Body Composition in Children on Peritoneal Dialysis

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Dual-energy X-ray absorptiometry (DEXA) can be used to evaluate total-body bone mineral content (BMC), bone mineral density (BMD), fat-free mass (FFM), and fat body mass (FBM), which are all frequently affected in patients (PD) on peritoneal dialysis. We used DEXA to evaluate body composition in children on PD and to establish whether relationships existed with nutrition status, dialytic parameters, and biochemical data.

We evaluated 20 PD patients (12 boys, 8 girls). The mean age of the patients was 5.84 years (range: 0.16 – 14.66 years). We carried out DEXA, anthropometry (weight/age, height/age, and body mass index), and measurements of dietary intake (protein, energy, calcium, and phosphorus), nitrogen balance (NB), dialysis dose (Kt/V), peritoneal equilibrium test (PET), and plasma calcium, phosphorus, and bicarbonate at months 1 and 6 of the study. Energy intake was prescribed according to the United States Recommended Dietary Allowances, *and Kt/V and daily protein intake (DPI) according to the Dialysis Outcomes Quality Initiative (DOQI) guidelines.*

In the patients, BMD increased to 0.769 ± 0.174 g/cm^2 from 0.747 ± 0.166 g/cm^2 (p < 0.05), and BMC increased to 680.3 ± 666.1 g from 632.6 ± 597.5 g (p < 0.01). The mean BMD Z score for patients older than 4 years (n = 11) was –0.69 at month 1, with a significant increase to –0.35 at month 6. The FBM and FFM increased, but without reaching statistical significance. At months 1 and 6, the DPI was 144.3% and 129.9% respectively (p = nonsignificant) and showed a negative correlation with BMD, BMC, and FFM (p < 0.05). Comparing DPI to plasma bicarbonate showed a negative correlation at month 1 (p < 0.05). Negative correlations were also found between NB and the parameters BMD, FBM, and FFM (p < 0.05).

All patients showed a positive NB. No correlation was found between DEXA and anthropometric measurements, energy intake, serum calcium, serum phosphorus, or Kt/V. Dialysate-to-plasma creatinine from the PET showed a negative correlation with BMD and FFM (p < 0.05).

In terms of positive NB and controlled Kt/V, we observed an increase in bone mineralization within the 6 months of follow-up. A high protein intake seems to negatively affect acid–base status, bone mineralization, and FFM.

Key words
Dual-energy X-ray absorptiometry, bone mineral content, bone mineral density, children

Introduction

In children with chronic renal failure (CRF) treated conservatively with dialysis, alterations of nutrition, metabolism, and fluid homeostasis may occur, critically affecting the acute and chronic well-being of the patients (1). In pediatric dialysis, malnutrition has been considered a major determinant of morbidity and mortality, and overcoming malnutrition remains one of the most important goals in the management of children on chronic peritoneal dialysis (PD) therapy (2,3).

Nutrition status can be monitored by dual-energy X-ray absorptiometry (DEXA), a noninvasive method of estimating bone mineral content and fat and lean body mass. Because of their varying density, bone, lean tissue, and fat attenuate the energy beams differentially. Therefore, by using dual-energy beams, it is possible to solve for three tissue compartments. Dual-energy X-ray absorptiometry is becoming increasingly available for clinical and research use. Radiation exposure in DEXA is extremely low (0.3 cGy), and whole-body estimates of body composition for infants, children, and adolescents can be obtained in less than 5 minutes (4).

Although the growing evidence about the critical meaning of nutrition in the long-term prognosis for

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dialyzed children is well documented, management for optimal nutrition in children on PD requires strict dietary prescription (energy, proteins); dietary recall; monthly weight, length, head circumference (up to 2 years), mid-arm circumference, skin-fold thickness measurements; physical examination; and tests of biochemical and hematologic parameters and dialysis adequacy (5,6).

In the present prospective study, we used DEXA to evaluate the nutrition status of children on PD. We studied bone mineral content and fat and lean body mass; measured daily protein intake, daily energy intake, nitrogen balance, and dialytic parameters; and studied the correlations between those variables.

Patients and methods

We performed prospective DEXA measurements in 20 stable PD patients, all of them being treated as outpatients at the Nephrology and Nutrition divisions of Luis Calvo Mackenna Children's Hospital. The group included 12 boys and 8 girls whose mean age was 5.84 years (range: 0.16 – 14.66 years) and whose mean duration on PD was 11 months (range: 2 – 46 months). Underlying renal disorders included renal dysplasia (n = 10), reflux nephropathy (n = 3), hemolytic uremic syndrome (n = 1), obstructive uropathy (n = 1), chronic glomerulonephritis (n = 4), and an unknown disorder (n = 1). At the start of the study, 11 patients were on continuous ambulatory PD, and 9 were on automated PD. Four patients had no residual renal function. Patients with fever, infections, nephrotic syndrome, gastrointestinal absorption disturbances, steroid treatments, endocrine diseases, genetic syndromes, and compliance or behavioral disturbances were excluded. The study protocol was evaluated and approved by the ethics committee of the hospital, and written informed consent was obtained from all parents before the study was initiated.

Each month, we evaluated anthropometry, dietary intake, nitrogen balance, serum bicarbonate, and dialysis dose. Whole-body DEXA was performed every 6 months, and a peritoneal equilibration test (PET) was performed at the start of the study.

Whole-body DEXA

The DEXA examinations were performed using a Lunar DPX-L 7660 densitometer (Lunar Radiation Corporation, Madison, WI, U.S.A.). We obtained bone mineral content (BMC), lean body mass (LBM), and fat body mass (FBM) in kilograms from the DEXA by using pediatric software for children with a weight less than 30 kg. All measurements were performed and analyzed by the same investigator.

Anthropometry

With the patient in minimum clothing, weight was measured on a mechanical Seca scale (Seca Corporation, Hamburg, Germany) of 0.1 kg precision and 150 kg capacity. All children on PD were weighed with a known dialysate volume in the peritoneal cavity, and the weight of the solution was deducted from the observed weight. Height was measured with 1 mm precision. All measurements were performed by the same investigator.

Dietary intake

Once each month, 24-hour-recall and a food frequency questionnaire were used to estimate intake of energy, macronutrients, and micronutrients. Usual portions were obtained from earlier studies plus food weighing during the interview when necessary. A Chilean food database stored in an Excel spreadsheet (Microsoft Corporation, Redmond, WA, U.S.A.) was used for the calculation. A nutritionist obtained the information. Food intake adequacy was compared with Dialysis Outcomes Quality Initiative (DOQI) guidelines for energy and protein requirements (5). Calcium and phosphorus intakes were compared with U.S. *Recommended Dietary Allowances* [RDA (7)].

Nitrogen balance studies

Blood samples and 24-hour dialysate and urine were collected on an outpatient basis. To avoid generation of urea secondary to bacterial activity, thimerosal was added to urine and dialysate samples. All samples obtained under noncompliance conditions were discarded. Total protein and albumin (turbidimetric assay) were measured in plasma, urine, and dialysate.

Dialysis dose

We calculated weekly Kt/V urea, both peritoneal and residual using the equation

$$\text{Kt/V urea} = [\text{24-h dialysate volume (L)} \times \text{D/P urea} \times 7] / [0.60 \times \text{weight (kg)}]$$

Dialysis dose was prescribed to meet a minimum weekly Kt/V of 2 as specified in the DOQI guidelines

(8), but no attempt was made to define a maximum Kt/V value in our patients.

Peritoneal equilibration test
The PET was performed according to a previously published protocol (9,10). Briefly, a standardized volume (1100 mL/m^2 body surface area) of Dianeal 2.5% solution (Baxter Healthcare SA, Castlebar, Ireland) was instilled into the peritoneal cavity, and dialysate samples were taken from the overnight exchange bag at 0, 120, and 240 minutes. A serum sample was taken at 120 minutes. Results were analyzed for the dialysate-to-plasma (D/P) creatinine and final-to-initial dialysate (D/D_0) glucose equilibration ratios at 4 hours, and each patient was categorized as a high, high-average, low-average, or low transporter according to pediatric values published by Warady *et al.* (9).

Biochemical measurements
We obtained plasma measurements of bicarbonate (mEq/L, by bromcresol blue), phosphate (mg/dL, by phosphomolybdate complex colorimetry at 340 nm), calcium (by the cresolphthalein complexone method), alkaline phosphatase (by 4-nitrophenyl phosphate), and hemoglobin (by cyanmethemoglobin).

Statistical analysis
Means, standard deviations, correlation coefficients, and *t*-tests were performed using Excel 5.0 (Microsoft Corporation) and Statistica for Windows, version 4.5 (StatSoft, Tulsa, OK, U.S.A.). Values of $p < 0.05$ were accepted as statistically significant.

Results

Body composition
Between the start of the protocol and month 6, the 20 patients evaluated by DEXA showed an increase in BMD to 0.769 ± 0.174 g/cm^2 from 0.747 ± 0.166 g/cm^2, $p < 0.05$. The BMC in the group also increased to 680.3 ± 666.1 g from 632.6 ± 597.5 g, $p < 0.01$.

The mean BMD Z score at the beginning of the study in patients older than 4 years ($n = 11$) was –0.69 (range: 0.3 to –2.2). The mean BMD Z score for those 11 patients showed a significant increase to –0.35 at month 6. The FBM and FFM also increased, but without reaching statistical significance.

The patients' DPI showed a negative correlation with BMD, BMC, and FFM ($p < 0.05$; Table I).

Anthropometry
The mean Z score for height/age was –2.17 (range: –4.75 to –0.3) at the start of the study, and –2.14 (range: –3.98 to –0.2) at month 6 [p = nonsignificant (NS)]. The Z score for weight/age was –1.6 (range: –3.15 to –0.39) and –1.94 (range: –2.25 to 0.39) at the same time periods (also p = NS).

Dietary intake
Most of the patients showed a caloric intake above the RDA recommendations (mean values: 115.11% ± 37.21% at month 1 and 108.16% ± 35.84% at month 6). In addition, the patients' DPI exceeded the DOQI (5) recommendations (mean values: 144.77% ± 48.74% at month 1 and 140.85% ± 52.13% at month 6, p = NS). Table II shows other dietary intake values.

The patients' mean DPI was 3.32 ± 1.6 g/kg/day at the beginning of the study and 3.3 ± 1.3 g/kg/day at month 6 (p = NS). A comparison of DPI versus bicarbonate showed a negative correlation at the beginning of the study ($r = –0.46$, $p < 0.05$), but only a tendency toward a negative correlation at month 6.

Nitrogen balance studies
All patients showed a positive NB initially and at month 6 of follow-up. Initially, mean DPI was 3.32 ± 1.05 g/kg/day, and mean daily protein losses were 1.19 ± 0.47 g/kg/day, for a mean net protein balance of +2.1 g/kg/day. At month 6 of the study, mean DPI was 3.30 ± 1.7 g/kg/day, and mean daily protein losses were 1.7 ± 0.47 g/kg/day, for a net protein balance of +1.6 g/kg/day. We observed no difference in the protein balance between month 1 and month 6 of the study. We found a negative correlation between BN and the parameters BMD, FBM, and FFM ($r = –0.8$, $r = –0.55$, and $r = –0.7$ respectively; $p < 0.05$).

Dialysis dose
The mean weekly total Kt/V urea was 3.31 ± 1.1 at the beginning of the study and 2.57 ± 1.53 at month 6. The mean weekly peritoneal and residual Kt/V urea values were, respectively, 1.7 ± 0.81 and 1.5 ± 1.24 at the beginning of the study, and 1.6 ± 0.58 and 1.5 ± 1.18 at month 6.

Peritoneal equilibration test
The mean 4-hour D/P creatinine was 0.78 ± 0.02 initially and 0.74 ± 0.13 at month 6 (p = NS). The mean

TABLE I Evaluation of body composition by dual-energy X-ray absorptiometry in 20 children during peritoneal dialysis

	Month 1	*Month 6*	p *Value*
BMC (g)	632.6 (32–2066)	680.3 (118–2227)	<0.05
BMD (g/cm^2)	0.747 (0.504–1.097)	0.769 (0.575–1.031)	<0.05
FBM (g)	3336 (516–12471)	3375.2 (822–11833)	NS
FFM (g)	15426 (4276–40943)	16405.6 (5466–36509)	NS
FBM (%)	17.3 (5.5–35.5)	14.8 (6.6–24.5)	NS
FFM (%)	80.0 (63.5–91.8)	82.2 (72.5–90.9)	NS

BMC = bone mineral content; BMD = bone mineral density; FBM = fat body mass; FFM = fat-free mass.

TABLE II Food intake in 20 children on peritoneal dialysis

	Month 1	*Month 6*	p *Value*
% Protein requirement (DOQI)	144.77±48.74	140.85±52.13	NS
% Energy requirement (RDA)	115.11±37.21	108.16±35.84	NS
% Calcium requirement (RDA)	88.23±25.91	94.6±49.05	NS
% Phosphorus requirement (RDA)	90.57±34.15	99.96±51.90	NS

DOQI = Dialysis Outcomes Quality Initiative guidelines; RDA = United States *Recommended Dietary Allowances.*

D/D_0 glucose was 0.33 ± 0.11 and 0.34 ± 0.08 for the same observation periods (p = NS). The mean 4-hour D/P creatinine showed a negative correlation with BMD and FFM ($p < 0.05$).

Biochemical measurements

Table III lists values for serum concentrations of creatinine, calcium, phosphorus, and intact parathyroid hormone, and for alkaline phosphatase activity. No correlations were found between BMD, BMC, LBM, or FBM and weight/age, height/age, body mass index, energy intake, or serum concentrations of calcium or phosphorus.

Discussion

Body composition has been measured by whole-body DEXA in a number of wasting diseases (including HIV, cystic fibrosis, pulmonary disease, CRF, and renal transplantation), but experiences in children on PD are scarce (11–14). Historically, the pediatric dialysis population has been characterized by progressive growth retardation. That trend is reflected in the 2001 Annual Report of the North American Pediatric Renal Transplant Cooperative Study (16), in which the mean height standard deviation score (SDS) of the PD patients was –1.69 at baseline and –1.92 at 24 months after initiation of PD.

TABLE III Serum biochemistry values in children on peritoneal dialysis

	Month 1	*Month 6*	p *Value*
pH	7.36 (7.23–7.48)	7.35 (7.29–7.47)	NS
HCO_3 (mmol/L)	24.3 (17–33.9)	24.7 (18.2–29)	NS
Creatinine (mg/dL)	4.25 (1.6–11.6)	3.52 (1.2–11.4)	NS
BUN (mg/dL)	43 (11–80)	51 (19–72)	NS
Ca (mg/dL)	10.2 (6.7–11.3)	10.1 (5.9–11.7)	NS
PO_4 (mg/dL)	4.7 (2.9–7.8)	4.5 (3.4–6.6)	NS
ALP (U/L)	599 (235–1605)	740 (266–1810)	NS
Albumin(g/dL)	3.5 (2.7–4)	3.6 (3–4.4)	NS
PTH (pg/dL)	158 (1.5–2500)	323.5 (1–1294)	NS
Ferritin (ng/mL)	201 (34.4–951)	135 (10–677)	NS
Hct (%)	29.8 (22–38)	33 (12–40.8)	NS

BUN = blood urea nitrogen; ALP = alkaline phosphatase; PTH = parathyroid hormone; Hct = hematocrit.

In renal failure, growth is acknowledged to be influenced by a variety of endocrine, nutritional, and metabolic factors. The impact of dialysis dose on growth remains undetermined (15,16). Thus, to obtain a more detailed nutrition assessment and follow-up in CRF patients, it could well be imagined that DEXA could be used as a complementary method of assessing body composition, as suggested by the ad hoc European committee on the assessment of growth and nutrition status in children on chronic PD (6).

The reproducibility of DEXA measurements is excellent: 1.2% for total fat-free and fat mass, and 0.5% for bone mineral content. The precision is 1.0% and 2.0% for FFM and fat mass respectively. The fat mass derived from DEXA measurements correlates well with the fat mass determined by hydrodensitometry and total-body ^{40}K. A limitation of DEXA is that it does not measure total body water (TBW); instead, an assumption is made that TBW is 73.2% of FFM. However, that assumption could result in an underestimation of protein mass in underhydrated individuals and an overestimation of protein mass in overhydrated individuals (4,11).

A limitation of the present study is a lack of local reference values. As a result, we had to compare our results with the NHANES (National Health and Nutrition Examination Survey) curves with SDS for BMD for whole-body DEXA for children under 4 years of age (17). The same is true for FFM and FBM. That bias must be taken in account when the data presented here are discussed.

In terms of controlled dialysis and nutrition, we observed a significant increase in bone mineralization: at 6 months of follow-up, BMD had risen to 0.769 ± 0.174 g/cm^2 from 0.747 ± 0.166 g/cm^2, and BMC had risen to 680.3 ± 666.1 g from 632.6 ± 597.5 g. The BMD Z score is available from 4 years of age, and, in our patients older than 4 years (n = 11), we found a significant increase to –0.35 from –0.69 (range: 0.3 to –2.2) during the observation period. An increase in FBM and FFM that did not reach statistical significance was also observed.

Most of the patients showed a daily caloric intake higher than the RDA (mean of $115.11\% \pm 37.21\%$ for energy and $108.16\% \pm 35.84\%$ for protein). Values for DPI were higher than the DOQI recommendations ($144.77\% \pm 8.74\%$ at month 1 and $140.85\% \pm 52.13\%$ at month 6, p = NS). But despite the high dietary intake, we did not see catch-up growth in all patients. Recent reports have identified certain factors that could interfere with control of protein turnover in CRF patients and therefore interfere with growth. Those factors include acidosis, inflammation, and resistance to anabolic hormones (18).

Schaefer *et al.*, (19) observed a significant negative correlation between delta height SDS and the creatinine equilibration rate in the initial study PET ($r = –0.31$, $p < 0.05$). Multiple regression analysis confirmed a negative effect of the high transport state (partial $r^2 = 0.07$) on delta height SDS. In the present study, it is interesting that we found a negative correlation between the mean 4-hour D/P creatinine and both the BMD and FFM parameters ($p < 0.05$), suggesting for the first time that a high transport state is an adverse risk factor for nutrition status in children on PD.

Conclusions

In terms of positive NB and controlled Kt/V, we observed an increase in bone mineralization within a 6-month period of follow-up. A high protein intake seems to negatively affect acid–base status, bone mineralization, and FFM. We also observed that a high transport state, as measured by 4-hour D/P creatinine, may adversely affect the fat and mineral content of the body.

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