

Do bioimpedance measurements of over-hydration accurately reflect post-haemodialysis weight changes ?

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Abstract

Introduction

Bioimpedance spectroscopy (BIS) devices are being used to determine ultrafiltration requirements to achieve target weight for haemodialysis (HD) patients. Pre-dialysis measurements are more convenient for patients and staff. We wished to compare the changes in pre-and post-dialysis hydration measured by BIS with actual weight loss.

Methods

We compared paired BIS measurements made pre and post-haemodialysis using a BIS device based on a 3 compartmental model, designed to provide information on extracellular water (ECW) excess .

Results

BIS was measured in 49 HD patients, 35 male (71.4%), mean age 67.6 \pm 14.2 years. Weight fell significantly from 69.2 \pm 17.8 to 67.6 \pm 17.4 kg, and BIS over hydration (OH) from 4.5 \pm 3.3.4 to 3.4 \pm 2.9 L, and ECW from 16.8 \pm 4.8 to 15.5 \pm 4.4 L, but there was no change in intracellular water (ICW). Weight loss correlated positively with the change in ECW, but exceeded the fall in OH; mean bias -0.58 (95% confidence limits -3.6 to 4.8 kg).

Summary

We measured OH pre-and post-haemodialysis, but did not find that the change in OH correlated with changes in body weight. Although there was a correlation between changes in OH and ECW, there was none for weight. Our findings do not support total reliance on pre-dialysis BIS alone for assessing

volume status in haemodialysis patients, but rather BIS should be considered as an aid to clinical assessment of volume status.

Introduction

Despite the success of haemodialysis, with more than 2 million patients now treated world-wide, the mortality of haemodialysis patients remains high and is greater than that for some of the more common solid organ malignancies. Most deaths are cardiovascular in nature, with an increased risk of sudden deaths, thought to be due to dysrhythmias. For patients dialysing thrice weekly more haemodialysis patients are admitted to hospital or experience sudden death in the hours before the first dialysis session of the week, [1], when they most volume overloaded. As such achieving a target weight, when patients are no longer volume expanded, by achieving a normal extracellular water (ECW) volume has been reported to improve patient survival [2].

Bioimpedance devices estimate the amount of fluid in the body by measuring the electrical resistance to a series of alternating currents flowing between electrodes placed on the hand and foot [3,4]. There are a number of bioimpedance devices commercially available, they varying in the number of electrical frequencies and whether they measure body segments or total body [5,6]. Bioelectrical impedance spectroscopy (BIS) assessments of total body water (TBW), ECW and intracellular water (ICW) have been validated against "gold standard" isotopic methods [7]. In every day clinical practice BIS measurements are made pre-haemodialysis to determine ultrafiltration

requirements to achieve a normally hydrated status, or target weight post-dialysis. Most bioimpedance devices have used a similar model to dual energy X ray absorptiometry (DXA) scanning, in terms of dividing the body into two basic compartments; fat mass and fat free mass, from which ICW and ECW are derived. However, for the dialysis patient it has been difficult to express the amount of excess fluid (over hydration (OH)) that a dialysis patient needs to lose to restore euvolaemia using this approach, with studies reporting ratios of ECW/TBW [8], or using equations to estimate ECW excess based on a normal ratio of ECW to ICW [9]. Newer BIS devices are now available, expressing OH, by using a 3 body compartmental approach, dividing lean body mass into normally hydrated tissue and the excess fluid as OH [3,7].

The assumption is that OH measured pre-dialysis provides information to guide the clinical team as to how much fluid should be during the dialysis session to return the patient to their target or post-dialysis weight. We therefore reviewed , pre and post dialysis bioimpedance measurements [10], to determine whether change in OH corresponded to the change in body weight following dialysis, to determine whether pre-dialysis measurement of OH by bioimpedance could be used to guide intra-dialytic weight loss.

Methods

We audited the results of pre and post haemodialysis BIS measurements (BodyStat multiscan 5000, Douglas, Isle of Man). All haemodialysis sessions were performed with patients lying on a bed, and using Fresenius 4000H dialysis

machines (Fresenius MC, Bad Homburg, Germany), with a high flux dialyzer (Elisio, Nipro Corporation, Osaka, Japan) [11] anticoagulated with low molecular weight heparin (tinzaparin, Leo Laboratories, Princes Risborough, UK) [12], using ultra-pure quality dialysis water. Dialysis machines were regular serviced and dialysate sodium checked [13]. Dialysate bicarbonate was fixed at 32 mmol/L, with an acetate of 3.0 mmol/L and magnesium 0.5 mmol/L. Serum chemistries were measured pre-dialysis with a standard laboratory analyser (Roche Cobra II, Basingstoke, UK), by a UK accredited laboratory

The amount of fluid to be removed during the dialysis session was determined by the clinical team, and if required ultrafiltration was set at a constant rate. Patients were restricted to one small drink during the dialysis session (approximately 180 ml) and no food was given.

Bioimpedance measurements were made with the patient lying in bed. Four electrodes were placed according to the manufacturer's instructions on the contra-lateral hand and wrist, ankle and dorsum of the foot to the arterio-venous fistula. Electrodes remained in position for the course of the dialysis session, and for post dialysis measurements. The BIS device measures whole body resistance and reactance with 50 different alternating electrical current frequencies ranging from 5-1000 kHz. Due to different amount of water in body tissues, the BIS device computes ECW, ICW and from an estimation of normo-hydrated tissues ECW excess as over hydration (OH) L.

To allow time for re-equilibration post dialysis measurements were made after the fistula needle sites had stopped bleeding, patients had been re-

weighed using the same scales, returned to bed and then rested. To ensure that patients were at a stable state, we repeated measurements up to four times in a number of patients.

Statistical methods

Statistical analysis was by parametric or non-parametric pair testing, ANOVA with appropriate post hoc testing, and univariate correlation, using Pearson or Spearman correlation (Prism 6.0, Graph Pad, San Diego, USA), and Bland Altman analysis (version 3.0, Analyse It, Leeds, UK), with significance at the $p < 0.05$ level. Data is reported as mean \pm standard deviation, median and interquartile range or percentage.

Ethics

Standard clinical practice in our centre is to measure bioimpedance pre and post-dialysis as standard equipment uses a 2 compartmental model. We audited the results of pre and post haemodialysis BIS measurements made with bioimpedance device using a 3 compartmental model in consecutive patients to determine whether bioimpedance derived body composition should be measured pre or post dialysis to be the standard of care for routine clinical practice. Ethical approval fulfilled UK NHS clinical service development and audit (UK NHS guidelines for clinical audit and service development (<http://www.hra.nhs.uk/documents/2013/09/defining-research.pdf>)).

Results

Pre and corresponding post BIS measurements were retrospectively reviewed in 49 consecutive adult patients receiving in-centre haemodialysis session who had corresponding pre and post dialysis session BIS measurements, 35 male (71.4%), mean age 67.6 ± 14.9 years, 22 Caucasoid (44.9%), 14 South Asian (28.6%), 7 African-Afro-Caribbean (14.3%) and 6 Far Asian (12.2%). Twenty two patients were diabetic (44.9%), and the median Davies co-morbidity score [14] was 2 (1-3). Pre-dialysis haemoglobin was 103.4 ± 19.1 g/L, serum albumin 36.4 ± 4.8 g/L, potassium 4.3 ± 0.9 mmol/L, urea 18.4 ± 6.2 mmol/L, calcium 2.32 ± 0.14 mmol/L, C reactive protein 8 (4-28) mg/L.

Median dialysate sodium was 137 (136-138.5 mmol/L, potassium 2.0 (1-2) mmol/L, with a calcium 1.35 (1.0-1.35) mmol/L. Dialysate was cooled, median temperature 35.0 (35.0 - 35.5)°C. The median dialyzer surface area was 2.1 (1.7 - 2.1) m².

To ensure that patients were in a stable state when post dialysis BIS measurements were made, three sets of measurements were made after 38 of the dialysis sessions. There was no significant change by ANOVA in measurement of OH, ICW or ECW over time (table 1). In 12 patients, four separate measurements were made post-dialysis, to determine whether there was any change over time, and there were no differences noted between measurements (1st measurement ECW 17.0 ± 4.6 vs 4th measurement 17.0 ± 4.6 L; and ICW 17.0 ± 5.6 vs 17.0 ± 5.4 L, respectively).

Clinician notes of clinical volume assessments made pre-dialysis were reviewed and the patients assigned into 4 groups dehydrated, no overt clinical signs of ECW excess, pitting ankle oedema or elevated jugular venous pulsation, or gross ECW excess and clinical heart failure. OH measurements increased sequentially in these 4 groups from 3.05 ± 0.07 (n=2), to 3.97 ± 3.69 (n=16), 4.29 ± 2.8 (n=23) and finally 6.7 ± 2.56 kg (n=8), in keeping with clinical assessment of increasing fluid retention. As there were so few patients thought clinically to be dehydrated, we compared the group clinically thought to be euvolaemic and those with signs of ECW excess. As clinical assessment of ECW excess increased, then so did OH measured by BIS, $p < 0.05$ by ANOVA testing. Pre-dialysis there was a correlation between OH and ECW ($r=0.69$, $p < 0.001$), but not TBW ($r=0.25$, $p=0.062$) or ICW ($r=-0.13$, $p=0.34$).

We compared the paired pre and post dialysis BIS measurements for each session, and as expected weight, and BIS measurements of TBW, ECW and OH fell significantly post dialysis (table 2). There was a simple correlation between the change in weight following dialysis with the change in TBW ($r=0.55$, $p=0.03$). We then compared the change in weight and TBW by Bland Altman analysis, which showed that the change in weight was greater than that in TBW, mean bias -0.03 (95% limit of agreement -8.2 to 8.1 L-kg) (Figure 1). However there was no significant correlation between the change in pre and post dialysis weight and OH ($r=-0.10$, $p=0.51$).

We then compared the change in patient weight and OH by Bland Altman analysis (Figure 2). Again, the difference in weight was greater than that for

OH following dialysis, mean bias 0.58 (95% limits of agreement -3.6 to 4.8. The change in weight with dialysis correlated with the change in ECW ($r=0.44$, $p<0.01$), but not with ICW ($r=-0.18$, $p=0.70$). The change in OH was positively associated with a change in ECW ($r=0.31$, $p=0.03$), and ratio of ECW/TBW ($r=0.84$, $p<0.001$) (Figure 3).

To consider other factors which may have affected the change in ECW, we considered body size, in terms of weight and BMI. However there was no statistical association between body size pre-dialysis and the change in OH or change in the ratio of OH/ECW. Similarly there was no association with age, sex, diabetes or co-morbidity score. We did however find an association between the change in OH with the difference between pre-dialysis serum sodium and the dialysate sodium concentration † ($r=0.43$, $p=0.02$) and negatively with CRP ($r=-0.45$, $p<0.01$). We also noted an association between pre-dialysis serum sodium and dialysate sodium gradient and the change in ECW ($r=0.73$, $p<0.001$) but not with ICW.

Discussion

One of the goals of haemodialysis treatment is to correct volume overload, and return patients to their target weight. As such most patients would be expected to lose weight, with corresponding reductions in TBW, ECW and ICW [15]. We measured BIS pre and post dialysis sessions and compared the results from consecutive patients. A clinical decision was made in each case to determine the ultrafiltration target. We found a step wise increase in the mean

pre-dialysis assessment of volume status made by BIS and clinical assessment of volume status, and there was a positive correlation between pre-dialysis OH and ECW volume.

We chose to measure weight loss, rather than ultrafiltration rates or ultrafiltration measured by the dialysis machine to exclude errors in calculating volume loss due to fluid changes with connecting patients to the dialysis machine and differences in wash back at the end of the dialysis session. As expected, following dialysis there was a reduction in weight for the cohort. The weight loss was greater than both the change in TBW and OH. This is to be expected as normal plasma water has a higher density than water, and that from dialysis patients even greater due to the effects of urea and other azotaemic retention solutes. As such one litre of ultrafiltrate weighs more than 1.0 kg. However in calculating OH, it was assumed that one litre of OH was equivalent to one litre of water (1.0 kg) [3]. Although there was a correlation between the change in weight following dialysis and both ECW and TBW, but there was no statistical association with change in ICW. Other reports have noted that changes in skin temperature due to differences in local blood flow lead to changes in bioimpedance measurements, with cooling and vasoconstriction resulting in an increase in impedance, whereas vasodilatation reduced impedance [16]. However the algorithm used by the BIS is based on determining OH as being the amount of ECW excess for normally hydrated tissues, and as such ICW using this model would not be expected to change post-dialysis. However a recent study reported

removing sodium from tissues during dialysis [17], and as such this would be expected to cause changes in ICW.

Previous reports have suggested that using a lower dialysate sodium can lead to a greater reduction in ECW [18], and we also noted an association between the serum to dialysate sodium gradient with both the change in OH and ECW.

Our results demonstrate that the majority of change in OH is due to a change in ECW, which supports a previous report of using BIS and a 3 compartmental body composition model [19,20]. As such pre-dialysis measurements of OH have been used to aid clinical decision making in terms of the amount of ultrafiltration required to return patients to a normo-volaemic state [21]. Most studies have only reported pre-dialysis measurements [20,22], and there has been an assumption that the pre-dialysis OH measurement was correct. However our data, although showing an increasing OH with clinical assessment of volume status suggest that the actual measurement of OH pre-dialysis should be used in conjunction with clinical assessment of volume status, and not replace clinical judgment.

Previous studies on BIS have reported on Caucasoid and African-American haemodialysis patients [2,3,22], and we did have patients from other ethnic groups, and reports have suggested that some bioimpedance measurements may vary between ethnic groups, but not in terms of ECW status [23,24], and we also did not find any association with ethnicity.

In theory post-dialysis bioimpedance measurements, could be affected by the electrolyte shifts occurring during the session [25]. This effect has been thought to be of minimal clinical relevance by some groups [3], whereas others have suggested that the change in resistivity during the course of a haemodialysis session could potentially lead to an ECW change of around -3.2% to 1.4% and -3.7% to 1.7% for ICW. This would potentially introduce an error in estimating ICW of 20% or more, and a lower ECW error of less than 15% [25]. We did note an effect of CRP and the change in OH with dialysis.

Inflammatory conditions can lead to increased capillary permeability and ECW expansion [26], and as such this may affect the amount of fluid which can be readily removed during a dialysis session, in keeping with a negative association between CRP and change in OH.

We allowed time for changes in blood flow and electrolyte shifts to re-equilibrate at the end of the dialysis session [27], and also the potential effect of a change in posture [28], so that when we repeated up to 4 measurements post-haemodialysis we found no significant differences. Unlike with some other BIS devices, the electrodes remained in place during the dialysis session [29], and no electrode had to be replaced, so eliminating error due to changes in electrode position.

Our retrospective audit has several limitations. There were a number of outlying data points, for the change in TBW, one patient was thought to be dehydrated pre-dialysis and had their weight increased with dialysis, and conversely another patient was thought to be markedly overhydrated and had a

large weight loss following dialysis. As this was an audit and not a study we do not have any comparative measurements of body volume by isotopic methods, or bioimpedance equipment, using a standard two body compartment model [4].

Compared to standard bioimpedance devices [30], we have compared pre and post-haemodialysis measurements with a BIS device using a 3 body compartmental model determining fluid overload. Although there was a trend between clinical assessment of fluid overload and the OH measured by bioimpedance this was not significant. We observed that the change in patient weight did not correlate with the measured changes in OH, or ICW. Weight change was predominantly related to changes in ECW. Previous studies targeting weight loss according to pre-dialysis BIS measurements have reported premature loss of residual renal function [31]. As such we would suggest that pre-dialysis BIS determination of OH should be used in conjunction with clinical assessments of volume status, and not replace clinical judgment, particularly for patients with evidence of systemic inflammation.

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Figure 1. Bland Altman plot of the change in patient weight (Wt) (kg) and total body water (TBW) (litres) following haemodialysis. . Mean bias and 95% confidence limits are depicted as dotted lines.

Figure 2. Bland Altman plot of the change in patient weight (Wt) (kg) and over hydration index (OH) L following haemodialysis. Mean bias and 95% confidence limits are depicted as dotted lines.

Figure 3. Relationship between change in the ratio of extracellular water (ECW) to total body water (TBW) and change in over hydration index (OH) following haemodialysis

Table 1. Reproducibility of post-haemodialysis bioimpedance spectroscopy derived measurements of over hydration (OH), extracellular water (ECW) and intracellular water (ICW). There were no significant differences between the 3 measurements in 38 patients.

| measurement | Over hydration | Extracellular water | Intracellular water |
|-------------|----------------|---------------------|---------------------|
| first | 3.71±2.95 kg | 15.60±4.48 L | 14.85±4.62 L |
| second | 3.72±2.96 kg | 15.61±4.48 L | 14.90±4.63 L |
| third | 3.66±2.96 kg | 15.58±4.48 L | 14.99±4.65 L |

Table2: Pre and post haemodialysis session weight and volume assessments made by bioimpedance spectroscopy. Values expressed as mean ± standard deviation

| variable | Pre dialysis | Post dialysis | p value |
|-----------|--------------|---------------|---------|
| Weight kg | 69.2±17.8 | 67.6±17.4 | <0.001 |

| | | | |
|-----------------------|-----------|-----------|--------|
| Over hydration kg | 4.5±3.4 | 3.4±2.9 | <0.01 |
| Total body water L | 31.2 ±9.9 | 30.5 ±8.4 | <0.001 |
| Extracellular water L | 16.8 ±4.8 | 15.5 ±4.4 | <0.001 |
| Intracellular water L | 15.4 ±6.4 | 15.0 ±4.8 | 0.47 |