APPLICATION OF BIOELECTRICAL IMPEDANCE TO CLINICAL ASSESSMENT OF BODY COMPOSITION IN PERITONEAL DIALYSIS

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Patients on peritoneal dialysis (PD) develop complex changes in body composition. These changes reflect hydration, nutrition, and body fat, all important elements reflecting patient well-being and efficacy of therapy that should be assessed and monitored as guides to patient management. They are all notoriously difficult to accurately measure in clinical practice and simultaneous abnormalities may obscure detection, as in the malnourished fluid-overloaded patient where body weight is misleadingly stable. Malnutrition is a serious complication in PD that carries an adverse prognosis. Assessment of hydration in PD is important in determining “dry weight” to allow adjustment of dialysis prescription to optimize fluid balance. A number of techniques have been investigated to measure body composition in clinical practice. Of these, bioelectrical impedance analysis (BIA) has attracted most interest and seems to be of greatest promise. Cases illustrating different aspects of the use of BIA in PD patients are described, and the background, possible uses, and limitations of BIA in PD patients are discussed. To be of clinical value, BIA must be used to distinguish between extracellular water (which reflects hydration) and body cell mass, or intracellular water (which declines in wasting and malnutrition). The high precision of BIA is ideally suited to detecting changes in body composition and its main role may be in longitudinal monitoring. However, inaccuracy of absolute measurements and variability of normal values in the general population make precise diagnosis of the degree of normality of body composition in an individual subject a more difficult task for body composition analysis.

KEY WORDS: Fluid balance; bioelectrical impedance; body composition; nutrition.

Bioelectrical impedance analysis (BIA) is a promising method for the objective assessment and monitoring of hydration and nutrition in patients on peritoneal dialysis (PD). We describe four cases illustrating differing patterns of abnormality and change in body composition detected by BIA in PD patients. We discuss the theory of body composition analysis and BIA with particular reference to application in patients on PD, and describe the potential application and pitfalls of this technique in routine clinical practice.

CASE 1

A 19-year-old woman commenced on automated PD for end-stage chronic renal failure due to Henoch–Schönlein purpura. One month after starting PD she was hypertensive, with blood pressure 180/120 mmHg despite being on four antihypertensive agents. She weighed 49.9 kg and bioimpedance spectroscopy (BIS; Xitron Hydra; Xitron Technologies, San Diego, California, USA) demonstrated extracellular water (ECW) 12.5 L and total body water (TBW) 23.5 L, with ECW/TBW ratio 53.1%. Compared with our age- and gender-specific normal ranges, the mean normal ratio for her would be 44.1%; her value was 3.6 standard deviations greater than this. Changes in fluid management achieved weight reduction of 4.6 kg over a 7-week period. Extracellular water reduced by 2.8 L and TBW reduced by 2.1 L, thus with an increase in intracellular water (ICW) of 0.7 L. This resulted in ECW/TBW ratio of 45.1%, only 0.3 standard deviations greater than this.
deviations above mean normal value. Blood pressure fell to 117/57 mmHg, despite significant reduction in anti-hypertensive therapy. These data suggest the patient initially had significant ECW expansion resulting in hypertension, which was corrected by fluid management changes leading to normalization of ECW and improved control of hypertension.

CASE 2

A 65-year-old woman with end-stage chronic renal failure due to adult polycystic kidney disease commenced treatment with automated PD. Her initial weight was 89.4 kg, with body mass index 31.7 kg/m². Her clinical course was complicated by low mood and reduced appetite with poor caloric intake, despite adequate small solute clearances. Two years later her weight had progressively fallen to 80.5 kg, with body mass index 28.5 kg/m². Initial BIS demonstrated ECW 14.7 L and TBW 29.5 L, with ECW/TBW ratio 50.0% (1.4 SD above mean normal value). On repeating BIS after 2 years, ECW was very similar to baseline, at 14.8 L, with a rise in TBW of 0.8 L to 30.3 L. These data suggest that, over 2 years, hydration was stable and there may have been a small increase in ICW [and thus body cell mass (BCM)]. Thus the marked reduction in body weight and body mass index was attributable to marked loss of body fat, requiring further dietetic intervention.

CASE 3

A 79-year-old woman with end-stage chronic renal failure of unknown cause commenced automated PD. She weighed 55.9 kg and assessment by BIS demonstrated ECW 12.2 L and TBW 24.1 L, with ECW/TBW ratio 50.5% (1.2 SD above mean normal value). Over time, she developed reduction in ultrafiltration and lost her residual renal function, requiring increasing use of more hypertonic glucose dialysate to achieve adequate fluid ultrafiltration. On repeating BIS after 2 years, her weight had increased by 2.6 kg to 58.5 kg, ECW had reduced by 1.6 L to 10.6 L, and TBW reduced by 3.4 L to 20.7 L (with reduction in ICW of 1.8 L). These data suggest that, over the 2 years, treatment had been successful in maintaining and further improving her state of hydration, despite ultrafiltration problems and loss of residual function. However, over that time she had suffered loss of BCM, and the increase in weight, despite reduction of ECW and decline in BCM, would be explained by body fat gain, possibly due to high glucose absorption due to requirement for hypertonic exchanges.

CASE 4

A 66-year-old man with end-stage chronic renal failure due to glomerulonephritis commenced automated PD. Early assessment demonstrated weight of 65.3 kg and BIS demonstrated ECW 17.5 L and TBW 33.3 L, with ECW/TBW ratio 52.5% (with normal population mean 44.9%, this result was 3 SD greater). He was hypertensive, with blood pressure 160/95 mmHg. Dialysis prescription was altered to increase ultrafiltration. On assessment 5 months later, his weight was 1.3 kg less and blood pressure low, at 96/65 mmHg. Complications during this time included a stroke, an episode of PD peritonitis, and development of impaired appetite and dietary intake. Bioimpedance spectroscopy demonstrated ECW reduced by 2.5 L to 15.0 L and TBW reduced to 27.8 L, with ICW reducing by 3.0 L, from 15.8 L to 12.8 L, and ECW/TBW ratio actually increasing to 54.1%. These data suggest that dialysis prescription had improved hydration by reducing ECW volume and blood pressure, but that BCM wasting, related to his intercurrent clinical problems, had also occurred. The discrepancy between degree of fluid loss and lesser fall in body weight suggests some gain in body fat also occurred over this time period. The rise in ECW/TBW ratio, despite improvement in hydration with fall in ECW and blood pressure, was due to ICW reduction (and thus greater TBW reduction) due to BCM wasting, demonstrating that ECW/TBW ratio reflects nutritional state and not just hydration.

The changes of body composition in these cases are summarized in Table 1.

DISCUSSION

BODY COMPOSITION ABNORMALITIES IN PD

Body composition techniques subdivide the body into compartments on the basis of differing physical properties (1). The different compartments reflect hydration, nutrition/wasting, body fat, and bone mineral content, which are all of great importance in patients on PD. There is a significant body of literature assessing the validity and applicability of these techniques in assessing patients with renal disease, and utilizing them in clinical research in this patient group. The challenge is to usefully incorporate these methods into clinical practice.

Wasting and malnutrition are common and serious complications in patients on PD (2–4) and are strongly associated with adverse outcomes (5,6). Techniques for assessing nutrition have limitations and, due to metabolic effects and confounding effects of altered hydration and
other body composition abnormalities, these limitations are greater in the context of renal failure.

Disordered regulation of fluid balance is a crucial abnormality in dialysis patients. Adverse effects of fluid retention include the development of hypertension and cardiovascular disease. There is increasing evidence for the importance of fluid status in determining outcome in PD patients (7,8). Fluid retention may confound assessment of nutritional state by artificially maintaining body weight and preserving body contours, thus masking the presence of malnutrition. Failure to detect the need to reduce dry weight in dialysis patients leads to the highly undesirable situation of a patient simultaneously developing malnutrition and fluid overload. Some studies have suggested that, despite the potential for PD to maintain stable hydration, PD patients can frequently be fluid overloaded (9–13). However, more recent studies show that, with current practice and PD therapies, patients are not necessarily overhydrated and that there is potential for PD to achieve adequate fluid removal to attain good control of hydration and blood pressure, with beneficial effects on cardiac function (14–18). Accurately determining ideal “dry weight” remains a major challenge. In hemodialysis this is often achieved by progressive dehydration to assess the lowest tolerated weight. Theoretically, this approach would be even better applied to the gradual change of steady state hydration in PD. However, evidence suggests that periods of dehydration promote loss of residual renal function on PD (19). Residual renal function is a crucial determinant of outcome (20) and is better preserved in PD, which may account for the impression that PD offers an early survival advantage compared with hemodialysis (21). Thus, we aim to preserve residual renal function for as long as possible in PD, and clinical management entails a delicate balance between avoiding or treating fluid overload on PD and avoiding excess fluid removal resulting in loss of residual renal function. Thus, we need objective measures to determine what the correct state of hydration is for the individual patient, to allow us to optimally adjust fluid management, and to detect changes in hydration over time.

**BODY COMPOSITION ANALYSIS: BACKGROUND, THEORY, AND LIMITATIONS**

A range of techniques have been used to study body composition. More complex “gold-standard” techniques, such as dilution methods, densitometry, in vivo neutron activation, and measurement of total body potassium, have been crucial in the development of the field of body composition analysis and act as standards for evaluation of newer techniques, but they are not applicable to routine clinical practice (1). Of the simpler bedside techniques, BIA has attracted particular interest as a technique with potential to provide detailed clinically useful information about hydration and nutritional state.

To correctly interpret the results from body composition studies, it is important to understand the basic theory of body composition analysis and the different compartments that may be measured (1,22). It is also necessary to know how the technique being used derives these measurements. It is easy to uncritically accept results at face value, risking misinterpretation of the clinical meaning of the data, which leads to inappropriate patient management. In particular, some values are derived indirectly and may also be subject to error arising from effects of disease states such as renal failure.

The basic two-compartment model divides the body into fat and fat-free compartments (Figure 1). Whereas fat is fairly homogenous, fat-free mass (FFM) is heterogeneous, with important and differing constituents, leading to important issues in understanding methodology. Fat-free mass includes bone mineral and the remaining “lean” tissue. The major component of lean tissue is water. Typically, TBW accounts for 73% of FFM. However, this percentage may vary among normal individuals (23) and is likely to vary more in disease states with disturbed water homeostasis, such as renal disease. Fat-free mass or lean tissue can be estimated by a variety of methods. Impor-

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**TABLE 1**

Summary of Changes in Body Composition from Four Clinical Cases

<table>
<thead>
<tr>
<th>Case 1</th>
<th>Change in weight (kg)</th>
<th>Change in ECW (L)</th>
<th>Change in TBW (L)</th>
<th>Change in ICW (L)</th>
<th>Change in ECW/TBW</th>
<th>Clinical comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 2</td>
<td>−4.6</td>
<td>−2.8</td>
<td>−2.1</td>
<td>+0.7</td>
<td>53.1% to 45.1%</td>
<td>Reduction in fluid excess</td>
</tr>
<tr>
<td>Case 3</td>
<td>−2.6</td>
<td>+0.1</td>
<td>+0.8</td>
<td>+0.7</td>
<td>50.0% to 48.9%</td>
<td>Weight reduction due to fat loss</td>
</tr>
<tr>
<td>Case 4</td>
<td>+2.6</td>
<td>−1.6</td>
<td>−3.4</td>
<td>−1.8</td>
<td>50.5% to 51.2%</td>
<td>Reduced ECW; BCM loss and fat gain</td>
</tr>
<tr>
<td>Case 5</td>
<td>−1.3</td>
<td>−2.5</td>
<td>−5.5</td>
<td>−3.0</td>
<td>52.5% to 54.1%</td>
<td>Reduced ECW excess, despite ECW/TBW increase</td>
</tr>
</tbody>
</table>

ECW = extracellular water; TBW = total body water; ICW = intracellular water.
BIA FOR ASSESSING BODY COMPOSITION IN PD

Tantly, although used as a measure of nutritional state or wasting, changes in FFM also reflect hydration. Thus, change in lean tissue could represent either nutritional or hydration changes, or composite of both such that a stable measurement could actually represent simultaneous changes in hydration and nutrition in opposite directions (e.g., wasting and fluid retention occurring together with no net change in FFM). Some techniques, such as BIA and measurement of TBW by dilution, primarily measure TBW, with subsequent derivation of lean tissue mass based purely on the assumption that TBW represents 73% of FFM, which is estimated as TBW/0.73 (figure of 73.8% used by Xitron Hydra).

To be clinically useful in PD, measurement of body composition must separately assess hydration and nutritional state. Total body water can be split into ECW and ICW, and lean tissue into ECW and BCM. Extracellular water is the compartment that predominantly changes with hydration; thus, to measure hydration, we need information about ECW specifically, rather than TBW. Body cell mass is the compartment reflecting nutrition and wasting (24). Unlike lean or FFM, it is a more specific marker of these aspects, being unaffected by hydration. Intracellular water comprises 72% of BCM and is unaffected by iso-osmotic changes in ECW; thus ICW is a useful marker reflecting and allowing measurement of BCM.

Body fat is estimated in a variety of ways. Some techniques depend on physical characteristics of body fat (e.g., densitometry, computed tomography, magnetic resonance imaging, dual-energy x-ray absorptiometry), others measure it indirectly by estimating FFM mass and deriving fat as accounting for the remainder of body weight. These latter techniques, which include BIA and dilution, are dependent on normal hydration, such that abnormal hydration causing erroneous estimate of lean tissue, or FFM, will produce a corresponding error in estimation of body fat.

BIOELECTRICAL IMPEDANCE ANALYSIS

The basic principle of BIA is that an alternating electrical current (which in whole-body BIA is passed between skin electrodes placed at the hands and feet) passes through body water, with fat being anhydrous, and that the measured impedance is inversely proportional to body water content (25). Bioelectrical impedance analysis actually covers a range of different systems and methods of analysis and it is crucial to understand that this is not a single uniform test when evaluating literature involving BIA, or when applying it to our patients.

The earliest use of BIA was with single frequency, 50 kHz, whole-body BIA techniques. Various regression equations have been developed to estimate TBW using BIA. These usually incorporate the “impedance index” term of height²/impedance. Total body water thus estimated includes both ECW and ICW, so does not provide separate independent assessment of hydration of nutrition. Fat-free mass, or lean tissue, is estimated by assuming TBW content is 73%, and fat is derived as weight minus FFM. Thus, both of these are potentially unreliable in situations with abnormal FFM hydration.

Development of BIA has allowed the technique to provide information about ECW (reflecting hydration) and ICW (reflecting nutrition/wasting). Impedance is comprised of a dominant resistance component (R) and a smaller reactance (Xc) component that results from the capacitance effect of cell membranes. The relationship between R and Xc is described by the phase angle and is determined by ECW volume and the relationship of ECW to ICW. Piccoli et al. used this property in developing the concept of the R/Xc graph (26). On this graph, regions reflecting the 95% confidence limits for healthy subjects are indicated. A subject’s readings are plotted on the graph to determine whether they fall within the range of the normal population, and if not, the direction of deviation from normality may explain the underlying abnormality. In particular, a decreased phase angle may represent increased hydration or wasting and is an adverse prognostic marker for survival in PD (27).

A further development was the use of multiple-frequency techniques. Alternating current passes freely through the ECW space regardless of the frequency, but penetration of the ICW space is frequency dependent. At low frequency, current passes predominantly through ECW. With increasing current frequency, there is increasing passage through the ICW space. The most commonly used method utilizing this property is BIS (28).
Bioimpedance spectroscopy measures resistance and reactance values at a wide range of different frequencies. Mathematical modeling then estimates the theoretical impedance at zero frequency, where passage of the current would be exclusively through the ECW space, and at infinite frequency, where the electrical current would pass freely through the entire TBW space, including ICW as well as ECW. This allows estimation of ECW, ICW, and TBW volumes.

CAN WE DIAGNOSE ABNORMAL BODY COMPOSITION WITH A SINGLE BIA MEASUREMENT?

Ideally, we would like a diagnostic tool that can be applied to a patient to tell us on a particular occasion whether their body composition is normal or whether clinically relevant abnormalities exist. There are a number of factors that make this a difficult task. There are clearly wide ranges of normality in normal body composition, with wide variation in body fat and skeletal muscle/BCM in healthy individuals. Thus, it may be possible for an individual to undergo significant changes in nutritional state or hydration before they would fall outside the ranges of normality for the general population. Normal population data may also vary between populations of different countries or ethnic origin, and populations studied at different times. Also, while measurements by BIA correlate well with gold-standard methodology, there is potentially significant error of measurement in individual subjects, which may be greater in patients with renal disease than in normal subjects (29,30). This error may partly relate to the body not acting as a geometrically uniform electrical conductor as the underlying theory assumes. Extracellular water will also increase with body adipose tissue, which is not accounted for (31).

Assessment of hydration and setting dry weight is an area of particular interest. There is a fundamental issue of what should be defined as normal hydration. Extracellular water volume reflects hydration but clearly will vary between subjects of different sizes. Thus to “diagnose” state of hydration, ECW volume needs to be “normalized” to that individual subject’s body size. Popular terms include ratios of ECW/ICW and ECW/TBW. These have the attraction of producing measurements of hydration purely from BIA data. There is significant variation in these ratios among healthy individuals, with the ratios being higher in women than in men and with increasing age (due to lesser or decreasing BCM and thus ICW). We have developed normal ranges for ECW/TBW, accounting for gender and age, based on regression against age from a group of 199 normal (predominantly Caucasian) subjects (32). Thus, an individual measurement can be plotted on a graph of ECW/TBW against age, comparing with the normal regression line and ranges according to SD from the mean, to determine whether it sits on the line of normality or how many SD away from the population norm it lies. In Case 1, the patient’s BIA ECW/TBW was greater than 2 SD above normal range, with associated hypertension; progressive fluid removal resulted in normalization of ECW/TBW ratio and blood pressure control. However there are some limitations to this approach. From clinical experience, we know that modest adjustments to dry weight can have significant clinical impact. The spread of these normal ranges is such that we are unlikely to precisely pinpoint the ideal hydration state for an individual. Thus, at present, we cannot distinguish between normality and significant but modest-sized abnormalities for an individual to be able to use BIA well enough to set a dry weight. Also, the denominator in these ratios reflects BCM; thus wasting, as well as fluid overload, will also produce an elevation of these ratios (as in Case 4) (33). Therefore, a high ECW/TBW or ECW/ICW ratio corrected for age and gender may be a cause for concern, but could reflect either or both fluid excess or wasting and so should not be interpreted purely as a marker of hydration. One other limitation is that ECW can be further split into extravascular fluid (reflecting tissue hydration and edema) and intravascular volume (impacting on blood pressure, development of left ventricular hypertrophy, and cardiac dysfunction), which are both of clinical importance. For a given ECW, the ratio of these compartments may vary among individuals due to factors such as cardiac dysfunction and varying oncotic pressure. Thus, in individuals with otherwise identical body composition, the desirable target ECW may vary due to differences in these factors.

CAN WE MONITOR BODY COMPOSITION WITH SERIAL BIA MEASUREMENTS?

While the limitations of individual variation and described technique accuracy lead to some limitations in the use of BIA to specifically diagnose normality of body composition, the high precision of the technique suggests that its greatest value may be in its ability to detect changes in body composition (34). While there may be error in the absolute accuracy of values of detected changes, it is likely that changes in BIA parameters will reflect genuine trends of change in body composition. It may be these trends, rather than absolute estimates of values of body compartments, that are the most useful guide to patient progress and response to treatment or need to alter management. Bioelectrical impedance
analysis measurements of ECW and ICW should independently reflect changes in hydration and nutritional state. This could be of particular value in indicating that changes are occurring in the situation of the PD patient, where weight is artificially held at a steady level by dialysis prescription. Bioelectrical impedance analysis does not directly measure fat, but in a patient where body weight is changing without corresponding changes in ECW or ICW, it is most likely that there is a change in body fat, as in Case 2, that can be calculated, allowing for limitations of the two-compartment model. A practical issue is that there is normal modest physiological fluctuation of body weight and composition over time. Thus the trend of frequent serial BIS measurements rather than change between just a pair of readings may be most revealing.

CONCLUSIONS

The cases described illustrate examples where BIA has been useful in detecting clinically important changes in hydration and nutrition. In some examples, BIA data confirmed clinical impressions but in others it suggested changes that may not have been clinically apparent. It is important with all measurements in clinical practice to understand the nature and interpretation of the measurement technique, and the possible limitations in terms of accuracy and precision. Bioelectrical impedance analysis is a technique that is acceptable to patients and can be readily performed in clinical situations. Serial measurements in particular may be a useful addition to clinical assessment and may identify changes in hydration or nutrition earlier than would occur with routine monitoring, allowing appropriate changes to management. Variation in normal values in the healthy population and inaccuracy of BIA, however, may restrict our ability to accurately determine whether fluid state and nutrition are normal in an individual at any time point. The complexity and limitations of the technology and underlying theory necessitate careful interpretation of results, which should be taken in conjunction with other facets of clinical assessment rather than as an alternative. Ideally, further systematic studies may evaluate the ability of BIA to alter and improve clinical management compared with standard clinical assessment and refine its ability to define normality.

REFERENCES


