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Blood 142 (2023) 926–928

The 65th ASH Annual Meeting Abstracts

ORAL ABSTRACTS

114.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Rheological Characteristics of Elderly Individuals with Sickle Cell Disease Compared with an Adult Sickle Cell Population

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Introduction: Individuals with sickle cell disease (SCD) have a shorter life expectancy (median age 43 years in the US) compared with the general population. However, a subset of patients with SCD live ≥60 years. Prior case series examining conventional laboratory values found no significant differences between elderly and adult populations with SCD. Red blood cell (RBC) function, which is affected by RBC deformability and density, is abnormal in SCD, but the degree of impairment varies greatly among patients. Oxygen gradient ektacytometry measures RBC deformability as an elongation index (EI) under conditions of oxygenation (EI_{max}) and deoxygenation (EI_{min}). The oxygen partial pressure at which RBC deformability decreases is the point of sickling (PoS), and a higher PoS is associated with greater likelihood of a pain crisis. % dense RBCs (%DRBC), defined as RBCs containing >1.11 g/dL of hemoglobin (Hb), are associated with an increased likelihood of clinical complications. We hypothesized improved RBC function contributes to the longevity of patients with SCD and in this analysis we compared the RBC function of elderly patients with SCD vs an unselected adult cohort with SCD aged ≤45 years.
Methods: Peripheral blood samples (transfused samples excluded) and clinical data were collected from consenting patients with SCD treated at Grady Memorial Hospital, Atlanta, GA, from August 2022 to June 2023. Patients were assigned to groups by age (elderly, ≥60 years; controls, 18-45 years) and genotype (HbSS or HbSC). Complete blood count, absolute reticulocyte count (ARC), and %DRBC were determined using an ADVIA hematology analyzer. EI_{max}, EI_{min}, and PoS were measured using a Laser Optical Rotational Red Cell Analyzer. Tests were performed within 24 h of blood collection. Hydroxyurea (HU) use and % fetal Hb were collected via chart review.
Results: Thirteen elderly patients (HbSS, median age 63 years; 61.5% using HU) were compared with 78 control patients (HbSS, median age 28 years; 75.6% using HU). Apart from median ARC and absolute neutrophil count (ANC), which were significantly lower in the elderly group, all hematological parameters were comparable between HbSS groups (Table). The RBCs of the HbSS elderly group had improved deformability compared with the RBCs of the HbSS control group with a higher EI_{max} (0.506 vs 0.410; P=0.001) and EI_{min} (0.203 vs 0.125; P<0.001; Figure). PoS and %DRBC were significantly lower in the HbSS elderly group vs the HbSS control group (PoS: 20.48 mmHg vs 32.40 mmHg; %DRBC: 3.0% vs 7.4%; each P<0.001). Eleven elderly patients (HbSC, median age 64 years; 9.1% using HU) and 37 control patients (HbSC, median age 29 years; 18.9% using HU) were compared. Apart from median Hb, ANC, and mean corpuscular Hb concentration, which were significantly lower in the HbSC elderly group, all hematological parameters were comparable between HbSC groups (Table). Although there were no significant differences in EI_{max}, EI_{min}, or PoS between HbSC groups, %DRBC was significantly lower in the HbSC elderly group (8.5% vs 14.4%; P=0.003).
Conclusions: This is the first study to compare rheology as well as hematologic parameters between elderly patients with SCD and control patients with SCD aged ≤45 years to determine if RBC function contributes to longevity. Significantly lower %DRBC in HbSS and HbSC elderly groups, vs respective control cohorts, may contribute to improved rheology as denser RBCs have higher concentrations of HbS and are more prone to sickle. In the elderly groups, %DRBC was numerically higher in the HbSC group vs the HbSS group, and significantly lower vs respective control groups, emphasizing the dehydrating

effects of HbC and supporting phlebotomy to reduce %DRBC in HbSC disease. Only the HbSS elderly group demonstrated better RBC deformability regardless of oxygen conditions and a lower PoS, indicating less HbS polymerization at lower oxygen levels and suggesting increased relevance of deformability to pathophysiology and outcomes in HbSS vs HbSC disease. Even outside of SCD, older age is associated with more dehydrated, less deformable RBCs, and the reversal of this trend in HbSS groups is remarkable. Use of HU, a modifier of RBC function, was comparable between HbSS groups and cannot account for our findings. Overall, our results support the clinical relevance of RBC function testing and its potential role in assessing genotype-specific disease severity and expected longevity.

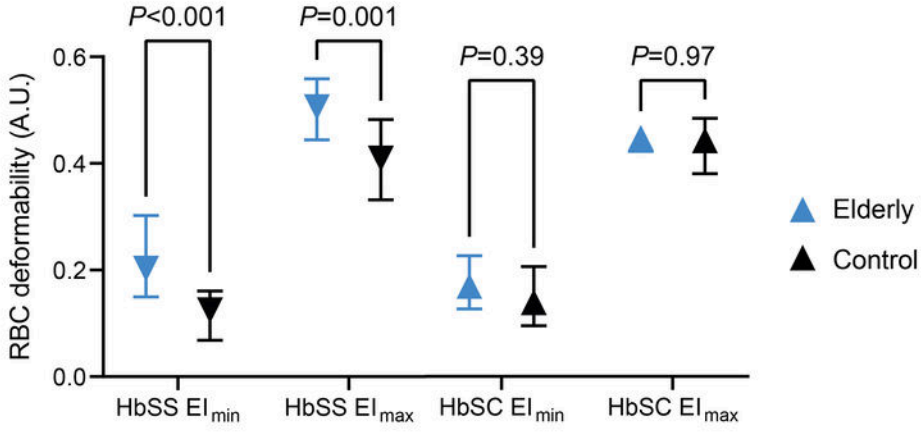
Disclosures El Rassi: *Novartis, Forma Therapeutics, Agios:* Research Funding. **Yu:** *Pfizer:* Current Employment. **Potdar:** *Pfizer:* Current Employment. **Sheehan:** *Refoxy Pharmaceuticals:* Research Funding; *Pfizer Inc:* Research Funding; *Beam Therapeutics:* Research Funding; *Novartis:* Research Funding; *Afimmune:* Research Funding.

Table. Baseline Demographics and Hematological Laboratory Testing in the Elderly and Control Patients by Genotype

	HbSS			HbSC		
	Elderly (n=13)	Control (n=78)	*P* value	Elderly (n=11)	Control (n=37)	*P* value
Demographics						
Median (range) age, y	63 (61–80)	27 (18–44)		64 (60–78)	29 (19–44)	
HU use, n (%)	8 (61.5)	59 (75.6)	0.29	1 (9.1)	7 (18.9)	0.45
Female, n (%)	11 (84.6)	38 (48.7)	**0.02**	7 (63.6)	22 (59.5)	0.80
Hematology labs[a]						
Hb, g/dL	8.5	9.4	0.21	10.4	12.0	**0.01**
MCV, fl	97.5	102.3	0.64	87.3	80.2	0.13
MCHC, g/dL	32.8	33.0	0.28	33.9	34.9	**0.002**
WBC, x10^3/uL	5.63	7.18	0.11	6.34	6.88	0.23
ANC, x10^3/uL	1.80	3.76	**0.02**	2.64	3.99	**0.004**
Platelets, x10^3/uL	292	378	0.24	315	258	0.88
ARC, x10^3/uL	174.4	328.4	**0.002**	214.6	215.5	0.85
HbF[b], %	23.1	13.8	0.19	–	–	–
Rheology[a]						
DRBC%, %	3.0	7.4	**<0.001**	8.5	14.4	**0.003**
EI_{max}, A.U.	0.506	0.410	**0.001**	0.448	0.444	0.97
EI_{min}, A.U.	0.203	0.125	**<0.001**	0.170	0.140	0.39
PoS, mmHg	20.48	32.40	**<0.001**	25.72	26.24	0.69

Statistical analysis performed using the Mann-Whitney test. Bold values indicate statistically significant differences with $P<0.05$.
[a] Presented values are medians. [b] HbF data are not presented for HbSC groups as this investigation is not routinely performed in patients with HbSC genotype in clinical practice.
ANC=absolute neutrophil count; ARC=absolute reticulocyte count; A.U.=arbitrary units; DRBC%=percent dense red blood cell; EI_{max}=maximum elongation index; EI_{min}=minimum elongation index; Hb=Hemoglobin; HbSC=hemoglobin SC disease; HbF=fetal hemoglobin; HbSS=homozygous for hemoglobin S; HU=hydroxyurea; MCHC=mean corpuscular hemoglobin concentration; MCV=mean corpuscular volume; PoS=point of sickling; WBC=white blood count.

Figure. Deformability of Deoxygenated and Oxygenated RBCs, As Measured by EI_{min} and EI_{max}, Respectively, in HbSS and HbSC Elderly Groups Versus Respective Control Groups



The HbSS elderly group demonstrated improved deformability of deoxygenated and oxygenated RBCs compared with the HbSS control group. There were no significant differences in deformability of deoxygenated or oxygenated RBCs between HbSC groups.
Statistical analysis was performed using the Mann-Whitney test. Presented values are medians with interquartile ranges.
A.U.=arbitrary units; EI_{max}=maximum elongation index; EI_{min}=minimum elongation index; HbSC=hemoglobin SC disease; HbSS=homozygous for hemoglobin S; RBC=red blood cell.

Figure 1

https://doi.org/10.1182/blood-2023-177791