Changes in serum osmotic pressure following haemodialysis treatments lead to changes in bioimpedance spectroscopy estimates of lean and adipose tissue

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Abstract

Haemodialysis (HD) patients are at risk of sarcopenia. Newer bioimpedance devices (BIS) using a 3 compartmental body composition model, separate extracellular water (ECW) over–hydration from normo-hydrated lean tissue mass (LTM) and adipose tissue mass (ATM). During HD hydration status changes, along with changes in electrolytes and solutes, and may alter body composition measurements. As such we measured BIS and serum osmotic pressure (sOP) pre and post-dialysis in 43 patients. There were no significant changes in LTM (39.5±15.1 vs 39.3±15.2 kg) or sOP (33.2±8.3 vs 35.9±9.7 mmHg). Higher post-dialysis sOP was associated with a greater percentage fall in LTM ($r=0.43$, $p=0.08$) and increase in ATM ($r=-0.43$, $p=0.017$). Increased sOP post-dialysis was associated with a reduction in LTM ($r=0.36$, $p=0.033$) and increased ATM ($r=-0.44$, $p=0.013$). Changes in sOP with HD are associated with changes in BIS body composition measurements. BIS measurements should preferably be made when patients are least over-hydrated.

Haemodialysis patients are at increased risk for sarcopenia, which is associated with increased mortality [1]. The European Society for Parenteral and Enteral Nutrition guidelines recommend dual X ray absorptiometry (DXA) and bioimpedance assessments to detect muscle wasting [2]. Bioimpedance is more convenient than DXA, and reports have shown equivalence in determining body composition [3]. Both methods typically divide the body into a two compartmental model of fat and fat free mass. However, assessments can be affected by hydration status [4]. Haemodialysis patients are volume overloaded pre-dialysis and fluid is removed during the dialysis session. Thus, post-dialysis measurements would potentially be more reliable when assessing muscle mass, but requires patients to remain behind after the dialysis session. More recently a three compartmental bioimpedance spectroscopy (BIS) model has been developed, separating extracellular water (ECW) over hydration from normally hydrated lean tissue mass (LTM) and normally hydrated adipose mass (ATM) [5]. Potentially this model would allow bioimpedance measurements of body composition to be made more conveniently pre-dialysis, as LTM and ATM should not change with removal of ECW excess. During haemodialysis, along with the change in ECW, there is also a change in electrolytes and serum osmolality, and as the bioimpedance model is based on the concept of measurement at a normo-hydrated state we investigated whether body composition changes with dialysis [6] were associated with the changes in osmolality, as haemodialysis patients will differ not only in terms of hydration status but also electrolyte balance and uraemic solutes.

As part of clinical service development (UK NHS guidelines for clinical audit and service development (http://www.hra.nhs.uk/documents /2013/09/ defining-research.pdf), we measured serum osmotic pressure (sOP) in 43 haemodialysis patients, using a colloid osmometer (Osmomat 050, Genotec, San Francisco, USA) and compared changes with pre and post-dialysis BIS (Body Composition Monitor, Fresenius AG, Bad Homburg, Germany), measured in a standardised manner, with electrodes placed in accordance with manufacturer's instructions contra-laterally to fistulae, and post measurements delayed to allow for equilibration [6,7]. Patient characteristics: 30 male (69.8%), mean age 64.5±17.8 years, median dialysis session was 3.5 (3.0-4.0) hours, dialysate temperature 35.0 (35.0-35.4)^{0}C, sodium 138 (137-140) mmol/L potassium 2.0 (1-2) mmol/L, and ultrafiltration rate 8.1 ±4.3 ml/kg/h. Weight and serum urea fell post-dialysis, and there were no statistically significant overall changes in body composition (table 1). Calculated serum osmolality, using serum urea, sodium, potassium and glucose, fell from 314 ±15.1 to 303.9±10.0 mOsmol/kg, but no significant change in measured sOP (table 1). There was a correlation between measured pre-dialysis sOP and calculated osmolality (r=0.37, p=0.04), and serum urea (r=0.53, p=0.001), but not between post-dialysis measurements. There was no correlation between pre-dialysis measured sOP and body composition or ECW status. The post-dialysis measured sOP correlated with the percentage fall in total body water (TBW), intra-cellular water (ICW), LTM, and negatively with ATM (table 2). However, there was no correlation with the change in patient weight, or ultrafiltration rate.

We then compared the change in sOP and changes in body composition. An increase in sOP post-dialysis was associated with a fall in body cell mass (BCM), and LTM and negatively with ATM (Table 2).

Although overall the mean body composition values in terms of LTM, ATM , and BCM measured with BIS did not significantly change post-dialysis, at the individual patient level there were changes in body composition. Total body weight and serum urea fell post-dialysis. Although there was a correlation between sOP and both serum urea concentration and calculated serum osmolality pre-dialysis, there was no such correlation post-dialysis. Standard equations for calculating serum osmolality are based on serum sodium, potassium, glucose and urea concentrations. Whereas measured sOP pre-dialysis would also include the other uraemic osmolytes and proteins, and then post dialysis the competing effects of osmolyte clearances, changes in electrolytes and the effect of plasma water volume contraction. Depending upon the balance between the fall in osmolytes and plasma water contraction, sOP post-dialysis increased in some patients and fell in others.

We found that the greater the post-dialysis sOP, then the greater the percentage fall in ICW and TBW and also LTM, whereas ATM increased. There was no correlation between post-dialysis sOP and either relative weight change or ultrafiltration rate.

Similarly, an increase in sOP post-dialysis was associated with a reduction in LTM and BCM, and an increase in ATM . Conversely when sOP decreased post

dialysis, then LTM and BCM increased, and ATM fell. Previous bioimpedance studies have variously reported a fall in fat free mass and increase in fat mass, or an increase in ICW and BCM [8]. Over estimation of fat free mass has been ascribed to increased ECW pre-dialysis, as muscle contains more water than fat. In theory, as the 3 compartmental model separates ECW excess from normally hydrated LTM and ATM, then there should be no changes in LTM or ATM following haemodialysis. However, the model is based on the concept of normally hydrated tissue, and tissue hydration will vary between haemodialysis patients due to hydration status, but also electrolyte balance and retention of uraemic solutes. During dialysis not only are there changes in hydration status but also electrolyte fluxes and removal of uraemic solutes, leading to differences in estimation of ECW and ICW during dialysis [8,9]. As such this will lead to changes in intra-cellular osmolality and cell hydration, which will vary between patients, leading to differences in tissue hydration status compared to the bioimpedance estimated normo-hydrated state [10]. However, as with any measuring device, there are error ranges for impedance predictions and some of the observed pre-post differences may be within these limits, although the changes we have demonstrated linked to osmolality would suggest an effect on BIS measurements.

We have demonstrated that using a 3 compartmental model estimates of lean and adipose tissue mass change post-dialysis, and that this is related in part to changes in osmotic pressure. Post-dialysis, patients are less over-hydrated, with a more normal electrolyte balance. Thus, for more reliable screening for

sarcopenia and measurements of lean tissue mass, then bioimpedance measurements should preferably be made post-dialysis.

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Table 1. Pre and post-haemodialysis session body composition as measured with bioimpedance spectroscopy, and serum chemistries. Results expressed as mean ±SD, or median (inter-quartile range). * $p<0.05$, ***<0.001 vs Pre-dialysis by appropriate paired testing.

variable	Pre-dialysis	Post-Dialysis
Weight kg	70.2 ±17.3	68.6 ±17.1 ***
Lean Tissue mass kg	39.5 ±15.1	39.3 ±15.2
Adipose Tissue mass kg	28.9 ±15.9	29.4 ±13.4
Fat tissue kg	25.4 ±17.1	22.5 ±11.2
Body Cell Mass Kg	21.9 ±10.2	20.8 ±10.3
Serum urea mmol/L	21.4 ±10.8	7.6 ±4.9
Serum sodium mmol/L	137.2 ±5.1	138.4 ±2.3
Serum potassium mmol/L	5.3 ±0.8	3.7 ±0.5 ***
Serum glucose mmol/L	7.7 ±2.5	7.2 ±1.6
Serum Albumin g/L	31.3 ±5.9	32.6 ±5.2 *
Osmotic pressure mmHg	33.2 ±8.5	35.9 ±9.7

Table 2. Spearman univariate correlation between post dialysis measured serum osmotic pressure and percentage change in body composition (Pre-post dialysis variable/pre dialysis) and change in measured serum osmotic pressure and change in body composition (Pre –Post). Median (interquartile range).

variables	r	p
Post serum osmotic pressure		
% change total body water 0.9 (-6.4 to 10.1)	0.33	0.036
% change intracellular water -1.8 (-12.6 to 8.3)	0.34	0.030
% change lean tissue mass -1.3 (-16.7 to 13.2)	0.43	0.008
% change adipose tissue mass 26.5 (-16.7 to 37.6)	-0.43	0.017
Change measured osmotic pressure -4.3 (-9.6 to 5.6) mmHg		
Change body cell mass -0.8 (-4.8 to 2.9) kg	-0.38	0.025
Change lean tissue mass -1.0 (-6.7 to 4.4) kg	-0.36	0.033
Change adipose tissue 2.1 (-3.8 to 5.9) kg	0.44	0.013