REVIEW ARTICLE

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Volume control and bioimpedance analysis in peritoneal dialysis

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ABSTRACT

Peritoneal dialysis patients develop a wide variety of changes in body composition, mainly reflecting hydration, nutrition and body fat mass. Volume status is now of enormous importance in the outcomes of PD patients, but its assessment is notoriously difficult in clinical practice. Clinical evaluation and chest X-ray, although of major importance, are not sensitive, and the abnormalities are often revealed at a late stage. Serum natriuretic peptides, although useful in the diagnosis of heart failure in the general population, are influenced by the existence of renal and cardiac disease, and thus their isolated use in volume evaluation may be cumbersome. The new techniques of body composition monitoring, namely bioimpedance analysis, have shown promising results in the evaluation of both hydration and nutritional status. Although their use in single measurements is not precise, serial evaluations are useful in the determination of clinical relevant changes in body composition. The purpose of this article is to review the available tools for volume evaluation, focusing on bioimpedance analysis and its clinically relevant advantages.

Key-Words:
Bioimpedance analysis; fluid overload; peritoneal dialysis.

INTRODUCTION

Many landmark studies published in recent years (EAPOS[1] or ADEMEX[2]) have pointed out the importance of volume control in the achievement of better outcomes in peritoneal dialysis (PD), relative to solute clearance. The Evidence Based Practice Guidelines 2005 included a minimum target for net ultrafiltration in anuric patients of 1.0 L/day[3].

The consequences of volume expansion (quite frequent in end-stage renal disease (ESRD), and thus in patients on PD programmes) are well known and adversely interfere in the prognosis of these patients. In addition to all the deleterious effects on the cardiovascular system (hypertension, left ventricular hypertrophy and lately congestive heart failure), some studies have shown a complex interaction between volume overload and inflammation[4] or malnutrition. Inflammation itself has been recognised as a predictor of mortality in ESRD, mainly cardiovascular mortality[5], and the association with malnutrition and atherosclerosis (MIA syndrome) could help to explain these complex relations. In PD patients, the relationship between extracellular volume (ECV) expansion and inflammation is bidirectional: the ECV expansion could be the origin of inflammation[6], but an inflammatory process may trigger volume expansion due to an increased peritoneal permeability and secondary fluid retention.

In patients on PD, the evaluation of fluid status and the definition of euvolaemia are two major challenges for the nephrologist. Indeed, fluid status in these patients is influenced by many factors (gender, race, comorbidity – namely the cardiac function and inflammation) and not only by balance between input and output of water and salt. The "dry weight" (euvolaemia) concept is also difficult to define: fluid overload is associated with worse cardiovascular outcomes[7], but its depletion is a threat to the preservation of residual renal function[8].

The purpose of this work is to review the methods of assessment of volume status in PD patients, focusing on bioimpedance analysis (BIA) and its advantages compared to others.

FLUID STATUS EVALUATION

The monitoring of hydration and the diagnosis of fluid balance problems is crucial in the standard evaluation of PD patients. Prompt detection of fluid abnormalities is essential to implement therapeutic changes and to ameliorate outcomes. At the current status of PD development, many tools are at the disposal of the practitioner, some quite easy to use (physical examination, chest X-ray), while others need specialised equipment and training to be correctly performed (BIA).

Routine physical examination, although useful, is a quite imprecise picture of fluid status. When common symptoms/signals of fluid overload (dyspnoea, peripheral oedema, crackles on lung auscultation) appear, a large amount of fluid excess has been accumulated, and so the absence of these signs of congestion does not exclude fluid overload. Hypertension and consecutive increments in the prescription of antihypertensive drugs are sometimes the only features of overload. Weight measurement, another essential tool in PD management, can be cumbersome in the evaluation of fluid or nutritional status. Indeed, malnutrition is a common and serious complication in these patients, and thus a stable body weight may mask protein-calorie malnutrition due to a concomitant increase in extracellular fluid retention.

Chest X-ray is another simple tool to monitor hydration; in fluid overloaded patients, signs of pulmonary venous congestion (as well as an increase in cardiac diameter) can be seen. However, these changes occur at a late stage, and thus this approach is not practical for short-term monitoring.

The measurement of inferior vena cava diameter with ultrasound and its collapsibility with respiration reflect the hydration status in dialysis patients, but the clinical value of this finding is debated[9].

BRAIN NATRIURETIC PEPTIDES (BNP)

Some recent studies have focused on the importance of natriuretic peptides in volume status evaluation. These particular peptides are secreted by the ventricular myocytes in response to stretching, cardiac disease (such as ischaemic) or hormonal stimulation (angiotensin II, catecholamines), and thus have a marked utility in the diagnosis/prognosis of acute and chronic heart failure. However, their interpretation can be cumbersome in the simultaneous presence of heart and renal failure (cardiorenal syndrome), because their excretion is exclusively glomerular[10]. In the presence of renal insufficiency, new cut-off levels are needed to diagnose heart failure. A recent study, including haemodialysis outpatients, found that N-terminal pro-brain type natriuretic peptide (NT-proBNP) was not associated with cardiac dysfunction as assessed by transthoracic echo but was dependent on factors associated with volume overload[11].

In PD, several studies have tried to use BNP monitoring in the diagnosis of the hydration status. The Lee *et al.* study found no association between BNP and extracellular water (evaluated with BIA)[12]. Hiramatsu *et al.* found a relation between icodextrin use and the decrease in NT-proBNP levels, due to extracellular water contraction[13].

Despite these conflicting results of BNP in hydration monitoring, two studies, one from Wang *et. al.*[14], and another from the ADEMEX group[15], have shown that NT-proBNP levels are highly predictive of survival and cardiovascular mortality in PD.

BODY COMPOSITION MONITORING TECHNIQUES AND BIOIMPEDANCE ANALYSIS

Body composition monitoring techniques are probably the most promising tools for objective evaluation of fluid and nutritional status in PD patients. Among these methods, bioimpedance analysis (BIA) is the most extensively studied, with an intrinsic capacity to predict survival[7].

To a better interpretation of the results of body composition monitoring technique (including BIA), it is useful to understand the principles of body composition analysis[16]. This theory divides the body into two major compartments: fat mass and fat free mass (lean tissue). Whereas fat is homogenous, fat free mass (FFM) is heterogeneous, with different components, including bone mineral content. The major component of FFM is water, and total body water (TBW) normally accounts for 73% of FFM, although this percentage can vary with disease states, mainly those with disturbed water homeostasis. The assessment of lean tissue with BIA reflects nutritional state and hydration[17]. However, to give clinical usefulness in PD patients, body composition monitor must evaluate hydration and nutrition separately. For this purpose, TBW must be further divided into extracellular (ECW) and intracellular water (ICW) and lean tissue into body cell mass (BCM) and ECW. ECW reflects hydration degree, whereas BCM is a more specific marker of nutrition and wasting virtually unaffected by the hydration state. Fat mass, the other big compartment of the organism, could be evaluated by direct (densitometry, magnetic resonance imaging, for instance) or indirect (BIA) methods. With this latter methodology, fat is estimated indirectly from FFM and derives as the remainder of body weight. However to be precise, these techniques are dependent on a normal hydration status, so that an abnormal hydration causes erroneous estimate of lean tissue[18].

PRINCIPLES OF BIA

BIA is based on the measurement of body's impedance to passage of a small alternating electric current between two skin electrodes (at the hands and feet). This electric current freely passes through body water (the major component of lean tissue), with fat acting as an electric insulator. The obtained impedance is inversely proportional to body water content[19].

In the earlier times, BIA was performed with single frequency (50 kHz) and TBW was estimated by regression equations. This method was unable to evaluate nutrition and hydration separately. Nowadays commercially available analysers use bioimpedance spectroscopy, with which reactance and resistance are evaluated with multiple frequencies. In fact, impedance comprises a resistance and a reactance component (the latter resulting from the capacitance effect of cell membranes); the relationship between these components is determined by ECW and by ratio ECW/ICW. Mathematical models of the obtained data estimate the resistance at frequency zero (where all current passes freely through ECW) and at infinite frequencies (where current passes through TBW). By plotting the subject's readings on a graph, this technique gives precise information about TBW, ECW and ICW, and thus determines whether they fall on normal range, and if not, the direction of deviation from normality[20].

CLINICAL APPLICABILITY OF BIA

With single measurements of BIA, on a particular occasion it is difficult to determine whether the body composition is normal or clinically relevant changes exist. Normal body composition widely varies among healthy individuals, in accordance to ethnicity and to the population used as referential. Thus, it is possible for an individual to develop significant bodily changes in hydration and nutritional status before they fall outside the normal range. In renal patients, the problem of defining normality is greater, because of the changes in body composition induced by the disease itself[21]. However BIA has brought insight into the volume status issue in PD and haemodialysis (HD) patients. While 24% of a population still have clinically relevant volume overload (more prevalent in PD and pre-HD patients than a post-HD group), comparable volume status can be obtained in PD and HD patients[17]. Also similar volume status was achieved either by continuous ambulatory and automated PD[22].

For the nephrologist, it is quite attractive and helpful to use single measurements of BIA to assess hydration and to define dry weight. Although ECW reflects hydration status, it widely varies among subjects of different sizes. In this situation, ECW volume must be normalised to the patient size through the calculation of the ECW/ICW or the ECW/TBW ratios[23]. However even with normalisation, these ratios suffer significant variations, and are higher in the female gender and in the elderly. By plotting these ratios on graphs against age and gender and by comparing the curves with the 95% confidence intervals for the general population, it is possible to obtain a more correct vision of the patient's hydration status. As a normality range is wide, however, a normal extracellular volume might not correspond to the ideal hydration status or to the dry weight. Considering the high prevalence of cardiovascular disease in PD patients, some will need higher ECW to avoid hypotension, while others will need a lower one to control pulmonary congestion. Also, because the denominators in these ratios reflect BCM, an elevation could not only reflect hyperhydration, but also wasting. The clinician should be aware of these possibilities and so, high ECW/TBW or ECW/ICW ratios cannot be simply interpreted as hydration indexes. Some authors proposed the normalisation of ECW to height or body surface area to assess hydration, in order to overcome the limitations associated with ECW/ICW or ECW/TBW ratios[23,24].

Additionally, BIA is also a useful tool to depict the complex relations between malnutrition-inflammation-atherosclerosis and volume status[25]: fluid overload is often correlated with inflammation markers. Hypoalbuminaemia was found to be an important predictor of tissue overhydration which was not associated with increased plasma volume[26]. Noteworthy, the BIA derived ratio extracellular mass (ECM)/body cell mass (BCM) shown to an independent predictor of long-term survival in PD patients[27].

Single BIA measurements have limitations in the evaluation of body composition, and there is a disagreement with other techniques of body composition analysis[28]. However, the great advantage of multifrequency BIA seems to lie in the detection of changes in body composition, with serial measurements[29]. Trends of changes in BIA parameters reflect trends of change in body compartments. These trends could be useful to monitor the patient's progress in response to treatment changes. In this setting, alterations in ICW and ECW independently reflect nutritional and hydration changes, respectively, even when the weight is stable. Despite BIA's inability to measure fat, in a patient where the weight is increasing, but ECW and ICW remain stable, the alterations are probably due to an increase in fat mass. Therefore routine BIA measurements could be a more informative tool in the evaluation of the hydration and the nutritional status in a single patient. However, the complexity and limitations of this technique necessitate careful integration of the results with other clinico-laboratory data.

CONCLUSION

In recent years, volume control has gained a huge importance in achieving better outcomes in PD. Although it is quite difficult to evaluate, the clinician has a wide variety of methods at his/her disposal. Some are quite simple and in routine use (physical examination, chest X-ray). Others, while promising and more sensitive, need more investigation to confirm the results outlined until now (BNP measurement, BIA). Among the latter, BIA is an acceptable technique for patients and readily performed in a clinical setting to detect changes in hydration and nutrition, despite the wide variation in normal values in healthy populations. With this methodology, single evaluations are not totally reliable and need cautiously interpretation. Serial measurements, however, may be useful to detect variations in nutrition or in hydration earlier (in addition to clinical assessment) and to implement therapeutic changes, ameliorating overall results.

Conflict of Interest statement. None declared.

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