Blood rheology in lupus erythematosus

E Ernst, A Hein, M Meurer, T Ruzicka

Abstract

Blood rheology is one of the determinants of perfusion and might therefore have an impact on the thromboembolic complications of lupus erythematosus. This study aimed at defining the flow properties of blood in patients with various types of lupus erythematosus. Results for 51 patients were compared with those for 20 controls matched for sex. The patients were divided into subgroups—chronic discoid, subacute cutaneous, and systemic lupus erythematosus—according to their clinical or laboratory characteristics. Blood and plasma viscosity, packed cell volume, red cell aggregation, and red cell deformability were used as parameters of blood rheology. Blood and plasma viscosity and red cell aggregation were significantly different in patients compared with controls, indicating reduced blood fluidity in lupus erythematosus. There were no marked sex differences. The rheological effects were greater in those with systemic lupus erythematosus than in those with chronic discoid or subacute cutaneous lupus erythematosus. The presence of a positive antinuclear antibody titre or methods of treatment (systemic steroids or retinoids) had no apparent effect on the parameters tested. It is suggested that a complex haemorheological deficit exists in lupus patients.

Haemorheological abnormalities have been described in a number of autoimmune diseases.¹ These may be a mere epiphenomenon,² but might also indicate an ability to hinder micro-circulatory blood flow.³ In patients with lupus erythematosus blood rheology is known to be disturbed,⁴⁻⁶ but there have been no comprehensive studies on large, well defined groups. This study aimed at providing a detailed analysis of blood rheology in various clinical subsets of lupus erythematosus.

Patients and methods

Fifty one consecutive patients with confirmed diagnosis attending the lupus erythematosus clinic in the department of dermatology of Ludwig Maximilian University, Munich, were included in the study. Table 1 gives details of the patients. The patients were divided into subgroups—chronic discoid, subacute cutaneous, systemic lupus erythematosus—according to American Rheumatism Association definitions.⁷ Further subgroups were constructed according to sex, treatment status, and anti-nuclear antibody test (see below). The control

group comprised 20 subjects matched for sex who were clinically healthy and were not taking any drugs (table 1).

Blood was taken from an antecubital vein by a standardised protocol and anticoagulated with lithium heparin. Within one hour of sampling the following haemorheological determinations were performed in triplicate:

- Native blood viscosity at two defined (94.5 and 0.7 s⁻¹) shear rates and 37°C using the LS30 Contraves rotational viscometer⁸
- Standardised blood viscosity as above but standardised for a packed cell volume of 0.45⁹
- Packed cell volume by centrifugation¹⁰
- Plasma viscosity at 37°C using the Luckham clinical viscometer¹¹
- Red cell deformability by a filtration technique with 5 µm Nuclepore filters and a red cell suspension in autologous plasma at packed cell volume 0.05¹²
- Red cell aggregation by an optical method¹³ with an automated cone and plate viscometer at stasis (M) and at low (3 s⁻¹) shear rate (M1)
- Erythrocyte sedimentation rate, applying the standard Westergren method.

The statistical analyses were performed as cross sectional comparisons. After testing for normal distribution of the rough data significance was evaluated by the *t* test for unpaired data. The null hypothesis was rejected when *p* was less than 0.05. Results are expressed as means (SEM).

Results

Values of all rheological variables were significantly higher in patients than in controls. The only exceptions were packed cell volume and

Department of Physical Medicine,
L M University, Munich
A Hein

Department of Dermatology,
L M University, Munich
M Meurer
T Ruzicka

Hemorheology Laboratory,
Department of Physical Medicine and Rehabilitation,
AKH University of Vienna, 1090 Vienna, Austria
E Ernst

Correspondence to:
Professor Ernst.

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Table 1 Details of patients and controls. Numbers of patients are given

Patients (n=51)	
Mean (SEM) age (years)	40.8 (2)
Men:women	15:36
Subtypes:	
Chronic discoid lupus erythematosus	27
Subacute cutaneous lupus erythematosus	16
Systemic lupus erythematosus	18
Non-related diagnoses	10
Raynaud's syndrome	11
Treatment:	
Sun screens	51
Steroids (topical)	24
Steroids (oral)	13
Oral retinoids	8
Antimalarial drugs	3
Immunosuppressive drugs	3
Controls (n=20)	
Mean (SEM) age (years)	50.7 (2.5)
Men: women	6:14
Clinical diagnosis	None
Treatment	None

Table 2 Haemorheological comparison of patients with lupus erythematosus and controls. Results are given as means (SEM)

Variable†	Patients (total)	Controls
BV1 (mPa.s)	29.75 (1.17)**	25.57 (1.05)
BV2 (mPa.s)	4.76 (0.07)**	4.46 (0.08)
st BV1 (mPa.s)	33.79 (1.12)**	29.84 (0.72)
st BV2 (mPa.s)	5.03 (0.05)**	4.79 (0.06)
Packed cell volume	0.43 (0.006)	0.43 (0.006)
RCA (M1) (units)	5.19 (0.20)***	3.17 (0.21)
RCA (M) (units)	9.57 (0.27)***	7.30 (0.40)
RCD (units)	0.66 (0.02)	0.72 (0.02)
PV (mPa.s)	1.27 (0.01)***	1.22 (0.01)
ESR (mm/1 h)	11.44 (1.66)**	6.0 (0.58)
ESR (mm/2 h)	25.88 (2.85)***	12.0 (1.17)

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

†1=shear rate 0.7 s^{-1} ; 2=shear rate 94.5 s^{-1} ; BV1=native blood viscosity (0.7 s^{-1}); BV2=native blood viscosity (94.5 s^{-1}); st BV=standardised viscosity (packed cell volume 0.45); RCA=red cell aggregation at stasis (M) and at low (3 s^{-1}) shear rate (M1); RCD=red cell deformability; PV=plasma viscosity; ESR=erythrocyte sedimentation rate.

red cell deformability (table 2). The largest percentage differences were found in red cell aggregation and erythrocyte sedimentation rate.

A comparison of the 36 female patients and the 14 female controls showed similar results, except that there was also a significant difference in red cell deformability ($0.66 (0.03) v 0.74 (0.02)$ units), indicating reduced deformability in patients. Red cell deformability values in the male patients and controls were almost the same ($0.67 (0.04) v 0.68 (0.04)$ units). When male and female patients were compared the only significant difference was in packed cell volume and in variables dependent on the packed cell volume, such as native blood viscosity—data not shown.

When subgroups with chronic discoid or subacute cutaneous lupus erythematosus were compared with the total lupus group no tested variable differed significantly. In contrast, a comparison between patients with systemic lupus erythematosus and the total group showed significantly higher standardised blood viscosities at high shear rate ($5.5 (0.13) v 5.03 (0.05)$ mPa.s), a significantly lower packed cell volume $0.40 (0.001) v 0.43 (0.006)$, and significantly higher red cell aggregation (M1) ($6.55 (0.55) v 5.19 (0.20)$ units) in the former group. Other variables, like plasma viscosity, were numerically higher but the difference was not significant ($1.33 (0.04) v 1.27 (0.01)$ mPa.s).

A comparison of the groups with systemic lupus erythematosus and subacute cutaneous lupus erythematosus showed that only high

shear standardised blood viscosity differed significantly ($5.5 (0.13) v 5.01 (0.09)$ mPa.s in subacute cutaneous lupus erythematosus). By contrast, patients with systemic lupus erythematosus and chronic discoid lupus erythematosus showed significant differences in both standardised blood viscosities, packed cell volume, and red cell deformability (table 3).

Thirty eight of the 51 patients were antinuclear antibody positive. These patients showed no significant (or large numerical) differences in any of the tested variables when compared with the total group.

Patients with Raynaud's symptoms were found to have a significantly lower packed cell volume than those without ($0.40 (0.01) v 0.44 (0.06)$). Of the 11 patients with Raynaud's symptoms, five had systemic lupus erythematosus, three subacute cutaneous lupus erythematosus, and three chronic discoid lupus erythematosus.

Patients receiving oral steroids (13), and those receiving oral retinoids (eight) were compared with the untreated patients (31). No significant difference was detected in any variable in either case (data not shown).

Discussion

Our findings suggest the existence of a marked haemorheological abnormality in patients with lupus erythematosus, which apparently is not grossly influenced by sex, antinuclear antibody titre, Raynaud's syndrome, or treatment. The haemorheological deficit comprises most of the ex vivo measurable determinants of blood rheology. Plasma viscosity and red cell aggregation are raised (the latter obviously leading to increased erythrocyte sedimentation rate), red cell deformability is reduced. These changes lead to a marked increment of blood viscosity both at standardised and native packed cell volume. Thus in lupus erythematosus a markedly altered rheological behaviour of the red cells exists in addition to abnormalities in the plasmatic component of blood as reported earlier.⁴⁻⁶ The rheological properties of the red cells are known to be important determinants of microcirculatory blood flow.¹⁴ Therefore, increased red cell rigidity in lupus erythematosus might contribute to the malfunction of exchange vessels.

The plasmatic changes of lupus erythematosus have been shown to be due to increased concentrations of fibrinogen, serum globulins, and IgG.^{6,15} The red cell aggregation (and erythrocyte sedimentation rate value) depends on the presence of large aggregating plasma proteins, predominantly fibrinogen.¹⁶ The increase in this parameter is thus explained by the above abnormalities in plasma proteins.

The reason for the limitation in red cell deformability, however, is unclear at present. One possibility is that this abnormality is related to a deficit in intraerythrocytic antioxidant enzymes, as reported in rheumatoid arthritis.¹⁷ Clearly, the phenomenon of reduced red cell deformability in lupus erythematosus deserves more detailed study.

Table 3 Haemorheological comparison of patients with systemic lupus erythematosus (SLE) and chronic discoid lupus erythematosus (CDLE). Results are given as means (SEM)

Variable†	Patients with SLE	Patients with CDLE
BV1 (mPa.s)	27.69 (2.67)	31.24 (1.73)
BV2 (mPa.s)	4.61 (0.15)	4.86 (0.11)
st BV1 (mPa.s)	43.62 (5.15)*	31.26 (0.78)
st BV2 (mPa.s)	5.50 (0.13)***	4.90 (0.05)
Packed cell volume	0.40 (0.01)**	0.45 (0.008)
RCA (M1) (units)	6.55 (0.55)**	4.70 (0.21)
RCA (M) (units)	11.29 (0.91)*	9.06 (0.22)
RCD (units)	0.63 (0.05)	0.70 (0.03)
PV (mPa.s)	1.33 (0.04)	1.26 (0.01)

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

†For abbreviations see table 2.

It is noteworthy that subsets of lupus erythematosus with a fairly good prognosis¹⁸ are associated with relatively less haemorheological changes (table 3). The 10 year survival rate of systemic lupus erythematosus, the group with the strongest rheological abnormalities, is only around 70%.¹⁹ Patients with systemic lupus erythematosus have a high incidence of arterial occlusive disease, and various mechanisms might be considered. Possibly, future investigation could test whether the haemorheological deficit and the thromboembolic tendency are linked. Similar haemorheological changes are found in rheumatoid arthritis²⁰ and ankylosing spondylitis.²¹ The pathophysiological meaning of rheological abnormalities in rheumatic illness is as yet unclear.

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