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Application of phase angle for evaluation of the nutrition status of patients with anorexia nervosa

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Summary

The evaluation of the nutrition status of patients has been the subject of interest of many scientific disciplines. Any deviation from normal values is a serious clinical problem. There are multiple nutrition status evaluation methods used including diet history, scales and questionnaires, physical examination, anthropometric measurements, biochemical measurements, function tests, as well as bioelectric impedance analysis or adipometry. Phase angle, obtained by means of bioelectric impedance analysis, is another parameter that is being more and more frequently applied in nutrition status monitoring. It is proportional to body cell mass. Its direct correlation with the cellular nutrition status has been documented. High phase angle values signify well-being, while low phase angle values indicate poor condition of cells. The purpose of this paper was to review the current state of knowledge about the application of phase angle in evaluation and monitoring of the nutrition status of patients with anorexia nervosa on the basis of available literature. It was proven that the phase angle values in patients with anorexia nervosa are much lower compared to healthy people. Detailed observations showed phase angle value increase in the course of treatment. The relevance of the commonly used body mass index (BMI) has been questioned due to significant degree of generalization in the nutrition status evaluation. Thus, there is a need for new, objective parameters for nutrition status evaluation, which will assist in the treatment and monitoring of patients in a more meaningful and reliable way. The existing independent studies equivocally confirm the usefulness of phase angle in the evaluation of nutrition status of patients with anorexia nervosa and its broader application in clinical practice is only a matter of time. However, these are merely attempts and they have not yet found wider application in clinical practice in the treatment of anorexia nervosa.

Key words: anorexia nervosa, nutritional status, phase angle

Introduction

In recent years we have observed enormous interest in human nutrition status evaluation. This is an interdisciplinary subject drawing attention of various specialists. Body mass disturbances – being underweight/cachectic or overweight/obese – are more frequently a serious problem in many medical disciplines and they constitute one of basic risk factors for occurrence of many diseases of civilization like hypertension or diabetes. According to a definition by the European Society for Clinical Nutrition and Metabolism (ESPEN), malnutrition is "a state resulting from lack of uptake or intake of nutrition leading to altered body composition and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease" [1, p. 335–336]. Compared to overnutrition/obesity, malnutrition, as significant clinical factor of high mortality, is still poorly understood. According to DSM-5, anorexia nervosa (AN) has been defined as food intake disorder characterized by purposeful body mass loss, consciously induced and maintained by the patient [2].

The purpose of this paper was to present the current state of knowledge about the application of phase angle in evaluation of the nutrition status of patients with anorexia nervosa. To that end, we have reviewed literature available in PubMed and Google Scholar databases using the following key words: phase angle, anorexia nervosa, bioelectric impedance analysis, and time descriptors: 1990–2015.

Nutrition status evaluation tools

Studies attempting at comprehensive evaluation of nutrition status commonly use: interview (including diet history), physical examination, anthropometric measurements, and biochemical analysis.

Diet history

Taking a detailed medical history from a patient is still the basic method of evaluating the degree of malnutrition. Thanks to this, it is possible to estimate either the risk of occurrence of nutrition disorders or the degree of the process intensity. The evaluation of daily food intake constitutes extremely significant information.

Scales and questionnaires

There are many different tools that help in evaluation of nutrition status including scales and questionnaires. The most frequently used scale is the Subjective Global Assessment (SGA) [1].

Physical examination

The collected medical history is supplemented with physical examination. The most important element of this examination is the evaluation of patient's body mass and the measurement of body mass loss in correlation with time.

Anthropometric measurements

The most important and the most frequently used anthropometric measurements for the evaluation of nutrition status are [3]:

- body mass index (BMI);
- waist to hip ratio (WHR);
- measurement of skinfolds in appropriate places, i.e., most frequently over the biceps, triceps, under the shoulder blade and over the hip;
- arm circumference;
- fat tissue percentage calculated using anthropometric formulas.

Function tests

The most important function tests are:

- direct stimulation of muscles (most frequently electric stimulation of adductor pollicis muscle);
- respiratory resistance measurement;
- handgrip.

Biochemical analyses

The most frequently used laboratory examinations evaluating nutrition status estimate the levels of: albumins, hemoglobin, transferrin, retinol binding protein, fibronectin, CRP, IL-6, and the number of lymphocytes in peripheral blood [3].

In clinical diagnostics, indirect parameters describing the body content are still routinely used, i.e.: current body mass compared to appropriate mass, BMI, WHR, skinfold thickness in designated points and the SGA. The commonly used BMI or skinfold thickness measurement are more and more often questioned due to significant degree of generalization in the evaluation of nutrition status and the fact that they do not indicate quantitatively important changes in patients' body content. Additionally, in order to properly analyze body content, it is necessary to know the organism hydration level, which is crucial for appropriate cell metabolism, as well as dry tissue component magnitude, i.e., muscular tissue, fat tissue. Opportunities to obtain such data are provided by bioelectric impedance analysis, which is presented in more detail below.

Bioelectric impedance analysis

Bioelectric impedance analysis (BIA) is a non-invasive, repeatable, method of specific, adequate and fast evaluation of body composition, which utilizes distinct electric properties of various tissues. Electric current (most often of 50 kHz frequency) flowing through the organism is conducted in different manner by separate tissues. Bioelectric impedance is the total resistance of the body to alternating current. It consists of resistance (*R*), which is the resistance of water and electrolytes dissolved in it, and reactance (*Xc*), which is the capacitive resistance of body cells acting like condensers [4]. It can be used in both healthy people and patients suffering from various chronic conditions associated with undernutrition including anorexia nervosa.

It is a method that allows for evaluation of the fat and fat free mass content and also defines the proportions in the watery spaces of the system, that is, the amount of intracellular and extracellular water and its balance. This method – on the basis of bioelectric impedance analysis of the body (*Z*), consisting of: resistance (*R*) and reactance (*Xc*) – using algorithms, calculates such parameters as: phase angle (PA), fat mass (FM), fat free mass (FFM), lean body mass (LBM), body cell mass (BCM), total body water (TBW), intracellular water (ICW) and extracellular water (ECW), system hydration level (ECW/ICW), which together provides full, detailed analysis of body composition and constant monitoring of structural changes of the organism in the course of therapy.

Phase angle – definition and clinical significance

Phase angle is calculated on the basis of resistance (*R*) and reactance (*Xc*) obtained by means of bioelectric impedance analysis according to phase angle formula PA = arc tangent *Xc*/*R* [4]. Biological significance of the phase angle is not fully understood but it is considered to be an indicator of cellular health. Phase angle value is closely correlated with body cell mass (BCM) [5]. Higher phase angle value is correlated with better cell function. It is an indicator of cell membrane integrity. Its value is influenced by the difference between the potential on the internal and external side of cell membranes. In the case of well nourished cells, their reactance is high, which implicates high PA value. In contrast, cells in bad condition lose membrane integrity, which is reflected by low PA value. Thus, it depends on the condition of integral components of cells responsible for biochemical and energetic activity [6, 7]. In this aspect, the value of this parameter reflects the efficiency of energy processes and proteolysis, indicating direct relationship with patient's health status [7].

The studies conducted so far were aimed at establishing the range of population standards for phase angle value and finding ways to apply them in clinical practice. The studies carried out on large group of volunteers of various nationalities revealed that there are differences in phase angle value in relation to sex, age and ethnic group [8]. Despite differences, it is believed that phase angle value in healthy adults is 5–7° [8, 9], and value below 5° indicates malnutrition.

The studies showed that phase angle value is not only a prognostic marker in serious conditions [10] but also a useful tool in evaluation of nutritional treatment efficiency [11, 12]. Low values of this parameter negatively correlate with prognosis in the case of such diseases as liver cirrhosis, HIV and cancer of many organs [6, 10, 13–18]. Decreased PA values were also found in malnourished children compared to control group [19].

Anorexia nervosa – general characteristics

Anorexia nervosa (AN) is a mental disturbance leading to very serious consequences for physical and mental health of patients [20]. In Poland, the prevalence of AN in girls below 18 years of age is from 0.8 to 1.8% [21]. AN in western countries occurs in 0.9 to 4.3% of women and from 0.2 to 0.3% of men and is considered to be one of the most serious chronic disorders, with mortality rate estimated to be about 10% [22, 23].

One of the objective criteria for this disease classification according to ICD-10 is body mass below 15% of appropriate mass, which corresponds to BMI < 17.5 kg/m^2 [24]. Similarly, one of DSM-5 criteria indicates body mass below 85% of normal weight for height and age [2].

Two types of the disorder may be distinguished. In the case of restrictive type, the patients limit food intake to minimum and they sporadically use laxatives. The bulimic type is characterized with regular episodes of gorging accompanied by compensative behavior in form of vomiting, as well as abusing laxatives and diuretics.

Main causes of death in anorexia nervosa include cachexia and its complications, mainly heart failure and electrolyte disturbances as well as suicide [20, 25].

AN is characterized with rapid organism wasting which leads to irreversible changes involving metabolic and hormonal ones, as well as neurological disturbances including brain volume decrease [26, 27].

Studies concerning the application of phase angle in diagnostics and monitoring of treatment in anorexia nervosa

We have reviewed literature available in PubMed and Google Scholar databases using the following key words: phase angle, anorexia nervosa, bioelectric impedance analysis, and time descriptors: 1990–2015.

Results of studies comparing phase angle value in patients with anorexia nervosa at the beginning of treatment and during convalescence were analyzed. They were compared to values observed in healthy people. The results of studies with the use of phase angle conducted among patients with anorexia nervosa are presented in Table 1.

Table 1. **The results of studies with the use of phase angle conducted among patients with anorexia nervosa**

Author/year of publication	Study group/number of participants (n)	Parameter	Commentary
Marra et.al. (2009) [28]	AN (n = 30), Essentially slim women (n = 10), Ballet dancers (n = 15), Healthy participants (n = 30)	Phase angle	Lower phase angle values were observed in patients with anorexia nervosa compared to essentially slim people (respectively 5.09°±0.52 and 5.94°±0.93; p < 0.001). In the second group, despite low body mass, the phase angle range was within population standards. Ballet dancers' phase angle values were higher compared to values obtained in patients with anorexia nervosa (respectively 6.40°±0.51 and 5.09°±0.52; p < 0.001) and control group (respectively 6.40°±0.51 and 5,84°±0.55; p < 0.001).
Moreno et al. (2007) [29]	AN (n = 13), Healthy participants (n = 17)	Phase angle	Phase angle values in patients with anorexia nervosa (5.5°±1.0) were lower than in control group (6.4 °±0.6) indicating cachexia in the first group.
Piccoli et al. (2005) [30]	AN (n = 74)	BIVA	Vector analysis (BIVA) of reactance (Xc) and resistance (R) indicates significant deviation from the reference range in the case of patients with AN. Return of the vector to normal range (75% ellipsis) constitutes an indicator of treatment efficiency.
Marra et al. (2005) [31]	AN (n = 86)	Phase angle, Basic metabolism	Phase angle (2.54–6.49°) and reactance showed strict correlation with basic metabolism (BMR 3,782±661 kJ) in patients with AN (p < 0.001).
Mika et al. (2004) [32]	AN (n = 21), Healthy participants (n = 19)	Phase angle	Gradual increase of phase angle value was observed in patients with AN undergoing treatment (within the 3rd and 15th week of treatment) with 4.6°±0.4 to 5.2°±0.6. Phase angle values at the time of convalescence after long term treatment had the same values as in healthy volunteers group (5.5°±0.6), with simultaneous BMI differences between the two groups (convalescents: 17.4 kg/m^2±0.7; healthy participants: 21.3 kg/m^2 ±2.0).

table continued on the next page

Scalfi et al. (1999) [33]	AN (n = 13), Healthy participants (n = 25)	Phase angle of the whole body and limbs (segmental)	Phase angle values in patients with AN were lower compared to the control group. Changes of the phase angle values measured using whole body impedance analysis were correlated with BMI increase ($p < 0.025$). Changes of the phase angle values measured using limbs impedance analysis were not correlated with BMI increase ($r = 0.694$; $p < 0.10$) Phase angle value changes in the course of treatment demonstrated extracellular water volume decrease in favor of intracellular water, confirming nutrition status improvement.
Polito et al. (1998) [34]	AN (n = 20), Convalescents (BMI > 18.5 kg/m^2) (n = 9), Healthy participants (n = 10)	Phase angle	In the group of patients with AN, phase angle values were lower (4.4 °±0.8) compared to the control group (6.1 °±0,4; $p < 0.0000$), indicating disturbed distribution between extra – and intracellular water volume. In the case of convalescents, phase angle values were 5.0 °±0.7 and the values were still lower compared to healthy subjects despite normal BMI, which proves that the balance between extracellular and intracellular water was still disturbed.
Marra et al. (1997) [35]	AN (BMI < 16 kg/m^2) (n = 39), Anorexia nervosa (BMI < 16–18.5 kg/m^2) (n = 22), Healthy participants (n = 55)	Phase angle of the whole body and limbs (segmental).	The lowest phase angle values were observed in patients with BMI < 16 measured using whole body and segmental impedance analysis ($p < 0.01$). Patients with BMI 16–18.5 kg/m^2 demonstrate values similar to the control group in scope of phase angle measured using whole body and lower limbs impedance analysis, while the values measured using upper limbs impedance analysis remained low ($p < 0.01$).
Scalfi et al. (1993) [36]	AN (n = no data), Convalescents (n = no data) Healthy participants (n = no data)	Phase angle, Basic metabolism	Patients with AN exhibited the lowest phase angle values (3.70°±0.83; $p < 0.01$). In the case of recent convalescents, phase angle values (4.36°±0.82) still significantly deviate from the population standards (5.17°±0.40), ranking between results of patients with anorexia and healthy people. This indicates health improvement of patients treated due to anorexia nervosa, however, because of short therapy, this effect was not complete, which was reflected by low phase angle value. Basic metabolism was significantly decreased ($p < 0.01$) only in the group of patients with AN.

Phase angle values in patients with AN, as it was shown by studies, were similar to the values in malnourished patients or patients with cachexia (5.09°±0.52 [28]; 5.5°±1.0 [29]; 2.54–6.49° [31]; 4.6°±0.4 [32]; 4.4 °±0.8 [34]; 3.70°±0.83 [36]). At the same time, which is worth noting, in the course of treatment the values of this parameter were gradually increasing. Thus, phase angle became an indicator of nutrition status of patients with AN in the course of treatment.

Bioelectric impedance analysis allows for establishing the reason for nutrition state improvement by answering the question whether the change was due to fat tissue mass increase or extracellular or intracellular water volume increase. As it was mentioned earlier, bioelectric impedance analysis on the basis of direct parameters like impedance (*Z*), resistance (*R*) and reactance (*Xc*), by means of algorithms, facilitates the calculation of other parameters, i.e.: phase angle (PA), fat mass (FM), fat free mass (FFM), total body water (TBW), intracellular water (ICW) and extracellular water (ECW), which together allows for monitoring of body composition changes in the course of treatment.

Phase angle measurements can be performed using bioelectric impedance analysis of the whole body or particular segments [35]. As it was shown in a study, patients' convalescence in the course of treatment (and more precisely obtaining cellular wellbeing) is not symmetrical in the whole body but is different in particular parts.

At the same time, studies comparing phase angle values in healthy people and convalescents revealed differences between the groups. People treated due to anorexia nervosa, despite reaching satisfactory BMI, still had lower phase angle values (5.0°±0.7 [34] and 4.36°±0.82 [36]) compared to control group (respectively 6.1°±0.4 [34] and 5.17°±0.40 [36]). It proves that BMI is characterized with high degree of generalization in the evaluation of nutrition status.

Phase angle values, as it was shown in a different study, significantly differed in patients with low body mass (AN 5.09±0.52; essentially slim persons 5.94±0.93; ballet dancers 6.40±0.51; $p<0.001$). In contrast to traditional anthropometric measures, this parameter was the only measurable indicator having different values with respect to different forms of weight deficit, thus becoming a factor differentiating between the groups [28].

As studies showed, phase angle value, apart from direct correlation with cellular mass, constituted a predictive factor of basic metabolism in underweight subjects [31]. It points out to specific opportunity of using the phase angle not only for treatment effects monitoring but also in the course of preparing nutrition plan for these patients. Farther studies of this subject are still necessary.

Recapitulation

Phase angle measured in non-invasive way using bioelectric impedance analysis constitutes a potentially new, objective and useful indicator of correct nutrition status in clinical practice.

Many studies confirmed clinical usefulness of this parameter as a prognostic factor in serious diseases with cachexia. Anorexia nervosa is one of many disorders, in which, as yet single studies show strict correlation between phase angle value and

patient nutrition status. It indicates potential possibility to use this parameter for monitoring treatment results, while it remains a more reliable parameter of nutrition state improvement in patients with anorexia nervosa than mere BMI.

Thus, it confirms the usefulness of bioelectric impedance analysis as a fast, precise, cheap and non-invasive diagnostic tool with a potential to permanently enter daily clinical practice.

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