Clinical Nutrition 32 (2013) 824–829

Contents lists available at SciVerse ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Bioelectrical impedance parameters in critically ill children: Importance of reactance and resistance

Zina Maria Almeida Azevedo [a,g], Daniella Campelo Batalha Cox Moore [b,g], Flavia Aparecida Alves de Matos [c], Vania Matos Fonseca [d], Maria Virginia Marques Peixoto [d], Maria Ignez C. Gaspar-Elsas [e], Erika Santinoni [a], Luiz Antonio dos Anjos [f], Eloane Gonçalves Ramos [d,*]

[a] Intensive Care Unit, Pediatrics Department, Fernandes Figueira Institute, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil
[b] Internal Medicine Department, Fluminense Federal University (UFF), Niterói, Brazil
[c] Pediatric Intensive Care Unit, Instituto Nacional de Cancer, Rio de Janeiro, Brazil
[d] Quantitative Methods Laboratory, Research Department, Fernandes Figueira Institute, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil
[e] Laboratory of Human Pathophysiology, Pediatrics Department, Fernandes Figueira Institute, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil
[f] Nutritional and Functional Assessment Research Laboratory, Department of Social Nutrition, Fluminense Federal University, Niterói, Brazil

ARTICLE INFO

Article history:
Received 7 September 2012
Accepted 18 January 2013

Keywords:
Sepsis
Electric impedance
Child
Multiple organ failure
Critical illness

SUMMARY

Background & aims: Currently, there are no clinical or laboratory parameters that can be used efficiently to predict the prognosis of critically ill patients, but in some situations, raw bioelectrical impedance parameters have been shown to be useful. The purpose of this study was to investigate the behavior of reactance and resistance in the severity of the critically ill pediatric patient.
Methods: We prospectively analyzed bioelectrical impedance in a sample of 332 critically ill pediatric patients submitted to mechanical ventilation. The values taken on admission and discharge were correlated with major outcomes to the critically ill patient.
Results: We found an association of low values of Xc/H (<27.7 Ohm/m) and of R/H (<563.6 Ohm/m) on admission with multiple organs dysfunction greater or equal to 4. Both R/H and Xc/H increased significantly between admission and discharge among survivors, while among nonsurvivors there was a trend of decrease between admission and the last measurement before death.
Conclusions: Bioelectrical impedance is a useful tool for monitoring of critically ill pediatric patients. A possible role of R/H and Xc/H, especially the latter, as a predictive biomarker of evolution for septic shock and organ dysfunction still remains to be elucidated.

1. Introduction

Critically ill patients, especially those who develop systemic inflammatory response, generally present change in body fluid distribution with migration of fluid from the intravascular to the extra vascular space, orchestrated largely by the action of cytokines and other inflammatory mediators.[1] Despite the current scores to predict mortality,[2,3] there are no clinical or laboratory parameters that can be efficiently used to predict the prognosis of critically ill patients. Early identification of severity may enable the anticipation of some therapeutic measures that can be decisive in patient outcomes.

Bioelectrical impedance analysis is a useful tool in the evaluation of body composition in many clinical situations. The predictive equations used for this purpose are, however, not adequate for the critically ill patient since the fixed tissue hydration assumption cannot be assured.[4] However, raw bioelectrical impedance parameters (resistance and reactance) have already been shown to be useful in assessing the severity of illness and the prognosis of the critically ill patients.[5] Resistance (R) refers to the restriction to the flow of an electrical current through the body, primarily related to the amount of water present in the tissues. The state of sepsis causes profound changes between the content of lean body mass, total body water and its distribution. The increased capillary permeability and rupture of the membrane in sepsis are responsible for leakage of liquid, development of third space and hyperhydration of the

* Corresponding author. Instituto Fernandes Figueira – Unidade de Pesquisa Clínica, Av. Rui Barbosa, 716, Flamengo, Rio de Janeiro 22250-020, Brazil. Tel.: +55 21 2554 1912; fax: +55 21 2553 0790.
E-mail address: eloane@iff.fiocruz.br (E.G. Ramos).
[g] Due to the nature of this study, equally essential clinical and pathophysiological contributions were made by Z.M. Azevedo and D.B. Moore, respectively, who should, therefore, be considered joint main authors.

0261-5614/$ – see front matter © 2013 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.
http://dx.doi.org/10.1016/j.clnu.2013.01.011

lipophilic portion of the cell membrane. Reactance (*Xc*) refers to the resistive effect produced by tissue interfaces and cell membranes.[4] Part of the electric current is stored by the cell membranes, which act as capacitors. Many studies over the last years have described oxidative stress in patients with sepsis, with evidence of ROS (Reactive Oxygen Species) production and associated damage and antioxidant depletion. In this context the analysis of *Xc* and *R* seems to be relevant to the critically ill patients, when *Xc* would be related to the degree of severity and *R* to the presence of edema. Phase angle (PA) is a parameter directly derived from *R* and *Xc* and has been studied as a marker of prognostic value for some clinical conditions such as cancer,[6,7] HIV infection[8] and kidney diseases,[9–12] among others. However, in a previous study[13] there was no significant association of PA with MODS >3 in septic patients.

To this end, the purpose of the present study was to assess the possible role of reactance and resistance as biomarkers of severity, instead of phase angle, in critically ill pediatric patients. Severity was assessed by the following indicators: lung injury, sepsis severity and multiple organ dysfunction (MODS). Although these indicators represent separate well-defined entities, they all share the same pathophysiologic basis.

2. Subjects and methods

The subjects of the present study comprised patients admitted to the Pediatric Intensive Care Unit of the Fernandes Figueira Institute (IFF)/Fiocruz, a federal public hospital in Rio de Janeiro, between October 2004 and December 2011. All subjects were sedated, on mechanical ventilation, and received enteral nutrition by continuous infusion (or were fasting) with urinary output obtained predominantly by continuous bladder catheterization when assessed. All the patients in the intensive care unit had received fluid reposition according to international protocols for sepsis management. Exclusion criteria were: children under 3 kg of weight or less than 1 month old.

Demographic variables analyzed were age in months and sex. Clinical variables investigated were: presence of comorbidities and edema; final outcome (survivors and nonsurvivors); lung injury (acute lung injury, acute respiratory distress syndrome, cardiogenic involvement and support); sepsis severity (systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis or septic shock); and multiple organs dysfunction (MODS), graded as zero to six organs affected. The sepsis severity and MODS classifications followed the criteria from the International Pediatric Sepsis Consensus Conference.[14] Acute respiratory distress syndrome (ARDS) was defined according to the American European Consensus Conference definition,[15] which is based on four clinical parameters: (a) acute onset; (b) severe arterial hypoxemia resistant to oxygen therapy alone ($PaO_2/FiO_2 < 200$ mmHg for ARDS; <300 mmHg for acute lung injury − ALI); (c) bilateral pulmonary inflammatory infiltrates on chest X-rays and (d) absence of left atrial hypertension. Cardiogenic patients were defined as those requiring invasive mechanical ventilation for cardiac reasons, such as pulmonary hyperflux, congestive cardiac failure or congenital heart disease. The patients who did not present pulmonary injury but were submitted to mechanical ventilation for other reasons were defined as support. The considered determinants of severity were the development of: ARDS/ALI, septic shock and MODS >4. Two scores were used to predict the risk of mortality of critically ill children at the time of admission, the pediatric risk of mortality (PRISM 1)[3] and the pediatric index of mortality (PIM 2).[2]

2.1. Measurements

The measurements of bioelectrical impedance parameters and recumbent length were performed within 48 h of admission in the intensive care unit, every 7 days thereafter and at any time of worsening of the clinical status. For the cross-sectional analysis only the admission data was used. In the paired analysis, admission and discharge data were used. For nonsurvivors, the last bioelectric impedance measurement was used as endpoint if it was available 24 h prior to death. The bioelectrical impedance parameters were obtained with a portable plethysmograph BIA 101 Quantum II (RJL Systems, USA), calibrated weekly with a circuit of known impedance value provided by the manufacturer. Averages of triplicate measurements were used in the analysis. The measurement procedure was conducted using the standard tetrapolar electrodes distribution.[16] The inner arm electrode (sensor) was placed on the dorsal surface of the right wrist between the ulna and the radius. The leg electrode was placed on the anterior surface of the right ankle between the prominent portions of the bones. The external electrodes (source or injector) were placed on the dorsal surface of the third proximal phalanx of the right hand and right foot. In the infants, the position of the injector electrode was the same but the sensor electrode was moved proximally, leaving 5 cm of free skin between them, the minimal distance required to avoid interaction between electric fields, which could otherwise lead to an overestimation of impedance values.[17] Bioelectrical impedance PA and modulus were calculated and resistance and reactance values were corrected for height.[18]

2.2. Data processing and statistical analysis

A cross-sectional analysis was made by initially conducting *t*-tests (ANOVA for age groups), since R/H and Xc/H are considered to be normally distributed for normal adults.[18] Since this assumption may not apply for the critical ill patients nonparametric median tests were conducted. Receiver operating characteristic (ROC) curves were then created for each severity outcome, evaluating R/H and Xc/H as severity indicators. The best areas under the curve (AUC) were observed for MODS versus Xc/H and MODS versus R/H. Optimal cut-off values were established as the nearest point to the top left corner of the graphic, leading to a threshold of 27.7 Ohm/m for Xc/H and 563.63 Ohm/m for R/H. Using these threshold values, specificity and sensitivity were calculated for all three severity outcomes: MODS ≥4, septic shock and ARDS/ALI. Multivariate logistic regression analysis and calculated odd ratios (OR) for the three dichotomized outcomes were performed with adjustments of the models for age and sex, presence of edema and comorbidities.[19]

The significance of the difference in bioelectrical impedance parameters between admission and discharge was established by paired *t*-tests, only on survived data. To show the cross-sectional and paired behavior of the bioelectrical impedance vector a bivariate analysis (BIVA)[20] was conducted. This consists of analyzing the RXc graph to evaluate the vector difference between admission and discharge and between MODS categories.

Comparison between survivors and nonsurvivors was performed by calculating individual percent differences of the bioelectrical impedance vector between admission and discharge for survivors and between admission and the last measurement before death for nonsurvivors, as follows: $R/H_{\text{difference}} = (R/H_2 - R/H_1)/R/H_1 \times 100\%$ and $Xc/H_{\text{difference}} = (Xc/H_2 - Xc/H_1)/Xc/H_1 \times 100\%$. Then, the mean difference vector and their 95% confidence ellipse were calculated for both groups.

3. Results

We evaluated 356 critically ill pediatric patients on mechanical ventilation and had bioelectrical impedance measured in the first 48 h of admission. After excluding bioelectrical impedance missing data and outliers (values below or above 1.5 times the interquartile