REVIEW ARTICLE

Phase Angle, an Alternative Physiological Tool to Assess Wound Treatment in Chronic Nonhealing Wounds

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KEYWORDS:

Bioelectrical impedance;
Phase angle;
Reactance;
Resistance

Abstract

BACKGROUND: This exploratory study was conducted in an effort to demonstrate that bioelectrical impedance analysis (BIA) phase angle measurement is a novel tool for monitoring the effectiveness of a wound care regimen at a regional level and is valuable in comparing that status with the overall metabolic health of the patient. Isolating and measuring the extent to which nutritional supplementation contributes to the healing process is difficult and confounded by the many treatment modalities patients undergo.

OBJECTIVE: The authors conducted a limited exploratory study to determine whether regional phase angle measurements accurately reflected the status of chronic nonhealing wounds. This information would potentially provide the ability to quantitatively evaluate of the role of nutritional supplementation in wounds of varying etiologies by comparing regional BIA phase angle measurement with overall BIA phase angle measurement.

METHODS: Eleven patients with wounds of varying etiologies were selected to participate. Each patient underwent a treatment regimen specific to his or her condition, and all patients were given JUVEN® nutritional supplement.

RESULTS AND CONCLUSION: In all patients, the BIA phase angle measurement mirrored the health of the wound and provided an accurate tool for assessing the regional tissue health, a valuable insight in measuring the effectiveness of a systemic treatment.

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Introduction

Assessing the effectiveness of a wound care treatment regimen is an inexact science. Multiple factors contribute to the overall dynamic healing process, and it is difficult to get an objective and quantitative measurement of the

contribution of each factor. Wound healing has traditionally been measured by surface area and volume reductions, which do not provide insight into the role of individual therapies. Chemical analysis provides more insight and detail into the healing process, but extrapolation of these chemical measurements as a guide to effective wound treatment is speculative.

A patient's overall metabolic health is a crucial element in the healing process, impacting the integrity of the cell and its ability to respond effectively. Energy and nutritional requirements increase during the reparative process of

Conflict of interest: The authors report no conflicts of interest.

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wound healing. Inadequate or diminished metabolites compromise wound healing and delay or impede the healing process.¹⁻³ JUVEN® nutritional supplement contains arginine, glutamine, and β -hydroxy- β -methylbutyrate and is intended to improve metabolic status and thus facilitate wound healing. However, it is difficult to know the extent of the contribution nutritional supplementation makes in an individual patient. Traditional methods of measuring the healing process do not provide this insight. Total body bioelectrical impedance analysis (BIA) phase angle measurement provides a more precise assessment of the nutritional status of the patient.⁴ Phase angle measurements have been shown to reflect the overall metabolic state in a variety of chronic medical conditions.⁵ Lower phase angle measurements indicate a compromised metabolic state and are a predictor of negative outcomes.⁶ The authors undertook an exploratory study to determine whether regional phase angle measurements serve as an indicator for the local metabolic status of chronic nonhealing wounds and reflected the status of the wound and to demonstrate that phase angle measurement is an accurate measure, not only of a patient's overall nutritional status, but also that of the wound itself. Positive findings would provide a rationale for a future study comparing regional phase angle measurement of the wound to a total body phase angle measurement in patients receiving JUVEN® nutritional supplementation, in order to provide a quantifiable measurement of the impact of the patient's nutritional supplementation in wound healing. The comparison of the 2 measurements would also guide clinicians in determining appropriate regional intervention.

BIA provides a safe, noninvasive, and objective indication of cellular-level architecture and function during the healing process.⁴ BIA uses a highly controlled electrical circuit developed with a high-frequency, low-voltage signal that neither stimulates nor perturbs tissues by placing 4 contact electrodes adjacent to the margins of the wound.⁷ The electrical measurements of resistance (R; reduction in voltage as the applied current passes through the wound) and reactance (Xc; cell membrane capacitance or delay in transmission of the applied current as a result of bipolar membranes) indicate (1) extracellular fluid distribution and electrolyte composition and (2) cell membrane mass and function, respectively.

Bioelectrical phase angle is a measurement of the ratio of the R and Xc when an electrical current is applied to tissue. R and Xc are the 2 vector components that form the basis of impedance measurements. This measurement has been found to predict cell viability. Lower phase angles are associated with low Xc and cell breakdown or death. High phase angles are consistent with intact cell membranes and body cell mass.^{4,5,7} The measurement of phase angle has been effective in assessing cellular integrity and as an overall assessment of the metabolic status of patients with advanced-stage carcinomas.^{6,8}

Using bioelectrical impedance measurements, serial measurements were made to evaluate the status of chronic

nonhealing wounds. The initial phase angle values reflected the overall integrity of cellular components in the chronic nonhealing wound. Changes in the phase angle likewise assessed the effectiveness of treatment.

Methods

Patients with chronic nonhealing wounds who were treated at the Wound Institute and Research Center were sequentially selected to participate in the study. In all, 11 patients were entered into the study, 7 women and 4 men, and the average age was 62.54 years. Five patients had diabetes mellitus, with 3 having type 1 diabetes mellitus and 2 having type 2 diabetes mellitus. The etiologies (and numbers) of the wounds were arterial (1), venous (3), neurotrophic (3), traumatic (1), surgical (1), and infectious (2).

Patients continued to follow their established protocol regimen based on the etiology of their individual wound. All patients were administered JUVEN® nutritional supplement as part of their treatment therapy. All patients were examined weekly to ensure that patients did not have an active infection or cellulitis.

BIA was made with a Quantum IV analyzer (RJL Systems; Clinton, MI, USA). Measurements were made with the parameters established by Michael Singer:

Use in the U.S. of the measured values of BIA (whole-body and regionally applied) to determine the presence and progression of illness, the effect of treatment and survival in any biological entity, and/or to determine illness or progression to death, or timing of death of a biological entity, and/or to detect the presence and severity of illness, the effectiveness of treatment interventions, and the ability to change treatment to be more effective or aggressive, to optimize outcome, limit morbidity and mortality and illustrate the patient's prognosis, and/or to determine illness of, progression to nonacute death of, or timing of nonacute death of a biological entity, is the subject matter of U.S. Patents 6,587,715, 7,003,346 and 7,136,697. Please refer to the owner of these patents for further information.

Electrodes were placed at the edges of the wound and 10 cm from the edge of the wound when feasible. Calibration of the Quantum IV analyzer was done prior to each evaluation to ensure consistency. Phase angle measurements were made weekly for 12 weeks or until closure of the wound occurred.

Additional measurements included rate of closure and days to healing. Rate of closure was calculated by measurement of the wound closure area in square centimeters per day. Days to healing were calculated by recording the number of days between initiation into the study and the date on which the wound exhibited epithelialization.

Figure 1 Phase angle measurement as seen in the healing of a chronic nonhealing wound of traumatic etiology.

Results

In all patients, BIA measurements correlated with the clinical status of the wound. Of those patients whose wounds healed, a positive increase in both phase angle degree and slope was seen. Epithelialization was associated with increases in R. Phase angle measurements deteriorated with clinical and bacteriologic signs of infection. A rapid decrease in phase angle degrees and slope was observed in 2 patients who developed methicillin-resistant *Staphylococcus aureus* (MRSA) infections.

Some 64% of the patients experienced closure of their wounds; 46% healed within a 12-week period. Two patients healed after the 12-week period. Four patients did not heal. Of the 4 patients with wounds that did not heal, 2 were hospitalized because of methicillin-resistant infections. The average time to closure was 62.8 days, and the average rate of closure was 0.0424 cm² per day, with a range of from 0.03 to 0.07 cm² per day. Etiology of the wounds was not a factor in healing.

The following 4 figures illustrate the association between phase angle measurement and wound status among 4 patients with vastly different clinical courses and within

Figure 2 Phase angle measurements in a patient with a rapid rise in resistance associated with cornification of the patient's wound.

Figure 3 Increasing phase angle slope and values associated with healing.

varying periods during the study. The etiology of the wounds, the treatment administered, and the closure of the wound were unique in each patient; however, phase angle measurement followed the predicted pattern, increasing with healing and deteriorating on infection or subsequent to an intentionally disruptive treatment procedure, such as debridement.

Figure 1 demonstrates an expected decrease in phase angle measurement after the cellular disruption of

debridement, the gradual leveling off of the decrease, and the eventual positive slope of the phase angle measurement as the wound progressed to epithelialization during the course of 6 weeks. This patient received JUVEN® nutritional supplement approximately 2 weeks after initiation into the study. After the initiation of JUVEN®, regional measurements continued to record a negative phase angle slope for 6 days; then the phase angle slope began to rise. JUVEN® typically exhibits positive nutritional benefits

Figure 4 Deterioration of phase angle associated with methicillin-resistant *Staphylococcus aureus* infection. APG = autologous platelet graft.

after 1 to 2 weeks of supplementation; thus the lag between initiation of JUVEN® and increased phase angle is expected and possibly indicates increased total body nutrition in the local wound environment as well as the time necessary for the wound to reflect that nutrition.

Figure 2 documents an alternative pattern of increasing phase angle associated with the healing of a surgical wound in a 17-year-old patient. The 12-week period represented in the graph illustrates the expected drop in phase angle after debridement and grafting and a steady increase in phase angle as healing progressed. This patient experienced a desiccation of the epithelial cells of the wound, resulting in a hard, dry cornification of the wound. The significant rise in R is associated with the healing pattern of the patient's wound.

In Figure 3, the phase angle increase is representative of a steady and consistent 5-week healing pattern in an elderly patient after treatment with oxidative cellulose. The wound was of traumatic etiology.

In a dramatic departure from the model of a healed wound, Figure 4 demonstrates a precipitous drop in regional phase angle measurement, despite nutritional intervention, due to colonization of the wound with MRSA after 4 weeks of measurement. This is consistent with the expectation that regional phase angle will mirror the local health of the wound, irrespective of total body nutritional status. In the 3 weeks prior to the wound's colonization with MRSA, the phase angle measurements reflected the treatment and healing pattern. Phase angle dropped after the intentionally disruptive autologous platelet graft, then increased steadily after oxidized cellulose therapy.

Discussion

When a low-voltage, high-frequency alternating current is introduced into a person, the current is conducted almost completely through the fluid component of the fat-free muscle mass. The cellular membrane delays the flow of current into the cell. This lag of current is a function of cellular membrane vitality.⁴ The current is affected by the R and the capacitance of the tissue. The capacitance is a function of the cellular membrane integrity, and R is a function of the extracellular water. The cellular membrane's ability to "hold" a charge is measured as Xc and is related to protein cell mass. Higher Xc values indicate more cell mass and lower Xc values indicate diminished cell mass. Resistance is inversely proportionate to fluid volumes, with more fluid reflecting lower values and less fluid reflecting higher values. Phase angle reflects the relationship of Xc to R. Higher phase angles indicate cellular vitality, and lower phase angles are associated with a diminished cellular vitality.

Phase angle measurement has been shown to be a valuable tool in assessing a variety of clinical benchmarks.

Gupta et al. have shown that phase angle measurements in patients with breast, colon, and non-small-cell lung cancer act as prognostic indicators and that nutritional intervention targeted at improving phase angle could potentially improve survival in these patients.⁶ Spence and Pomeranz demonstrated that electrical R of the epidermis increased in surgically induced wounds in an animal model and could be used as a valid measure of healing.⁹ Wagner et al. were able to use bioelectrical impedance as a discriminator in the development of pressure ulcers, confirmed by tissue biopsy.⁷

JUVEN® is a dietary nutritional supplement containing arginine, glutamine, and β -hydroxy- β -methylbutyrate. Arginine induces the anabolic hormones insulin and growth factor; stimulates T-lymphocyte response to wound healing; is a metabolic precursor to nitrous oxide, which enhances macrophage killing of bacteria; and catabolizes ornithine to proline in protein synthesis. Glutamine facilitates collagen synthesis and supports immune response and gut integrity. β -Hydroxy- β -methylbutyrate is found in muscle, diminishes the inflammatory response, decreases muscle breakdown, and increases lean body mass. A double-blind clinical studies have shown that JUVEN® facilitates wound healing.³ However, a measurement of the contribution of the nutritional supplementation in the healing process has not been established, and wound healing is confounded by the multiple treatment modalities that patients undergo. The ability of JUVEN® to increase lean body mass and the fact that Xc is related to protein cell mass should be reflected in increases in phase angle, both in total body phase angle measurements and in regional phase angle measurements.

Present bioelectrical impedance technology affords the ability to obtain measurements on distinct anatomic areas. The authors conducted a limited exploratory study to assess the outcomes of regional phase angle measurements on patients with chronic nonhealing wounds of various etiologies. Clinical healing of the wounds was associated with a regional increase in Xc, R, and phase angle, which is consistent with the healing process. Deterioration of the wound due to infection or deliberate disruption was associated with a regional decrease in Xc, R, and phase angle. Etiology of the wound did not influence these positive and negative associations between slope and healing, though it is unknown whether etiology plays a more nuanced role in phase angle. Additionally, this study did not evaluate whether acute healthy wounds and those of a chronic nature exhibit different phase angle patterns within the expected trends associated with healing. Regional phase angle measurement provides a valid measure of healing and is a valuable reference point in analyzing the contribution of the patient's overall metabolic state and the role of nutritional supplementation in wound healing.

Based on the findings presented, the authors propose to measure total body phase angle and regional phase angle

of nonhealing wounds of a specific etiology in patients receiving JUVEN® nutritional supplement. It is postulated that regional phase angle measurements would reflect the metabolic activity of the wound treatment and status of the cellular components engaged in that process. Total body phase angle would reflect the overall metabolic state of the body and would be an indicator of the metabolic status of the body and its ability to deal with the metabolic demands of a chronic nonhealing wound. By evaluating these 2 parameters, regional and total body phase angle measurements, one could assess the effectiveness of treatment and justify interventional changes on a regional basis. This information would also provide a rationale for nutritional intervention prior to or in conjunction with regional therapy and could likewise be used to assess the ability of a chronic nonhealing wound to support regional intervention.

Acknowledgments

Support in the form of JUVEN® nutritional supplement was provided by Abbott Nutritional Laboratories a division of Abbott Laboratories.

References

1. Wild T, Rahbarnia A, Kellner M, Sobotka L, Eberlein T: Basics in nutrition and wound healing. *Nutrition*. 2010;26(9):862–866.
2. Himes D: Protein-calorie malnutrition and involuntary weight loss: the role of aggressive nutritional intervention in wound healing. *Ostomy Wound Manage*. 1999;45(3):46–51, 54–55.
3. Williams JZ, Abumrad N, Barbul A: Effect of a specialized amino acid mixture on human collagen deposition. *Ann Surg*. 2002;236(3):369–375.
4. Foster K, Lukaski H: Whole-body impedance—what does it measure? *Am J Clin Nutr*. 1996;64:388S–396S.
5. Hunter G, Weinsier R: Electrical impedance in assessing human body composition: the BIA method. *Am J Clin Nutr*. 1988;47:789–792.
6. Gupta D, Lammersfeld C, Vashi P, et al: Bioelectrical impedance phase angle as a prognostic indicator in breast cancer. *BMC Cancer*. 2008;8:249.
7. Wagner D, Jeter KF, Tintle T, Martin MS, Long JM III: Bioelectrical impedance as a discriminator of pressure ulcer risks. *Adv Wound Care*. 1996;9(2):30–37.
8. Schwenk A, Beisenherz A, Romer K, Kremer G, Salzberger B, Elia M: Phase angle from bioelectrical impedance analysis remains an independent predictive marker in HIV-infected patients in the era of highly active antiretroviral treatment. *Am J Clin Nutr*. 2000;72:496–501.
9. Spence D, Pomeranz B: Surgical wound healing monitored repeatedly in vivo using electrical resistance of the epidermis. *Physiol Meas*. 1996;17(2):57–69.