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Essential fatty acid composition and correlates in children with severe acute malnutrition

Esther Babirekere-Iriso [a, b, *], Lotte Lauritzen [b], Charlotte Gylling Mortensen [b], Maren Johanne Heilskov Rytter [b], Ezekiel Mupere [c], Hanifa Namusoke [a], Kim F. Michaelsen [b], André Briend [b], Ken D. Stark [d], Adam H. Metherel [d], Henrik Friis [b]

[a] Mwanamugimu Nutrition Unit, Department of Paediatrics, Mulago Hospital, Kampala, Uganda
[b] Department of Nutrition, Exercise and Sports, University of Copenhagen, Faculty of Science, Copenhagen, Denmark
[c] Makerere College of Health Sciences, Department of Paediatrics, Kampala, Uganda
[d] Department of Kinesiology, University of Waterloo, Canada

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SUMMARY

Background: Severe acute malnutrition (SAM) is a common condition in children living in low-income countries and may be associated with reduced polyunsaturated fatty acids (PUFA) blood levels. The purpose of this study was to describe whole blood fatty acid composition and correlates of PUFA in children admitted with SAM.

Methods: We conducted a cross-sectional study among children admitted with SAM at Mulago National Referral Hospital and healthy controls. Whole blood fatty acid composition was measured and correlated with clinical data such as oedema, levels of haemoglobin, C-reactive protein and HIV-infection status. Multiple linear regression analyses were used to identify correlates of PUFA.

Results: The relative contribution of saturated fatty acid to the fatty acids in whole blood (FA%) were lower in 108 children with SAM compared to 24 well-nourished controls whereas most mono-unsaturated fatty acids were higher in children with SAM. Total and all n-6 PUFA including linoleic (18:2n-6, LA) and arachidonic acid (20:4n-6, AA), as well as total n-3 PUFA and docosahexaenoic acid (22:6n-3, DHA) were lower in children with SAM. The n-6:n-3 PUFA ratio was also lower in the children with SAM. Haemoglobin was a positive correlate of AA, n-3 docosapentaenoic acid (22:5n-3, n-3 DPA), DHA, total n-6 long chain (LC) PUFA and total n-3 LCPUFA. HIV infected children had 0.87 (0.47; 1.58) %-points less n-6 LCPUFA and 0.61 (0.03; 1.19) %-points less AA than the un-infected children.

Conclusion: Children with SAM presented with lower FA% of LCPUFA. HIV infection and low haemoglobin were also associated with lower FA% of LCPUFA, which may be related to lower numbers of blood cells. Nutrition rehabilitation interventions need to pay more attention to the intake of PUFA.

1. Introduction

Malnutrition is common in low-income countries, and may also occur in hospitalized patients, elderly and socioeconomically underprivileged people in high-income countries. Severe acute malnutrition (SAM) affects more than 19 million children and contributes significantly to childhood morbidity and mortality [1].

Much research has focused on associations between malnutrition and deficiencies of specific micronutrients, while little data exist regarding essential fatty acids in children with SAM and their associations with clinical presentations. The two parent essential fatty acids, i.e. linoleic acid (18:2n-6, LA) and α-linolenic acid (18:3n-3, ALA), cannot be synthesized by vertebrates [2]. They must

Abbreviations: AA, arachidonic acid; ALA, α-linolenic acid; CI, 95% confidence interval; CRP, C-reactive protein; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentanoic acid; FA%, fatty acid percent; HIV, human immunodeficiency virus; LA, linoleic acid; LCPUFA, long chain polyunsaturated fatty acid; MUAC, mid-upper-arm circumference; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SAM, severe acute malnutrition; SD, standard deviation; SFA, saturated fatty acid; WHO, World Health Organization; WHZ, weight-for-height-z score.

* Corresponding author. Mulago National Referral Hospital, Kampala, Uganda. Tel.: +256 772611167.

E-mail addresses: ebabirekere@yahoo.com (E. Babirekere-Iriso), ll@nexs.ku.dk (L. Lauritzen), charlotte.gylling@gmail.com (C.G. Mortensen), marenrytter@hotmail.com (M.J.H. Rytter), mupez@yahoo.com (E. Mupere), n6471277@gmail.com (H. Namusoke), kfm@nexs.ku.dk (K.F. Michaelsen), andre.briend@gmail.com (A. Briend), kstark@uwaterloo.ca (K.D. Stark), adammetherel@hotmail.com (A.H. Metherel), hfr@nexs.ku.dk (H. Friis).

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be supplied from the diet to fulfil essential human functions, including maintenance of the skin water barrier, optimal brain function, regulation of the immune system and reproduction [3]. LA and ALA can be metabolized to long chain polyunsaturated fatty acids (LCPUFA) that mediate some of these essential functions [3]. Essential fatty acid deficiency will in practice be associated with low levels of LA and ALA as well as their long chain metabolites such as arachidonic acid (20:4n-6, AA), eicosapentaenoic acid (20:5n-3, EPA) and docosahexaenoic acid (22:6n-3, DHA) [4]. Growing children do not only need relatively large amounts of PUFA for deposition in growing tissues but also for the biosynthesis of specific eicosanoids necessary for regulatory purposes such as immune function [3]. An FAO/WHO expert consultation on fats and fatty acids has suggested that the intake of n-6 PUFA for infants and children from 6 to 24 months should be 3.0–4.5 energy percentage (E%) and n-3 PUFA should be between 0.4 and 0.6 E% [5]. For undernourished children there are no firm recommendations, but it has been suggested that children with moderate acute malnutrition should consume at least 4.5 E% of n-6 PUFA and at least 0.5 E% of n-3 PUFA [6].

SAM in children has been shown to be associated with lower relative contribution of PUFA in plasma phospholipids, cholesterol esters and erythrocytes compared with healthy subjects [7]. Data regarding the effect of different types of malnutrition on PUFA status are controversial [8,9]. Wolff et al. [8] reported lower relative contribution of LA in plasma and erythrocytes in Peruvian children with both kwashiorkor and marasmus compared with well-nourished controls, whereas AA was lower in kwashiorkor only. In a Nigerian study, children with kwashiorkor had lower AA and DHA in plasma phospholipids and erythrocytes while LA did not differ in children with different types of malnutrition [9]. Furthermore, the relative contributions of different PUFA differ depending on the specific study setting, due to differences in diet and malnutrition co-morbidities. The purpose of the present study was to describe the whole blood fatty acid composition and identify correlates of PUFA in children admitted with SAM in a clinical setting of malnutrition.

2. Patients and methods

2.1. Study design

This was a cross-sectional study of children admitted for in-hospital treatment of SAM, between October 2012 and February 2013.

The study was conducted at Mwanamugimu Nutrition Unit, Mulago National Referral Hospital, Uganda, which is the main national rehabilitation center for children with complicated SAM.

Children aged 6–59 months with SAM, defined as weight-for-height z-score (WHZ) <−3 on the WHO Growth Standard or mid-upper arm circumference (MUAC) < 11.5 cm or bilateral pitting oedema [10], were eligible for the study. On admission, children who were in shock, or had severe respiratory distress requiring resuscitation, had haemoglobin concentration <4 g/dl, body weight <4.5 kg or significant disability like cerebral palsy were excluded from the study. A control group of 29 children were recruited among siblings of admitted children and children of hospital staff. The inclusion criteria for these children were being 6–59 months of age, apparently healthy, and with a WHZ >−1. Control children were not tested for HIV.

2.2. Ethical issues

Approval of the study was obtained from the Makerere University School of Medicine Research Ethics Committee, and Uganda National Council of Science and Technology. A consultative approval was also obtained from the Danish National Board of Research Ethics. Before enrolment into the study, informed consent was provided by parents or guardians of the children, as evidenced by a signed consent form. Participation in the study did not affect routine medical and nutritional treatment, which was similar to that offered to the admitted children not participating in the study.

2.3. Questionnaire

The age of the child was noted by asking the caretaker the child's date of birth. When available, the child's immunization card was checked to confirm the date of birth. The child's breastfeeding history and fish intake in the household in the past two weeks were obtained from the mother/caretaker.

2.4. Physical examinations and anthropometric measurements

On admission, physical examination was performed and oedema was diagnosed according to WHO guidelines [11]. Length was measured using an infant length board (Infant/Child Shorr-Board®) and MUAC using measuring tape, both to the nearest 1 mm. Body weight was measured daily to the nearest 100 g using a digital scale (Seca 813). Anthropometric z-scores were computed using WHO Growth Standards [12], adjusting for the fact that length was measured even in children older than two years, and using the lowest weight recorded during admission, to determine weight free from oedema.

2.5. HIV

All biological mothers were offered counselling and testing for HIV, according to WHO guidelines [13]. If the mother was HIV infected or absent, the child was tested.

2.6. Blood sampling

On admission, haemoglobin was measured in venous blood collected in heparinized vacutainer tubes using HemoCue (Hb 201+, Ängelholm, Sweden). Plasma was obtained from a vacutainer with citrate (Cell-Preparation Tube, Becton Dickinson, USA) by centrifugation at 1300–2200 G for 10 min, stored at −80 °C until shipped on dry ice to the University of Copenhagen, Department of Nutrition, Exercise and Sports, Denmark, where plasma level of C-reactive protein (CRP) was measured by high sensitive kit on a ABX Pentra 400 (Horiba, France, no. A11A01611 and A11A01696).

Approximately 40 μl of whole blood was applied to an antioxidant-treated (with 1000 μg deferoxamine and 50 μg butylated hydroxytoluene) chromatography paper strip so that approximately 1 cm^2 was saturated with blood [14]. The blood spot was allowed to dry completely at room temperature. The samples were then stored in a sealed container (polypropylene 'ziplock' bag) in a refrigerator for up to two months until they were shipped to University of Waterloo, Department of Kinesiology, Canada for fatty acid analysis. Storage of whole blood on chromatography paper under these conditions is shown to be stable for this period of time [15]. Once in Canada, the samples were stored at −80 °C.

2.7. Fatty acid analysis

The whole blood spot was directly transesterified with the addition of 1 mL of 14% boron trifluoride in methanol (Pierce Chemicals), 300 μL of hexane and 3 μg of an internal standard (22:3n-3 ethyl ester; Nu-Check Prep, Elysian, MN, USA) and heated at 95 °C for 1 h [16]. Samples were allowed to cool to room