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Letter to the Editor

Erythrocyte aggregation in homozygous sickle cell disease

Amparo Vayá[a,*], Susana Collado[a], Rafael Alis[b,c] and Maria-Angeles Dasí[d]
[a]*Hemorheology and Haemostasis Unit, Service of Clinical Pathology, La Fe University Hospital, Valencia, Spain*
[b]*Research Universitary Institute "Dr. Viña Giner", Molecular and Mitochondrial Medicine, Catholic University of Valencia, "San Vicente Mártir", Valencia, Spain*
[c]*Faculty of Medicine, Catholic University of Valencia "San Vicente Mártir", Valencia, Spain*
[d]*Pediatry Service, La Fe University Hospital, Valencia, Spain*

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To the Editor. Patients with homozygous sickle cell disease (Hb SS) show a prothrombotic tendency characterized by vaso-occlusive crisis and cerebral and pulmonary thrombosis. Although it is clearly established that erythrocyte deformability is markedly diminished in this hemoglobinopathy, there are contradictory results regarding the role of erythrocyte aggregation (EA) in this respect. In this sense, some others [6] observed EA to be diminished although disaggregation threshold is higher; in other words, that in spite of Hb SS erythrocytes aggregate less, the shear rate needed to disaggregate them is higher. On the other hand, other authors have observed EA to be increased when measured by different methodologies [1].

To further clarify this issue, we have investigated EA in 10 Hb SS and in 10 controls by means of the Sefam erythro-aggregometer [2, 6] after adjusting haematocrit to 45% with autologous plasma. This device determines the aggregation time (Ta), the aggregation index at 10 sec (AI10), i.e. a measurement of the extent of EA and the disaggregation threshold (γD), i.e. the shear rate needed for erythrocytes to disaggregate. The temperature was adjusted to 37°C. Basic blood cell count and erythrocyte indices were determined by means of a Sysmex XE-2100 (Roche Diagnostics S.L, Bcn, Spain). Serum total cholesterol and triglycerides were determined by enzymatic techniques in an Olympus AU 5430 autoanalyzer. Fibrinogen was performed in an ACL-TOP autoanalyzer (Instrumentation Laboratory, Milan, Italy). Hb S

*Corresponding author: AmparoVayá, MD, PhD, Hemorheology and Haemostasis Unit, Service of Clinical Pathology, La Fe University Hospital, Avda. Campanar 21, Valencia 46009, Spain. Tel.: +34 963862714; Fax: +34 96 1973089; E-mail: vaya_amp@gva.es.

and Hb F were isolated and quantified by high-performance liquid chromatography (HPLC, Bio-radLab, Spain).

Our patients were in steady-state condition and had not been transfused or undergone a vaso-occlusive crisis for at least 3 months before sampling. Patients suffered no infectious, inflammatory or organic diseases. The control group was made up of outpatients of our hospital who had minor surgery. The non-parametric Mann-Whitney test was used to analyze the differences between continuous variables in both groups.

Data are shown in Table 1. No differences in total-cholesterol, triglycerides nor fibrinogen was observed between groups ($p > 0.05$). Sickle cell disease patients showed lower AI10 and correspondingly higher Ta ($p < 0.05$), although no differences in the disaggregation threshold were observed ($p = 0.163$).

It is a well-known fact that erythrocyte shape and geometry play a crucial role in the aggregation process [1, 4, 5], being therefore conceivable, that sickle erythrocytes aggregate less than controls, given the marked morphological alterations that characterizes this disease. It seems that plasmatic factors, mostly fibrinogen and lipids, have no influence on the EA process, as no differences were observed between groups. In disagreement with other authors [7] patients in the present study did not show differences in the disaggregation threshold, meaning that rouleaux do not need higher shear rates to be disaggregated, suggesting that EA is not related with the prothrombotic state of these patients. The disparity of results regarding EA in sickle cell disease [3, 7] may be attributed to patients heterogeneity, diverse methodology and low simple sizes. It would be desirable to perform multicentre studies with a higher simple size and a similar methodology to elucidate this rheological property of sickle red blood cells.

Table 1
Biochemical, hematological and erythrocyte aggregation parameters in homozygous sickle cell disease and controls

	Homozygous SS ($n = 10$)	Controls ($n = 10$)	*P*
Age (years)	10.5 (5–34)	12.50 (6 – 34)	0.425
Gender (M/F)	5/5	5/5	1.000*
Total cholesterol (mg/dL)	128 (107–177)	135 (141–201)	0.137
Triglycerides (mg /dL)	64 (33–125)	71 (51–144)	0.093
RBC (10^{12}/l)	2.83 (2.20–3.27)	4.94 (4–5.18)	<0.001
Haemoglobin (g/dL)	8.70 (7.30–10.70)	13.90 (10.20–15)	<0.001
Haematocrit (%)	25.45 (20.5–29.8)	42.35 (32.7–46)	<0.001
MCV (fL)	87 (76–114.2)	85.0 (71–90)	0.423
MCH (pg)	30.5 (24.9–40.5)	28.40 (22.3–29.9)	0.151
MCHC (g/dL)	34.25 (32.2–36.7)	33.20 (31.20–34.7)	0.064
Hb S (%)	83 (74–90)		
Hb F (%)	12 (7.60–23.70)		
Reticulocytes (%)	7.57 (6.40–15.80)	0.78 (0.59–0.98)	0.034
Fibrinogen (mg/dL)	336 (291–387)	334 (291–411)	0.772
Ta (s)	2.79 (2.10–5.55)	2.16 (1.44–2.58)	0.007
AI10	31.2 (18.4–44.9)	38.5 (24.3–49.5)	0.032
γD (s–1)	69 (51–87)	63 (24–84)	0.163

Data as median (min-max). RBC: red blood cell count. MCV: mean corpuscular volume. MCH: mean corpuscular haemoglobin. MCHC: mean corpuscular haemoglobin concentration. Ta: erythrocyte aggregation time. AI10: aggregation index at 10 sec. γD: total disaggregation threshold. *Chi-Square test.

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