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Original Investigation

Scaling Hemodialysis Target Dose to Reflect Body Surface Area, Metabolic Activity, and Protein Catabolic Rate: A Prospective, Cross-sectional Study

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Background: Women and small men treated by hemodialysis (HD) have reduced survival. This may be due to use of total-body water (V) as the normalizing factor for dialysis dosing. In this study, we explored the equivalent dialysis dose that would be delivered using alternative scaling parameters matching the current recommended minimum Kt/V target of 1.2.

Study Design: Prospective cross-sectional study.

Setting & Participants: 1,500 HD patients on a thrice-weekly schedule, recruited across 5 different centers.

Predictors: Age, sex, weight, race/ethnicity, comorbid condition level, and employment status.

Outcomes: Kt was estimated by multiplying V by 1.2. Kt/body surface area (BSA), Kt/resting energy expenditure (REE), Kt/total energy expenditure (TEE) and Kt/normalized protein catabolic rate (nPCR) equivalent to a target Kt/V of 1.2 were then estimated by dividing Kt by the respective parameters.

Measurements: Anthropometry, HD adequacy details, and BSA were obtained by standard procedures. REE was estimated using a novel validated equation. TEE was calculated from physical activity data obtained using the Recent Physical Activity Questionnaire. nPCR was estimated using a standard formula.

Results: Mean BSA was 1.87 m^2; mean REE, 1,545 kcal/d; mean TEE, 1,841 kcal/d; and mean nPCR, 1.03 g/kg/d. For Kt/V of 1.2, there was a wide range of equivalent doses expressed as Kt/BSA, Kt/REE, Kt/TEE, and Kt/nPCR. The mean equivalent dose was lower in women for all 4 parameters ($P < 0.001$). Small men would also receive lower doses compared with larger men. Younger patients, those with low comorbidity, those employed, and those of South Asian race/ethnicity would receive significantly lower dialysis doses with current practice.

Limitations: Cross-sectional study; physical activity data collected by an activity questionnaire.

Conclusions: Current dosing practices may risk underdialysis in women, men of smaller body size, and specific subgroups of patients. Using BSA-, REE-, or TEE-based dialysis prescription would result in higher dose delivery in these patients.

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INDEX WORDS: Hemodialysis target dose; dialysis dosing; Kt/V; metabolism; energy expenditure; dialysis adequacy; body size; physical activity; sex differences; end-stage renal disease (ESRD).

A major objective of dialysis is the removal of metabolic waste products derived from nitrogen protein metabolism that accumulate in patients with chronic kidney failure. Hence, it has been suggested that the minimum dialysis requirement should relate to the rate of metabolic waste production and could be based on factors that reflect metabolic activity. However, Kt/V, a dimensionless parameter, where K is dialyzer urea clearance, t is dialysis time, and V is urea distribution volume (or Watson volume) equating to total-body water is how hemodialysis (HD) adequacy is measured at present.[1] The V variable is linearly related to body weight such that smaller persons will need a relatively lower dialysis dose compared with their larger counterparts to achieve the same Kt/V target. However, the relative concentration of metabolic wastes per unit of body weight might be greater in small people[2] because the ratio of lean muscle mass and visceral organs is relatively higher compared to body fat[3] and hence they risk being underdialyzed in relation to their metabolic needs.

In the Hemodialysis (HEMO) Study, results of a subgroup analysis suggested that women had a survival benefit when administered greater dialysis doses.[4] Others have also demonstrated an inverse relationship between mortality and body size in patients receiving HD.[5-8] There are a number of possible explanations for this phenomenon, one of which may be the prescription of HD based on V rather than on the patient's metabolic

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need. A number of alternate parameters for scaling dialysis dose, which better reflect metabolic activity, have been suggested.[9-11]

Body surface area (BSA) has been proposed as an alternative for scaling dialysis dose because normalizing the dose based on BSA will provide more dialysis for women than when using Kt/V.[12]

Because resting energy expenditure (REE) is the sum of all metabolic activities at rest, it might reflect the rate of metabolic waste production. Physical activity increases the urea generation rate in HD patients[13] and as such, may increase dialysis requirements. Total energy expenditure (TEE) encompasses both REE and energy expenditure from physical activity and hence may reflect total metabolic waste production. Our aim in this study was to investigate the equivalent dialysis dose that would be delivered using the mentioned parameters for scaling corresponding to the existing recommended minimum Kt/V target of 1.2. We also aimed to determine patient characteristics that would be associated with risk for inadequate delivered dialysis doses with existing dosing practice.

METHODS

Ethics Review

The study was approved by the North Wales Regional Ethics Committee (12/WA/0060). All participants gave informed written consent to take part.

Participants

Maintenance HD patients older than 18 years and with dialysis vintage longer than 3 months were recruited from participating renal units. Exclusion criteria included patients dialyzing for other than thrice-weekly frequency, those with amputated limbs, and those with no capacity to consent. Study information sheet, consent forms, and questionnaires were translated into Bengali and Urdu to facilitate data collection from non−English-speaking patients in participating units.

Study Protocol

Data Collection

The following data were collected from each patient:

1. Demographic data, including age, sex, dialysis vintage, and employment status.
2. Anthropometric data, including height and weight, were collected by direct measurement pre- and postdialysis. Predialysis weight was used to estimate Watson volume (V).
3. Comorbid condition data were collected by using a self-report questionnaire.[14] This scale is based on self-reporting of the presence and severity (grades 1-3) of 7 potential comorbid conditions: arthritis, cancer, diabetes, heart disease, lung disease, liver disease, and stroke. The maximum score is 21. High comorbidity is designated as a composite self-report comorbid condition score > 3.
4. Routine pre- and postdialysis biochemistry and hematology results were obtained from the local pathology system. Single-pool Kt/V was calculated using the Daugirdas formula.[15]
5. Physical activity data were obtained through the Recent Physical Activity Questionnaire. The questionnaire enquires about activities performed at home, work, and leisure time and also the time spent on each activity in the preceding 4 weeks. It has been validated against the doubly labeled water technique in the general population[16] and has been shown to be a reliable tool for estimation of energy expenditure in patients with chronic kidney disease.[17]

Estimation of Alternative Scaling Parameters

BSA using the Haycock formula[18] and Watson volume (V)[1] were derived from these measurements.

Normalized protein catabolic rate (nPCR) was estimated using the following formula:

$$\text{nPCR} = 5.42 \times \text{G}/\text{V} + 0.17$$

where G is urea generation rate and V is total-body water.

REE was estimated from a newer predictive equation that was derived and validated in a cohort of HD patients.[19] This disease-specific equation was found to be at least as accurate, if not more, compared with previous equations derived from nondialysis populations but associated with less bias. The newer equation follows:

$$\begin{aligned}\text{REE} = &-2.497 \times \text{Age (years)} \times \text{Factor}_{\text{age}} + 0.011 \\ &\times \text{Height}^{2.023}\ (\text{cm}) + 83.573 \times \text{Weight}^{0.6291}\ (\text{kg}) \\ &+ 68.171 \times \text{Factor}_{\text{sex}}\end{aligned}$$

where $\text{Factor}_{\text{age}}$ is 0 if younger than 65 years and 1 if 65 years or older and $\text{Factor}_{\text{sex}}$ is 0 if female and 1 if male.

Concerning physical activity data, each reported activity was assigned a metabolic equivalent task (MET) value as per the Compendium of Physical Activities.[20] Sleep time per day was assumed to be 8 hours and any unreported time during the day was assumed as the time performing light activities at home as per the published literature.[17] Total daily MET value was calculated by summation of each individual MET value from the activities. A mean daily MET value was then calculated by dividing total daily MET by 24 hours.[17]

TEE was estimated from the following equation:

$$\text{TEE} = \text{REE} \times \text{Mean daily MET}$$

Scaling of Dialysis Dose

The NKF-KDOQI (National Kidney Foundation−Kidney Disease Outcomes Quality Initiative) HD adequacy guideline recommends a minimum single-pool Kt/V of 1.2 per dialysis session for a thrice-weekly schedule.[21] Hence, in order to compare minimum dialysis targets using alternative scaling parameters, Kt was calculated as below.

$$\text{Kt} = 1.2 \times \text{V}$$

Hypothetical target values of Kt/BSA, Kt/REE, Kt/TEE, and Kt/nPCR for each patient were calculated by dividing Kt by the observed value for each parameter.

Statistical Analysis

Statistical analysis was carried out using SPSS, version 19 (SPSS Software; IBM Corp). Normally distributed data are presented as mean ± standard deviation. The significance of differences between mean values was determined by *t* test. The significance of differences between multiple group mean values was assessed by analysis of variance (ANOVA), with differences between individual groups being assessed using the post hoc Bonferroni correction for multiple analyses, with $P < 0.05$ being assumed to indicate statistical significance. Multivariable regression models to examine predictors of Kt/TEE were