformability, expressed as elongation index (EI), and erythrocyte aggregation expressed as aggregation half-time (*t*_{1/2}), aggregation index (AI), and syllectogram amplitude (AMP) were measured with the laser-assisted optical rotational cell analyser (LORCA) [7]. EI was measured at different shear stresses (18.49, 33.20, and 60.03 Pa) due to correlation coefficient between these values, only results obtained at 60.03 Pa are demonstrated.

Autologous serum skin test (ASST)

Intradermal tests with patient's own serum were performed according to the method described by Sabroe et al. [13]. A serum-induced wheal of diameter greater by at least 1.5 mm than that of a control wheal induced with physiological saline was assessed as positive. Saline was used as a negative control and histamine served as a positive control.

Table 2 Rheological parameters in CU female patients with positive or negative response to ASST and in healthy controls

Analysed parameters (unit)	Control group (n = 15)	Positive-ASST/CU group (n = 15)	Negative-ASST/CU group (n = 14)
Hematocrit (%)	40.5 36–44	39 35–44	39.25 34–44.5
Plasma viscosity (mPas)	1.5 1.29–1.65	1.42 1.24–1.59	1.45 1.35–1.5
Blood viscosity (mPas)	3.8 3.32–4.31	3.89 3.51–4.47	3.72 3.09–4.76
Corrected blood viscosity to hematocrit 45% (mPas)	4.3 3.48–4.87	4.39 3.86–5.36	4.19 3.77–4.87
Aggregation index (%)	62.4 42.8–97.4	57.8 31.4–72.9	54.9 46.2–68.7
Aggregation half time (s)	2.06 1.28–5.1	2.74 1.26–8.56	3.15 1.62–4.52
Syllectogram amplitude (au)	9.77 0.1–14.2	10.9 7.41–14.6	9.35 6.18–13.4
Elongation index (EI%)	0.52 0.41–0.61	0.5 0.45–0.63	0.53 0.38–0.6

Values are expressed as median with range

CU chronic urticaria, ASST autologous serum skin test

Statistical analysis

Data are presented as medians with maximum and minimum values (range). Nonparametric ANOVA Kruskal–Wallis test and one-way ANOVA were used to screen differences between the groups. *P* values below 0.05 were considered significant.

Results

The hematocrit, whole blood viscosity and plasma viscosity did not show significant differences among the positive-ASST/CU group, the negative-ASST/CU group and the control subjects (Table 2). Also, RBC deformability, expressed by EI as well as RBC aggregability expressed by an aggregation $t_{1/2}$, AI, and AMP did not differ significantly between the three groups (Table 2).

Discussion

As mentioned above, chronic inflammatory processes and different psychological factors are associated with changes in blood rheology, including increased blood viscosity and RBCs aggregability as well as decreased RBCs flexibility [1, 2, 5, 11]. For example, blood and plasma viscosity and RBCs aggregation were significantly different in lupus patients, including chronic discoid and subacute cutaneous lupus erythematosus compared with controls, indicating reduced blood fluidity in lupus erythe-

matosis [6]. To the best of our knowledge only one study has evaluated hemorheology in urticaria. Liu and Su observed changes in hemorrheology in chronic urticaria patients [8]. The whole blood viscosity, plasma viscosity, and fibrinogen levels were found to be markedly increased in chronic urticaria patients [8]. However, the recent study showed no precise characteristic of chronic urticaria patients and RBCs deformability and aggregability, which also play an important role in blood fluidity. Neither did our study point to any significant differences in plasma and blood viscosity nor aggregation and flexibility of RBCs between urticaria patients and healthy controls. Moreover, no difference was observed between the rheological profile of urticaria patients with negative ASST and positive ASST, which suggest the autoimmune origin of the disease [13]. The results suggest that blood rheological abnormalities do not accompany immune and inflammatory events associated with chronic urticaria. In contrast to other chronic immune-inflammatory diseases [6, 12], blood rheological parameters may not be modified in the course of chronic urticaria. Such phenomenon appears favourable considering that abnormalities in blood rheological properties could impair microcirculatory blood flow and tissue oxygenation and play a role in atherothrombogenesis [1].

In conclusion, the study failed to detect any significant differences in blood rheological properties among two chronic urticaria groups during the active phase of the disease and in the healthy subjects. It seems that rheological properties of blood do not alter in patients with chronic urticaria, irrespective of their response to ASST.

Acknowledgments This study was supported by a research grant from the Committee for Scientific Research (NN-1-117/06).

References

1. Baskurt OK, Meiselman HJ (2003) Blood rheology and hemodynamics. *Semin Thromb Hemost* 29:435–450
2. Brun JF (2002) Hormones, metabolism and body composition as major determinants of blood rheology: potential pathophysiological meaning. *Clin Hemorheol Microcirc* 26:63–79
3. Brzoza Z, Kasperska-Zajac A, Badura-Brzoza K, Matysiakiewicz J, Hese RT, Rogala B (2008) Decline in dehydroepiandrosterone sulphate observed in chronic urticaria is associated with psychological distress. *Psychosom Med* 70:723–728
4. Caproni M, Giomi B, Volpi W, Melani L, Schincaglia E, Macchia D, Manfredi M, D'Agata A, Fabbri P (2005) Chronic idiopathic urticaria: infiltrating cells and related cytokines in autologous serum-induced wheals. *Clin Immunol* 114:284–292
5. Ehrly AM, Landgraf H, Hessler J, Saeger-Lorenz K (1988) Influence of videofilm-induced emotional stress on the flow properties of blood. *Angiology* 39:341–344
6. Ernst E, Hein A, Meurer M, Ruzicka T (1991) Blood rheology in lupus erythematosus. *Ann Rheum Dis* 50:710–712
7. Hardeman MR, Dobbe JG, Ince C (2001) The laser-assisted optical rotational cell analyzer (LORCA) as red blood cell aggregometer. *Clin Hemorheol Microcirc* 25:1–11
8. Liu CH, Su W (1992) Changes in hemorrheology in urticaria. *Chin Med J (Engl)* 105:144–146
9. Papadopoulou N, Kalogeromitros D, Staurianeas NG, Tiblalex D, Theoharides TC (2005) Corticotropin-releasing hormone receptor-1 and histidine decarboxylase expression in chronic urticaria. *J Invest Dermatol* 125:952–955
10. Piconi S, Trabattoni D, Lemoli E, Fusi ML, Villa ML, Milazzo F, Clerici M (2002) Immune profiles of patients with chronic idiopathic urticaria. *Int Arch Allergy Immunol* 128:59–66
11. Rampling MW (1998) Haemorheology and the inflammatory process. *Clin Hemorheol Microcirc* 19:129–132
12. Ricart JM, Vaya A, Todoli J, Calvo J, Contreras MT, Espana F, Aznar J, Corella D (2005) Haemorheological alterations in Behcet's disease are not related to a tendency for venous thrombosis. *Thromb Res* 115:399–404
13. Sabroe RA, Grattan CEH, Francis DM, Barr RM, Kobza Black A, Greaves MW (1999) The autologous serum skin test: a screening test for autoantibodies in chronic idiopathic urticaria. *Br J Dermatol* 140:446–453
14. Yang HY, Sun CC, Wu YC, Wang JD (2005) Stress, insomnia, and chronic idiopathic urticaria—a case-control study. *J Formos Med Assoc* 104:254–263
15. Zuberbier T, Asero R, Bindslev-Jensen C, Walter Canonica G, Church MK, Giménez-Arnau A, Grattan CE, Kapp A, Merk HF, Rogala B, Saini S, Sánchez-Borges M, Schmid-Grendelmeier P, Schünemann H, Staubach P, Vena GA, Wedi B, Maurer M (2009) EAACI/GA(2)LEN/EDF/WAO guideline: definition, classification and diagnosis of urticaria. *Allergy* 64:1417–1426