SHORT REPORT

Phase angle and n-3 polyunsaturated fatty acids in sickle cell disease

D J VanderJagt, Y-S Huang, L-T Chuang, C Bonnett, R H Glew

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Phase angle, an impedance parameter used for nutritional assessment, is reflective of the capacitance properties of cell membranes. We have shown a significant correlation between the proportions of specific n-3 polyunsaturated fatty acids in the serum phospholipids of Nigerian children with sickle cell disease and their phase angles determined by bioelectrical impedance analysis.

Bioelectrical impedance analysis (BIA) measures whole body resistance (R) and reactance (Xc) and is used for the determination of body composition and nutritional status. Phase angle, calculated as the arctan Xc/R, reflects the capacitance properties of cell membranes.

Sickle cell disease (SCD) is associated with poor growth[1][2] in a pattern that resembles protein calorie malnutrition. In addition to micronutrient deficiencies and skeletal abnormalities, differences in the fatty acid composition of serum phospholipids of children with SCD have also been observed.[3][4] Specifically, the serum phospholipids of children with SCD contain reduced proportions of the long chain n-3 polyunsaturated fatty acids compared to healthy controls.

Having observed alterations in both the serum phospholipid fatty acid composition and body composition of Nigerian children with SCD,[3][5] we were interested in knowing whether a relation exists between phase angle and the fatty composition of their serum phospholipids.

METHODS

Subjects were recruited from among the patients attending the Sickle Cell Clinic at the Jos University Teaching Hospital, Jos, Nigeria. The SS genotype of the SCD subjects was confirmed by electrophoresis. Age and gender matched controls were recruited from among children visiting the clinic for immunisations or for follow up examinations after recovery from non-chronic conditions.

Impedance analysis was performed using the BIA-Quantum analyser (RJL Inc., Clinton Township, MI) as described previously.[5] A blood sample was obtained for determination of the fatty acid composition of plasma phospholipids, as described elsewhere.[3] This study was approved by the Human Research Review Committee of the University of New Mexico Health Sciences Center, Albuquerque, NM and the Ethics Review Committee of the Jos University Teaching Hospital, Jos, Nigeria.

Two-sample *t* tests were used for comparing variables between SCD and controls (NCSS 2001 Statistical System for Windows, NCSS, Kaysville, UT). Regression analysis was used to examine the relation between phase angle and the content of specific fatty acids in serum phospholipids. A p value of 0.05 was considered significant.

RESULTS

A total of 72 subjects with SCD (34 males and 38 females) and 68 healthy controls (34 males and 34 females) were enrolled in the study (table 1). While no significant differences in the percentages of either of the two essential fatty acids, linoleic and α-linolenic acid, were found between SCD subjects and controls, significant differences were found in the percentages of the long chain polyunsaturated fatty acids that are derived from them (table 2). Specifically, the amounts of 20:5 n-3 (EPA), 22:5 n-3, and 22:6 n-3 (DHA) in the SCD subjects were approximately 50% those of the controls (table 2). The mean percentage of arachidonic acid (20:4n-6) was also significantly reduced, but only by 10%.

For the combined subjects, palmitic acid (16:0) and oleic acid (18:1n-9) were inversely correlated with phase angle (fig 1A). On the other hand, the three polyunsaturated fatty acids derived from 18:3n-3 (20:5n-3, 22:5n-3, and 22:6n-3) were positively correlated with phase angle (fig 1B). The only fatty acid that was different between SCD subjects and controls but not significantly correlated with phase angle was arachidonic acid (20:4n-6).

DISCUSSION

We observed a significant positive correlation between phase angle and several of the n-3 polyunsaturated fatty acids known to increase membrane fluidity, and, in contrast, an inverse correlation between phase angle and palmitate and oleic acid, which decrease membrane fluidity. These results suggest that the phase angle may reflect some property of cell membranes that is related to fluidity.

Changes in phase angle have also been observed in conditions such as trauma, sepsis, and cancer.[6–8] The changes in Xc in these conditions are usually more pronounced than the changes in R. In a study of patients with lung cancer,[8] changes in Xc preceded the onset of symptoms of cachexia, were more predictive of survival than was weight loss, and were attributed to some undefined electrical property of the tissue membranes.

Modification of the lipid composition of cell membranes affects diverse cell functions including ion transport, the activity of membrane bound enzymes, and receptor function.[9] However, the question remains as to whether the lipid content of membranes affects their electrical properties. Although changes in the fatty acid composition of membrane phospholipids have been shown to affect the membrane potential of cells in vitro,[10] there is a void in our understanding of the basis for the changes at the membrane levels that are responsible for disease related changes in the phase angle.

If the serum phospholipid fatty acids are indeed a surrogate for membrane phospholipids, then the correlations we observed between specific fatty acids and the phase angle of the subjects we studied should apply to the fatty acids of tissue membrane phospholipids as well. This assumption leads

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Table 1 Characteristics of the subjects with SCD and controls

	Males			Females		
	SCD (n=34)	Controls (n=34)	p value	SCD (n=38)	Controls (n=34)	p value
Age (y)	13.4 (2.7)	13.9 (2.8)	NS	13.2 (3.4)	12.9 (3.1)	NS
Weight z score	−2.66 (1.31)	−0.72 (1.07)	<0.001	−1.83 (1.04)	−0.53 (0.81)	<0.001
Height z score	−2.40 (1.04)	−0.70 (1.38)	<0.001	−2.21 (1.49)	−0.35 (0.95)	<0.001
Phase angle	4.21 (0.77)	6.02 (0.95)	<0.001	4.38 (0.69)	5.42 (0.76)	<0.001

Results expressed as mean (SD).

Table 2 Percentages of selected fatty acids in the serum phospholipids of controls and children with SCD

Fatty acid	SCD subjects (n=72)	Controls (n=68)	p value
Palmitic acid (16:0)	35.5 (3.05)	33.2 (2.28)	<0.001
Stearic acid (18:0)	13.7 (4.59)	13.8 (3.11)	NS
Oleic acid (18:1 n-9)	12.9 (2.36)	11.6 (1.65)	<0.001
Linoleic acid (18:2n-6)	20.8 (4.51)	21.6 (3.70)	NS
Arachidonic acid (20:4n-6)	7.41 (1.84)	8.17 (2.06)	0.018
α-linolenic acid (18:3n-3)	0.23 (0.14)	0.25 (0.11)	NS
Eicosapentaenoic acid (20:5n-3)	0.30 (0.21)	0.63 (0.36)	<0.001
Docosapentaenoic acid (22:5n-3)	0.33 (0.18)	0.53 (0.18)	<0.001
Docosahexaenoic acid (22:6 n-3)	1.65 (0.73)	2.93 (0.92)	<0.001

Results are expressed as mean (SD).
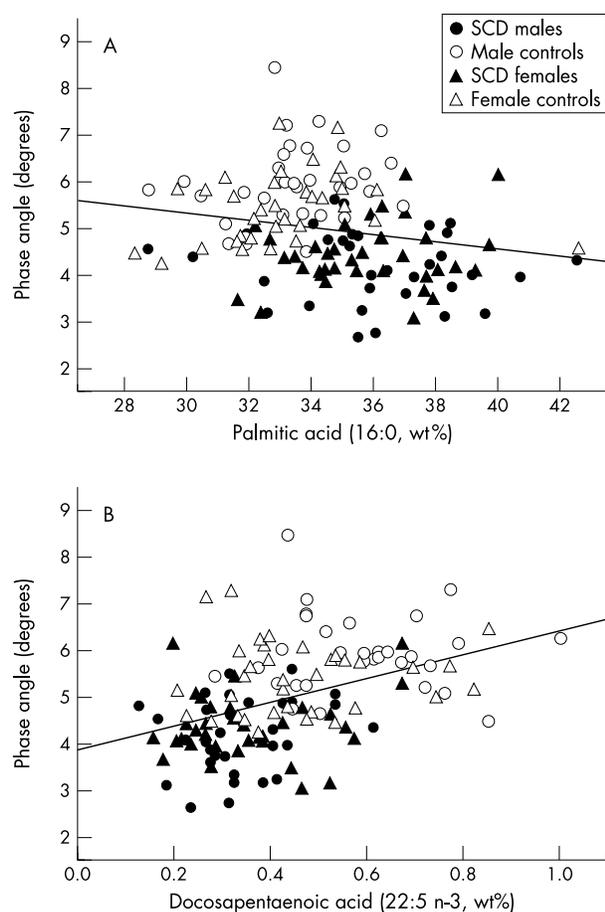
us to suggest that data from impedance analysis, specifically the phase angle, can be used to monitor changes in the composition of cell membranes as well as changes in body composition.

In summary, we found significantly lower phase angle values for Nigerian children with SCD compared to healthy controls. These decreases could be a result of either the presence of a malnourished state or of specific alterations in cell membrane properties, such as lipid content. We propose that impedance analysis, specifically determination of the phase angle, could be used to monitor any interventions, such as fatty acid supplementation aimed at addressing abnormalities in cell membranes that occur in SCD.

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Authors' affiliations
D J VanderJagt, C Bonnett, R H Glew, Department of Biochemistry and Molecular Biology, University of New Mexico, School of Medicine, Albuquerque, NM 87131, USA
Y-S Huang, L-T Chuang, Ross Products Division, Abbott Laboratories, Columbus, Ohio, USA

Correspondence to: Dr R H Glew, Department of Biochemistry and Molecular Biology, Room 249, BMSB, University of New Mexico, School of Medicine, Albuquerque, NM 87131, USA; rglew@salud.unm.edu

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Figure 1 (A) Relation between phase angle and the weight percent of palmitic acid (16:0) in serum phospholipids of subjects; p = 0.016, r = 0.20. (B) Relation between phase angle and the weight percent of docosapentaenoic acid (22:5n-3) in serum phospholipids of subjects; p < 0.001, r = 0.49.

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