Total Body Protein Mass: Validation of Total Body Potassium Prediction Model in Children and Adolescents

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ABSTRACT Protein is an important body component for monitoring growth, development, and nutritional status. We previously developed a total body potassium (TBK, in mmol) and bone mineral (Mo, in kg) model for predicting total body protein (TBPro, in kg) in adults (TBPro = 0.00252 × TBK + 0.732 × Mo). However, the applicability of the TBK-Mo model for children is unknown. The study aims were to develop a TBK-independent 6-component (6-C) TBPro approach as the criterion, and then to validate the TBK-Mo model in children. The following measurements were made in adolescents and children (n = 62, 38 boys and 24 girls, aged 5–17 y): body weight (BW, in kg), body volume (BV, in liters) by air displacement plethysmography, total body water (TBW, in kg) by 3H2O dilution, Mo by dual-energy X-ray absorptiometry, and TBK by whole-body counting. A 6-C model was derived as TBPro = 2.922 × BW − 0.301 × TBW − 2.039 × Mo − 2.632 × BV. The TBPro estimates did not differ between the 6-C and TBK-Mo models (mean ± SD, 0.20 ± 0.86 kg). There was a significant correlation between TBPro by the 6-C and TBK-Mo models (r = 0.94, P < 0.001). Bland-Altman analysis indicated that the differences between TBPro by 6-C and TBK-Mo models were not significantly correlated with the mean TBPro estimates by the 2 models (r = 0.032, P > 0.05). The TBK-Mo model can thus be used to estimate TBPro in healthy adults, adolescents, and children >5 y old. J. Nutr. 136: 1032–1036, 2006.

KEY WORDS: nutritional assessment • body composition • bone mineral • whole-body counting

Protein is a body component affected by many physiological and pathological processes, including growth, development, nutritional status, physical activity, and diseases. Alterations in protein can, in turn, serve as a biomarker of relevant physiological and pathological conditions.

Although total body nitrogen (TBN)1 measured by in vivo neutron activation (IVNA) analysis can be applied as the criterion for total body protein (TBPro) estimation, application is limited, especially for measurements in children and adolescents, due to radiation exposure (1). Therefore, the estimation of TBPro in healthy children and adolescents remains impractical or difficult, and there are only a few reports in the literature regarding protein mass in pediatrics (2–4).

We recently reported a model for predicting TBPro (in kg) from total body potassium (TBK, in mmol) and bone mineral (Mo, in kg): TBPro = 0.00252 × TBK + 0.732 × Mo (5). This model is based on observations that both potassium and protein distribute mainly within the intracellular compartment and that intracellular potassium and protein concentrations are relatively stable. In addition to this physiological model, we developed an empirical TBPro prediction method from fat-free mass (FFM, in kg) in healthy adults, TBPro = 0.199 × FFM − 0.45 (6).

Although the TBK-Mo TBPro model was validated in healthy adults and patients with several chronic diseases (5,7), it is not known whether the model is applicable in pediatric subjects. The aims of the present study were to first develop a TBK-independent TBPro model as a practical reference for estimating TBPro mass, and then to evaluate the applicability of the TBK-Mo models in children and adolescents. In addition, we evaluated the applicability of the adult FFM TBPro method in children and adolescents.

SUBJECTS AND METHODS

Six-component TBPro model

Total body nitrogen measured by IVNA is currently the criterion for TBPro estimation (1). However, IVNA is inappropriate for use in children and adolescents because of the associated radiation exposure (0.26 mSv). A 6-component (6-C) approach was thus developed and applied as a practical criterion in the present study. Body weight (BW) can be expressed as the sum of fat, total body water (TBW), TBPro, Mo, soft-tissue mineral (Ms), and glycogen (Gly) (8). Accordingly,

\[ BW = \text{fat} + \text{TBW} + \text{TBPro} + \text{Mo} + \text{Ms} + \text{Gly}. \]  

[1]

A 6-C TBPro model was derived from Eq. 1,

\[ \text{TBPro} = \text{BW} - \text{fat} - \text{TBW} - \text{Mo} - \text{Ms} - \text{Gly}. \]  

[2]

All of the major components in Eq. 2 are now measurable or calculable. Fat mass can be measured by a multicompartment model: fat
A single prediction equation was then calculated for all subjects pooled:

\[
TBPro = 0.0301 \times TBK + 0.34
\]

with \( r = 0.96, P < 0.001, \) SEE = 0.85 kg; \( n = 62 \) (Fig. 1A). In addition, a multiple regression analysis in which TBPro was the dependent variable and TBK was the major independent variable showed that age was not associated with TBPro.
Total body protein mass

**TBK-Mo model.** Total body protein mass calculated by the 6-C model was 7.76 ± 2.94 kg in boys, 5.86 ± 1.47 kg in girls, and 7.02 ± 2.98 kg in the combined sample subjects. There were significant correlations observed for TBPro estimated by the 6-C model and the TBK-Mo model for each gender separately and for all subjects (boys, r = 0.97; girls, r = 0.93; and all subjects pooled, r = 0.94; all P < 0.001; Table 2, Fig. 1B). TBPro estimates did not differ between the 2 models (7.02 ± 2.98 kg by the 6-C model vs. 6.82 ± 2.95 kg by the TBK-Mo model, with mean difference 0.20 ± 0.86 kg; P = 0.074).

Bland-Altman analysis indicated that the differences between TBPro by the 6-C model and the TBK-Mo model were not significantly correlated with the mean TBPro estimates by the 2 models for all subjects pooled (r = 0.032, P > 0.05) (Fig. 2A).

**FFM Model.** There were significant correlations for TBPro estimated by the 6-C model and the FFM model for each gender separately and for all subjects (boys, r = 0.97; girls, r = 0.94; and all subjects pooled, r = 0.94; all P < 0.001; Table 2). TBPro estimates did not differ between the 2 models (7.02 ± 2.98 kg by the 6-C model vs. 6.85 ± 2.75 kg by the FFM model, with mean differences 0.17 ± 0.82 kg; P = 0.10). However, Bland-Altman analysis indicated that the differences between TBPro by the 6-C model and FFM model were significantly correlated with the mean TBPro estimates by the 2 models for all subjects pooled (r = 0.28, P < 0.05) (Fig. 2B).

**DISCUSSION**

Although there is considerable interest in estimating protein mass during growth and development, there are only a few previous reports of TBPro mass in pediatrics (2–4,23). The main finding of the present study is that the TBK-Mo model derived in adults is applicable in children and adolescents. Therefore, the TBK-Mo model will allow investigators to predict TBPro in both healthy adults and children in a non-invasive manner.

**Six-component TBPro Model.** Because of its unique role as an essential element of protein, the assessment of total body nitrogen by IVNA has been used classically as the criterion for measurement of total body protein mass. However, IVNA is not advised for healthy children and adolescents, and is prohibited for these subjects in the United States due to radiation exposure.

In recent years, multicomponent models were developed for measuring TBPro mass. Siconolfi and colleagues (24) first estimated TBPro based on a 3-component (3-C) model in...
TABLE 2

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Model</th>
<th>Total body protein mass, kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boys</td>
<td>38</td>
<td>6-C</td>
<td>7.76 ± 2.94</td>
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<tr>
<td></td>
<td></td>
<td>TBK-Mo</td>
<td>7.32 ± 3.00</td>
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<tr>
<td></td>
<td></td>
<td>FFM</td>
<td>7.37 ± 2.79</td>
</tr>
<tr>
<td>Girls</td>
<td>24</td>
<td>6-C</td>
<td>5.86 ± 1.47</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TBK-Mo</td>
<td>6.05 ± 1.47</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FFM</td>
<td>6.03 ± 1.38</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
<td>6-C</td>
<td>7.02 ± 2.98</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TBK-Mo</td>
<td>6.82 ± 2.95</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FFM</td>
<td>6.85 ± 2.75</td>
</tr>
</tbody>
</table>

1 Values are means ± SD.

which TBPro could be assessed by using estimates of TBW, body volume, and body weight. However, these authors did not provide a complete equation for deriving TBPro and we were thus unable to evaluate their 3-C model in the current study.

The 3-C model concept advanced by Siconolfi et al. (24) was extended in later studies. Fuller et al. (25) developed a 4-component (4-C) TBPro model: \( \text{TBPro} = 3.65 \times \text{BW} - 0.290 \times \text{TBW} - 2.734 \times \text{BMC} - 2.74 \times \text{BV} \). In the present study a 6-C model for estimating TBPro (i.e., Eq. 3) was developed.

The multicomponent model approach provides an alternative method for making estimates of TBPro for body composition laboratories in which IVNA or whole-body \(^{40}\)K counters are unavailable. Unfortunately, we were unable to evaluate all of the existing multicomponent models, including 3-C, 4-C, and 6-C models against the IVNA-TBN method in children and adolescents.

**TBK-Mo TBPro model.** Both potassium and protein are distributed primarily within the intracellular compartment. The validated TBK-Mo model developed from healthy adults is based on relatively stable intracellular potassium and protein concentrations (5,26). If the intracellular potassium and protein concentrations in children and adolescents are the same as those observed in adults, the TBK-Mo model should also be applicable for use in pediatrics.

Ellis et al. (4) used a set of assumptions to predict TBPro from TBK: 150 mmol/L for the intracellular potassium concentration, 4 mmol/L for the extracellular potassium concentration, 0.16 kg N/kg protein, and 2.17 mmol K/g N for lean tissue. Based on these assumptions, a TBPro prediction equation was derived by Ellis et al. (4) from TBK: TBPro \((kg) = \{[(1/0.16) \times (1/2.17)] \times 10^{-3}\} \times \text{TBK} = 0.00288 \times \text{TBK} \).

Our results confirm that TBPro and TBK are correlated in both healthy boys and girls. The slopes and intercepts of the empirical derived equations for TBPro vs. TBK were 0.0030 and 0.71 for boys, and 0.0030 and 0.25 for girls. These observations are similar to Ellis’s empirical prediction formula for adult women with a slope of 0.00317 and an intercept of 0.95 (27). This observation supports the applicability of the TBK-Mo model in children and adolescents.

As a theoretically derived model, the TBK-Mo model should work well at different body composition laboratories, and in both adults and children. We recently evaluated the TBK-Mo model in adult subjects studied in New York and Melbourne. The TBPro estimates did not differ in the New York and Melbourne studies between the IVNA criterion and the TBK-Mo model in healthy adults and patients with AIDS, liver disease, chronic renal failure, and growth hormone deficiency (5,7). The present study shows the applicability of the adult TBK-Mo model in healthy children and adolescents. However, we do not yet know whether the TBK-Mo model can be applied reliably in children with acute and chronic diseases. In general, the TBK-Mo model could be applied in patients with disease if the intracellular ratio of potassium to protein remained stable and unchanged from that in healthy subjects. However, this deduction warrants evaluation in future studies.

**FFM TBPro model.** DXA can measure body fat and fat-free mass, and protein is one of the major components of FFM. Clinical studies designed to measure TBPro will benefit if TBPro can be measured using DXA because DXA are now widely available and relatively less expensive to purchase. Because the fraction of FFM as protein is often assumed to be stable, we derived an empirical equation for predicting TBPro from FFM with DXA measurements (6). Although the mean fractions of FFM as protein do not differ between healthy groups, there was a moderate variation in the range of TBPro/FFM within each group. For example, the ratios of TBPro to FFM were 0.194 ± 0.017 with a CV of 8.8% for healthy men and 0.186 ± 0.025 with a CV of 13.4% for healthy women (7). In the children and adolescents in the present study, the ratio of TBPro to FFM was 0.197 ± 0.024 with a CV of 12.0%. Therefore, FFM alone may not be a good predictor of TBPro mass in adults and children.
Study limitations and future directions. Although the mean difference in TBPro for the population of boys and girls tested was ~0, there was a relatively large discrepancy in estimates by the TBK-Mo and 6-C models for a few individuals (Fig. 2A). However, we did not find any connection between the discrepancy and biological factors such as age, gender, body weight, and adiposity. Therefore, these discrepancies are likely caused by measurement errors.

With the TBK-Mo prediction model, whole-body $^{40}$K counting provides a noninvasive approach for estimating TBPro that is applicable in a wide range of subjects including healthy children and adults, and patients with selected chronic diseases. However, the prohibitive construction costs of whole-body counters limit their widespread application, so that there are now only ~30 whole-body counters throughout the world.

It is not known whether our TBK-Mo model gives accurate estimates in newborns. Further studies of newborns and children <5 y old are warranted to explore the associations between TBK and TBPro. This future research has the potential of providing a noninvasive TBPro prediction method for newborns. Further studies are also required to evaluate the TBK-Mo model in pediatric patients with chronic diseases.

In conclusion, we previously developed a TBPro prediction model from TBK and Mo in healthy adults ($\text{TBPro} = 0.00252 \times \text{TBK} + 0.732 \times \text{Mo}$). The present study provides evidence that the same model can be used to estimate TBPro in healthy pediatric subjects ≥5 y old.

LITERATURE CITED