Phase Angle and Nutritional Status of Children in Antineoplastic Treatment

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Ângulo de Fase e Estado Nutricional de Crianças em Tratamento Antineoplásico

Ángulo de Fase y Estado Nutricional de los Niños Sometidos a Tratamiento Antineoplásico

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ABSTRACT

Introduction: Child cancer has a major impact on public health. The evaluation of body composition by bioelectric impedance provides the values of phase angle, causally related to functional changes in the cell membrane which have been used to evaluate nutritional status and prognosis. **Objective:** To evaluate the correlation between phase angle and parameters of the nutritional status of pediatric oncologic patients under treatment. **Method:** Cross-sectional study performed in a public university hospital. The nutritional status was evaluated by weight, height, arm circumference, triceps skin fold, body mass index and arm muscle circumference. The phase angle was determined by bioelectric impedance. **Results:** 13 patients were included with a mean age of 103.2±39.7 months, 61.5% males with prevalence of leukemia in the diagnoses. It was found that most (53.8%) of the patients were eutrophic. There was a strong correlation of the phase angle with the parameters of lean mass (r=0.923; p=0.000), cellular body mass (r=0.911; p=0.000), extracellular mass (r=0.897; p=0.000) and body weight (r=0.920; p=0.000). **Conclusion:** Expressive associations between phase angle and other anthropometric indicators were observed, reinforcing the hypothesis that it can anticipate the identification of changes in body composition, allowing early nutritional intervention and better prognosis.

Key words: Neoplasms/drug therapy; Body Composition; Electric Impedance/therapeutic use; Nutritional Status; Child.

RESUMO

Introdução: O câncer infantil gera um grande impacto para a saúde pública. A avaliação da composição corporal pela impedância bioelétrica fornece os valores de ângulo de fase, diretamente relacionados a alterações funcionais na membrana celular e que têm sido usados para avaliar o estado nutricional e o prognóstico. **Objetivo:** Avaliar a correlação entre o ângulo de fase e os parâmetros do estado nutricional de pacientes oncológicos pediátricos em tratamento. **Método:** Estudo transversal realizado em um hospital público universitário. O estado nutricional foi verificado por meio das medidas de peso, altura, circunferência do braço, dobra cutânea tricipital, índice de massa corporal e circunferência muscular do braço. O ângulo de fase foi determinado pela impedância bioelétrica. **Resultados:** Foram incluídos 13 pacientes com média de idade de 103,2±39,7 meses, sendo 61,5% do sexo masculino, com prevalência da leucemia entre os diagnósticos. Constatou-se que a maioria (53,8%) dos pacientes estava em eutrofia. Houve forte correlação do ângulo de fase com os parâmetros de massa magra (r=0,923; p=0,000), massa corporal celular (r=0,911; p=0,000), massa extracelular (r=0,897; p=0,000) e peso corporal (r=0,920; p=0,000). **Conclusão:** Observaram-se correlações expressivas entre o ângulo de fase e os indicadores antropométricos, reforçando a hipótese de que o ângulo de fase pode antecipar a identificação de alterações na composição corporal, possibilitando uma intervenção nutricional precoce e melhor prognóstico.

Palavras-chave: Neoplasias/tratamento farmacológico; Composição Corporal; Impedância Elétrica/uso terapêutico; Estado Nutricional; Criança.

RESUMEN

Introducción: El cáncer infantil tiene un gran impacto en la salud pública. La evaluación de la composición corporal por impedancia bioeléctrica proporciona los valores del ángulo de fase, directamente relacionados con los cambios funcionales de la membrana celular y que se han utilizado para evaluar el estado nutricional y el pronóstico. **Objetivo:** Evaluar la correlación entre el ángulo de fase y los parámetros del estado nutricional de los pacientes oncológicos pediátricos en tratamiento. **Método:** Estudio transversal realizado en un hospital universitario público. El estado nutricional se evaluó por peso, altura, circunferencia del brazo, pliegue de la piel del tríceps, índice de masa corporal y circunferencia muscular del brazo. El ángulo de fase fue determinado por la impedancia bioeléctrica. **Resultados:** Se incluyeron 13 pacientes con una edad media de 103,2±39,7 meses, de los cuales el 61,5% eran hombres con prevalencia de leucemia entre los diagnósticos. Se descubrió que la mayoría (53,8%) de los pacientes eran eutróficos. Hubo una fuerte correlación del ángulo de fase con los parámetros de masa magra (r=0,923; p=0,000), masa corporal celular (r=0,911; p=0,000), masa extracelular (r=0,897; p=0,000) y peso corporal (r=0,920; p=0,000). **Conclusión:** Se observaron asociaciones expresivas entre el ángulo de fase y otros indicadores antropométricos, lo que refuerza la hipótesis de que puede anticiparse a la identificación de cambios en la composición corporal, lo que permite una intervención nutricional temprana y un mejor pronóstico.

Palabras clave: Neoplasias/tratamiento farmacológico; Composición Corporal; Impedancia Eléctrica/uso terapéutico; Estado Nutricional; Ninõ.

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INTRODUCTION

Child and adolescent cancer (diagnosed between 0 and 19 years) includes several malignant neoplasms and the incidence varies in the whole world according to age, gender, ethnicity and geography. Regardless of being a cancer considered rare when compared with adult's, the number of new cases in this age range is a great impact for public health because the rates of mortality use to be high, in addition to important side effects the treatment causes[1].

It corresponds to 1% to 4% of the cases, when compared with other neoplasms[2]. The American Cancer Society[3] affirms that leukemias are the most prevalent (28%), followed by central nervous system (26%) and lymphomas (8%). It is estimated 4,310 new cases in males and 4,150 per year in females in Brazil in the period of 2020-2022[4].

The progressive weight loss and resulting nutritional depletion are typically encountered in oncologic patients with direct impact in unfavorable outcome. In this sense, the early detection of nutritional variations is essential to prevent functional and morphologic alterations ensuring the development and proper evolution of children and adolescents[5]. The fast and simple identification of the nutritional risk through screening and evaluation of the nutritional status should be the primary actions to treat these patients[6].

Anthropometry evaluates the body composition through measurement of weight, height, skinfolds and circumferences parameters. The nutritional evaluation of pediatric oncologic patients should look for the presence of edema, ascites and tumor mass that can lead to a misleading classification of the nutritional status[7]. Bioelectrical impedance (BIA) is a method for estimating body composition considered simple, of easy application, low cost, non-invasive and fast and can be done in bed.

With BIA, it is possible to determine the body components as lean and fat mass and water, in addition to the phase angle (PhA)[8]. PhA is a measure obtained through the ratio of the resistance (R), that is, the opposition of the tissues to the electric flow to reactance (Xc), which is the capacitance of the cellular membranes[8]. The value of PhA is related to functional alterations in the cell membrane with reflection in the body tissues and hydric distribution among the intra and extracellular fluid, being increasingly encouraged to assess the nutritional status and prognosis including oncologic patients. However, so far, the studies in the scientific literature evaluating the role of PhA in children with cancer are scarce[9,10].

The objective of the present study was to evaluate the correlation between PhA and parameters of nutritional status of pediatric patients in antineoplastic treatment.

METHOD

Cross-sectional study with 13 pediatric patients diagnosed with neoplasms and in antineoplastic treatment. All the patients enrolled through convenience sample underwent specific intervention. Their legal guardians accompanied them, were informed about the study objectives and procedures and both signed the Assent Form (AF). The data were collected from July to September 2018. Date of birth, gender, type of tumor, tumor staging, chemotherapy cycle and time of diagnosis were extracted from the electronic charts.

The Institutional Review Board approved the study, CAAE number 81081717.0.0000.5154 in compliance with Resolution number 466/2012[11]. The inclusion criteria were individuals between 0 and 19 years old, both genders with diagnosis of neoplasms in chemotherapy and/or radiotherapy treatment. Patients with incomplete charts, in relapse and other basal pathologies were excluded.

BIA (Byodinamics®, model 450, brand TBW Brazil) was used to evaluate the body composition according to the manufacturer's recommendations. Anthropometric measurements included: weight (kg), height (cm), arm circumference (AC) (cm) and tricipital skinfold (TSF) (mm), with calculation of the body mass index (BMI) (kg/m^2) and of the arm muscle circumference (AMC) (cm) as the "*Avaliação Nutricional da Sociedade Brasileira de Pediatria*"[12] (Brazilian Nutritional Pediatrics Society) recommends. The volunteers were evaluated pursuant to the anthropometric indicators of weight-for-age (WFA) (0 to 10 years), weight for height (WFH) (0 to 5 years), height for age (HFA) (0 to 19 years), body mass index for age (BMI/A) (0 to 19 years) and classified in score Z by the curves of growth of the World Health Organization (WHO) of 2006/2007 (software WHO Anthro version 3.2.2 and WHO Anthro Plus 1.0.4). For data of AM, AMC and TSF the Frisancho[13] patterns were used as references for classification.

The software Statistics 6.0® (StatSoft Incorporation, Tulsa, Ok, USA) was utilized for statistical analyzes. The Shapiro-Wilks test was applied to test the normality of the distribution of the data obtained. The variables were presented as mean and standard deviation for parametric variables and as median, minimum and maximum values for the non-parametric. The test t of Student was used to compare the groups (gender). Pearson correlation was adopted to evaluate the presence of the correlation among several parameters of the study, values of r between 0.1 and 0.3 are considered weak, between 0.4 and 0.6, moderate and between 0.7 and 1[14], strong.

RESULTS

The casuistic consisted of 13 patients, 8 males (61.5%) and five females (38.5%), with mean age of 103.2 ± 39.7 months. Eight patients were diagnosed with acute lymphocytic leukemia, one, low-grade unresectable glioma, one, Hodgkin lymphoma, one, osteosarcoma and one, Langerhans cell histiocytosis. All the patients were in chemotherapy cycle and two in radiotherapy. The patients presented median of 9 months from the time of the diagnosis until the intervention, minimum of three months and maximum of 21. Three patients had associated diseases as hypertension, depressive syndrome and suspected diagnosis of Cushing's syndrome.

The anthropometric data and the parameters obtained through BIA are presented in Table 1. Seven patients were eutrophic (53.8%), one (7.7%) with risk of overweight, three (23.2%) with overweight and two (15.4%) with obesity according to the classification of BMI/A. All the patients had correct height-for-age.

The patients presented mean of percent of match of 114.8% for AC and 117% for TSF considering the values of percentile 50 for gender and age[13]. The correlation of the values of PhA with other parameters of nutritional status is shown in Table 2. Only the variables AMC, AC and TSK did not hold strong correlation with PhA.

DISCUSSION

No patient in the present study was malnourished according to the BMI/A criteria. In addition, the PhA held strong correlation with other anthropometric parameters: lean mass, body cell mass (BCM), extracellular mass (EM), total water and body weight. Studies have been demonstrating the action of PhA as indicator of nutritional status in this population, low values of PhA would indicate nutritional risk even with BMI compatible with eutrophy. Changes of cellular level occur prior to tissue alterations detectable with traditional anthropometric methods, showing the relevance of PhA in clinical practice as tool of screening and indicator of prognosis[15,16].

BIA and consequently the values of PhA have been the objective of studies in the last years as tool of prognostic, nutritional value, of function of cellular membrane or indicator of health in several clinical conditions and in adults and children[15,17,18]. Its association with other evaluation tools as anthropometry in patients in nutritional risk can lead to a more accurate intervention[9].

The mean value of PhA the volunteers showed in this study was 4.5º. So far, there are no reference values of PhA established in the literature for the population of healthy Brazilian children for comparison. A study of De Palo

Table 1. Distribution of the variables of body composition of all the study volunteers according to gender

	All (n=13)	Female (n=5)	Male (n=8)
Body weight (kg)	30.2±11.9	26.1± 8.4	32.7±13.1
AC (cm)	20.1±3.8	19.8±2.2	20.3±4.6
TSF (mm)	14.4±4.8	13.2±1.78	15.1± 6.0
AMC (cm)	15.6±2.9	15.6±2.0	15.5 ±3.4
BMI (kg/m²)	17.7±3.0	17.5±1.95	18.6± 3.2
Lean Mass (kg)	23.6±7.9	21.4±8.3	25.1± 7.8
Lean Mass (%)	80.2±7.8	80.9±5.3	79.7±9.4
Fat Mass (kg)[1]	7.1±4.9	4.9±1.7	8.5 ±5.7
Fat Mass (%)	21.6±7.7	18.8±5.1	23.3±8.8
Water (L)	17.6±5.2	16.4±6.1	18.9±4.8
Total water (%)	75.8±4.4	77.5±2.1	74.7±5.3
BCM	10.9±3.4	10.3 ±4.1	10.9±4.2
EM	12.8±4.6	11.3±3.1	14±4.7
Phase angle (°)	4.6±1.0	4.7±1.4	4.5±0.7

Captions: AC: arm circumference; TSF: tricipital skinfold; AMC: arm muscle circumference, BMI: body mass index; BCM: body cell mass; EM: extracellular mass; [1]: $p<0.05$, test t of Student.

Table 2. Correlation of Pearson of the phase angle vs. parameters of nutritional status of all the study volunteers (n=13)

	Value of r	Value of p
Lean mass (kg)	0.923	0.000*
Fat mass (Kg)	0.734	0.004*
BCM	0.911	0.000*
EM	0.897	0.000*
EM/BCM	0.919	0.024*
Total water (L)	0.920	0.000*
Total water (%)	-0.773	0.002*
Current weight (kg)	0.920	0.000*
AMC (cm)	0.569	0.042*
AM (cm)	0.618	0.024*
TSF (mm)	0.471	0.104

Captions: BCM: body cell mass; EM: extracellular mass; AMC: arm muscle circumference; AC: arm circumference; TSF: tricipital skinfold; *Value of p considered significant <0.05[14].

et al.[17]with 2,044 healthy children between 10 and 15 years encountered a variation of PhA greater than what was found in the present study (between 5.7º and 6.2º).

In other studies, values of PhA between 0.7º and 3.1º were found in a population of malnourished pediatric patients[18,19]. A possible association between PhA and the anthropometric indicators can be explained by the fact that PhA reflects the function of the cellular membrane and of the BCM, predominantly formed by muscles. When low PhA values are found, it can suggest cell death or alteration of the integrity of the cellular membrane and the opposite indicates intact cellular membranes[9]. Therefore, it is suggested that low value of PhA can be attributed to the process of sarcopenia already reported in malnourished and oncologic patients[20].

Few are the studies in the literature addressing the role of PhA in children in antineoplastic treatment. Garofalo et al.[21] demonstrated in a study with 33 oncologic pediatric patients with mean age of 10 years the presence of low values of PhA when compared with healthy children (5.5º *vs*. 4.8 º, respectively). In critical patients, these low values of PhA were associated with poor nutritional status, worse clinical outcomes and high mortality[21].

The association of PhA and time of hospitalization and mortality of critical pediatric patients was evaluated in a study with 247 volunteers admitted in intensive care units. Higher survival was found in children with PhA bigger than 2.8º. Those with low values of PhA were hospitalized for more time[22].

In a study Pereira et al.[23] conducted in a Brazilian university hospital with children in chemotherapy treatment two groups were assigned: group I (leukemias, mean of 92 months of age) and group II (lymphomas and solid tumors, mean of 62 years old); BIA was performed in three moments: before the first session of chemotherapy, in the middle of the treatment protocol, at the end of the induction phase in leukemias and one week after the application of the last chemotherapy for solid tumors. Similar to the findings of this study, group I presented better values of PhA of 4.6º ± 1.2, 4.5º ± 1.1 and 4.5º ± 0.7, in three times, respectively. For solid tumors, the means of PhA were 5.1º ± 1.4, 4.8º ± 0.9 and 4.6º ± 0.7. No change of PhA was identified during the treatment in any of the groups, however, when patients of different groups were observed individually it was noticed that most of them presented reduction of the values of PhA during the treatment, regardless of the type of tumor[24].

Based in the reduction of values of PhA found in different studies, it was hypothesized that the patients could be at risk of malnutrition even when BMI values are compatible with eutrophy, which is justified by the fact that cell level alterations occur before tissue level alterations (which can be detected through usual methods for nutritional diagnosis as anthropometry)[23]. However, chemotherapics can promote low values of PhA too, since the cellular membrane acts to eliminate the drugs administered and PhA depends directly of its integrity[25].

Some of the limitations are the study's cross-sectional nature, not being possible to infer causal relations and not having control group. The size of the casuistic is another issue as it was a sample by convenience since the health service is not a reference in pediatric oncologic treatment.

CONCLUSION

Pediatric patients in antineoplastic treatment hold strong correlations among PhA and anthropometric parameters of lean mass, BCM/EM and body weight. BIA is a non-invasive, easily applicable method of evaluation and PhA detection can identify early the patients in nutritional risk, ensuring immediate intervention.

CONTRIBUTIONS

All the authors contributed for the study conception and/or design, data collection, analysis, and interpretation, wording, critical review and approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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