Comparison of different scaling parameters and energy expenditure in peritoneal dialysis patients

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Abstract

Objective

Peritoneal dialysis (PD) dosing is determined by urea clearance scaled to total body water (TBW). However, studies delivering greater peritoneal Kt/Vurea have failed to demonstrate improved survival. Body surface are (BSA) has been suggested as an alternative scaling factor. Cellular metabolism generates toxins, thus total energy expenditure (TEE) may be a preferable scaling factor. As TEE is cumbersome to determine, we wished to determine the association of anthropomorphic scaling factors with TEE.

Subjects/Methods

TEE was determined by the Recent Physical Activity Questionnaire combined with resting energy expenditure by validated equations using doubly labelled isotopic water, and body composition by multifrequency bioimpedance.

Results

148 adult PD patients were studied, 97 male (65.5%), mean age 60.6±20.6 years, with a median PD treatment of 9.1 (3.5-25.2) months. Their mean weight was 73.6±16.7 kg, body mass index (BMI) 26.0 ±4.9 kg/m^2 and BSA of 1.86 ±0.24 m^2. The mean TEE was 1974±414 kcal/day, and TEE correlated with BMI (men r=0.48, p<0.001, women r=0.36, p=0.018), BSA (men r=0.56, women r=0.63) and TBW (men r=0.62, women r=0.65), all p<0.001. Skeletal muscle mass correlated with BMI (men r=0.48, women r=0.50), BSA (men r=0.72, women r=0.63) and TBW (men r=0.98, women r=0.99), all p<0.001.

Conclusions

Comparing scaling factors, then TBW and BSA had stronger correlations with TEE than BMI. Skeletal muscle mass was most strongly associated with TBW. As such this study did not demonstrate any advantage for BSA as a scaling factor to adjust PD dialysing dosage compared to TBW.

Introduction

Cellular metabolism generates waste products. Patients with chronic kidney disease (CKD) fail to excrete many of these compounds, leading to their accumulation. Urea is generated as a by-product from the breakdown of proteins into amino acids, and recycling of amino-acids. Urea clearance is currently recommended to determine the amount of dialysis patients receive. In the case of peritoneal dialysis (PD) patients this is the sum of averaged 24-hour urinary urea and creatinine clearance and daily peritoneal urea clearance, adjusted to total body water estimated from anthropomorphic measurements (Kt/Vurea) [1,2].

However, prospective studies have failed to convincingly demonstrate that increasing peritoneal urea clearance results in greater patient survival [3]. This could be due to the differences in urea clearance compared to the clearance of other waste products of metabolism which may have greater biological toxicity. An alternative hypothesis would be that adjusting urea clearance for total body water does not adequately allow the comparison of urea clearance in different sized patients. As such, some researchers have suggested alternative scaling factors for urea clearance, to allow for inter-patient comparison are required [4]. For example, body surface area (BSA) rather than total body water (TBW) is used to scale urinary creatinine clearance, and for some visceral organs, such as left ventricular mass.

As urea is generated by cell metabolism, then in the steady state urea production is a marker of cellular protein turnover. Energy expenditure consists of both resting energy expenditure (REE) and that due to active energy expenditure (AEE). REE depends upon the activity of visceral organs; including muscles, liver, brain, gastro-intestinal tract, heart, and kidneys. Visceral organs such as the heart are typically reported scaled to BSA, whereas skeletal muscle is scaled to height squared. Patients with CKD are more vulnerable to muscle wasting, termed sarcopenia. As such, body composition may differ in PD patients, potentially due to increased muscle loss, on one hand and increased body fat, on the other. Thus, the standard scaling factors of BSA, TBW and body mass index (BMI), used to adjust for differences in patient sizes may differ compared to healthy patients. We therefore wished to compare scaling of PD urea clearance using these different scaling factors and REE and total energy expenditure (TEE).

Patients and methods

Adult patients with chronic kidney disease under the care of the Royal Free Hospital treated by PD were recruited when attending for outpatient assessments of peritoneal dialysis adequacy. Corresponding spent dialysate effluent and serum samples were analysed by standard methods, and weekly dialysis dose calculated as Kt/Vurea [1,2]. Nitrogen protein accumulate rate (PNA) was estimated using the Bergström equation (g/day) [2].

Multifrequency bioimpedance (InBody 720, Seoul, South Korea) was performed in a standardised manner. Patients were asked to empty the bladder, and then dialysate was drained out [5,6]. Skeletal muscle mass (SMM) and fat mass (FM) were determined by bioimpedance.

Physical activity data was obtained through the validated Recent Physical Activity Questionnaire (RPAQ) [7], which collects information about activities performed at home, work and leisure time and also the time spent on each activity in the preceding 4 weeks. The RPAQ has been validated and been shown to be a reliable tool for estimation of energy expenditure in patients with CKD [8]. Physical activity data was determined by each reported activity being assigned a Metabolic Equivalent of Task (MET) value according to the Compendium of Physical Activities [9].

Ethical approval was granted by the UK National Research Ethics Committee - Essex and the study was registered in UK Clinical Research Network (CRN) Portfolio number 14018. All patients provided written informed consent in keeping with the declaration of Helsinki.

Statistical analysis

Statistical analysis was by paired analysis, students' t tests, or Wilcoxon pair analysis, with appropriate correction for multiple testing, Pearson or Spearman's correlation (GraphPad Prism version 7.0, San Diego, USA). Data are presented as mean ± standard deviation, median (inter quartile range), or mean and 95% confidence limits (CL), or as a percentage.

Results

Data from 148 patients, 97 male (65.5%), mean age 60.6±20.6 years, with a median of 9.1 (3.5-25.2) months treatment with PD was collected. The mean weight was 73.6±16.7 kg, with a BMI of 26.0 ±4.9 kg/m^2 and BSA of 1.86 ±0.24 m^2. The mean REE was 1534±241 kcal/day and TEE 1974±414 kcal/day.

As expected there were highly significant univariate correlations between BMI, BSA and TBW and body composition (Table 1). However, whereas there was a highly significant correlation between fat mass and BMI, fat mass was not associated with TBW. When we compared these scaling factors with TEE, the univariate correlations ranged from r^2 0.13 for men, and r^2 0.23 for men with BMI, to r^2 0.38 for men and r^2 0.42 for women with TBW (Figure 1).

There was a correlation between TEE and PNA for men ($r=0.65$, $p<0.001$), but not for women ($r=0.28$, $p=0.058$). The strongest univariate associate for PNA was with TBW and least with BMI (table 1). Similarly, there were positive correlations between TEE and skeletal muscle mass for both men and women ($r=0.63$, and $r=0.66$ respectively), $p<0.001$.

Discussion

Clinical guidelines recommend that PD patients are given a target amount of dialysis based on urea clearance adjusted for TBW [1,2]. However, as prospective studies have failed to demonstrate a survival advantage for greater peritoneal urea clearance [3], some have questioned the paradigm of Kt/Vurea, and whether the dose of dialysis should be alternatively scaled [9]. As uraemic toxins are generated by cellular metabolism, then it has been suggested that the amount of dialysis a patient should receive be tailored according to metabolic rate [10]. However basal metabolic rate only includes REE [12] and does not take into account active energy expenditure [13].

We looked at the relationship between TEE and the three most commonly used scaling factors; BMI, BSA and TBW. On univariate analysis, the weakest association was with BMI, and the strongest TBW, which was only marginally greater than that for BSA. However, as shown in the figure the relationship between TEE and TBW was r^2 0.38 for men and r^2 0.42 for women, so around 40% of the variation in TEE could be explained by changes in TBW, or conversely 60% of the variation in TEE cannot be explained by differences in TBW.

As BMI, BSA and TBW use common factors, then there is mathematical coupling between these scaling factors. We used a validated method to determine body composition [5,11], and noted that BMI had a greater association with body fat compared to BSA and TBW. As with TEE, the univariate association was strongest between skeletal muscle mass and TBW, followed by BSA, and weakest with BMI. Previous reports have suggested that skeletal muscle mass regulates metabolism due to inter-organ cross talk [14]. We found positive correlations between TEE and skeletal muscle mass, of similar magnitude to TBW. It would therefore appear that the value of TBW as a scaling factor is linked to the underlying association between TBW and skeletal muscle mass.

This analysis comparing the three most common scaling factors, would suggest that for peritoneal dialysis patients TBW and BSA are preferable to BMI, which has greater linkage to body fat mass. TBW and BSA have greater linkage to skeletal muscle mass in this cohort of patients. This analysis demonstrates little difference between TBW and BSA as scaling factors. Previous reports have suggested that scaling using BSA was superior to TBW for haemodialysis patients [9,10]. The difference described for haemodialysis patients may be due to patient selection, in that much heavier patients (>120 kg) are generally offered haemodialysis rather than PD. As such, relatively more HD patients may have greater BMIs [15], and the relative greater proportional increase in fat mass compared to the increase in body weight may account for these differences.

Although TBW remains the current scaling factor used in clinical practice, there is considerable variation in TEE that cannot be readily explained by changes in TBW. This variation may provide some explanation as to why studies examining the effects of delivering greater urea peritoneal clearance, based on TBW scaling of dosage, have failed to demonstrate a survival advantage

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Figure 1. Univariate association between total energy expenditure (TEE) kcal/day and anthropomorphic estimated total body water (TBW) L, for male and female peritoneal dialysis patients. Spearman correlation for all patients.

Table 1: Univariate association between body mass index, body surface area, and total body water and body composition and total energy expenditure.

	Male		Female	
Body Mass Index	r	p	r	p
Weight	0.89	<0.001	0.90	<0.001
Body Surface Area	0.82	<0.001	0.85	<0.001
Total Body Water	0.46	<0.001	0.51	<0.001
Fat mass	0.78	<0.001	0.92	<0.001
Skeletal muscle mass	0.45	<0.001	0.50	<0.001
Protein nitrogen appearance	0.37	0.001	0.22	>0.05
Total Energy Expenditure	0.48	<0.001	0.36	0.018
Body Surface Area				
Weight	0.99	<0.001	0.90	<0.001
Body Mass Index	0.82	<0.001	0.85	<0.001
Total Body Water	0.75	<0.001	0.84	<0.001
Fat mass	0.63	<0.001	0.71	<0.001
Skeletal muscle mass	0.72	<0.001	0.83	<0.001
Protein nitrogen appearance	0.46	<0.001	0.40	0.008
Total Energy Expenditure	0.56	<0.001	0.63	<0.001
Total Body Water				
Weight	0.70	<0.001	0.78	<0.001
Body Surface Area	0.75	<0.001	0.84	<0.001
Body Mass Index	0.46	<0.001	0.52	<0.001
Fat mass	0.07	>0.05	0.25	>0.05
Skeletal muscle mass	0.98	<0.001	0.99	<0.001
Protein nitrogen appearance	0.62	<0.001	0.40	0.008
Total Energy Expenditure	0.62	<0.001	0.65	<0.001