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Protein losses in children on continuous cycler peritoneal dialysis

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Abstract. Peritoneal dialysis can result in significant protein losses through the dialysate effluent. Although protein loss in chronic ambulatory peritoneal dialysis has been examined, it has not been extensively studied in patients on continuous cycler peritoneal dialysis. Such losses can contribute to protein calorie malnutrition, especially in infants and children, many of whom are on continuous cycler peritoneal dialysis. We measured protein loss during continuous cycler peritoneal dialysis in patients ranging in age from 2 months to 18 years. There was an inverse correlation between body surface area and peritoneal protein loss, expressed both as milligrams of protein per kilogram body weight per day ($P < 0.000$l) and as milligrams of protein per meter square body surface area per day ($P < 0.05$). Peritoneal fluid protein losses in patients greater than 50 kg were similiar to those previously reported in adults treated with chronic ambulatory peritoneal dialysis. In contrast, infants had nearly twofold greater peritoneal protein losses per meter square body surface area than older children weighing more than 50 kg. Such protein losses in infants impair normal growth and may contribute to permanent loss of growth potential. Infants on peritoneal dialysis require early and aggressive nutritional supplementation with higher caloric and protein intake to compensate for such dialysate protein losses and maximize growth.

Key words: Peritoneal dialysis – Protein loss – Anthropometric measurements

Introduction

Peritoneal dialysis is widely accepted as a modality for renal replacement therapy and is usually delivered as chronic ambulatory peritoneal dialysis (CAPD) or continuous cycler peritoneal dialysis (CCPD) [1–4]. One drawback of peritoneal dialysis is the associated loss of significant amounts of body protein into the dialysate effluent [5–10]. The peritoneal protein losses in adults on CAPD are in the range of 6.9–13.3 g per day with an average of 9.4 g per day (134 mg/kg per day) [10–12]. In contrast, peritoneal protein losses in children on CAPD can be at least twice as high as in adults, when considered on a milligram per kilogram basis [5–8,13]. Protein losses in children on CCPD have only been studied in children older than 10 years and not in infants [14]. Given the popularity of CCPD in pediatric dialysis programs, the associated protein loss and its potential role in contributing to protein calorie malnutrition, knowledge of the magnitude of protein loss is clinically relevant. The poor nutritional intake common to many dialysis patients exacerbates protein calorie malnutrition and contributes to impaired growth and possibly to impaired development [15,16]. The purpose of this study is to examine the magnitude of peritoneal protein losses in all pediatric patients on CCPD.

Patients and methods

Six infants (2–24 months) and nineteen older children (6–18 years) from our peritoneal dialysis program were enrolled in our study. All infants were initiated on dialysis prior to 6 months of age. The etiologies of end-stage renal failure were obstructive uropathy in 6 patients, hypodysplasia in 4 patients, polycystic kidneys in 5 patients, focal segmental glomerulosclerosis in 3 patients, bilateral cortical necrosis in 2 patients, systemic lupus erythematosus in 1 patient, hemolytic uremic syndrome in 1 patient, Henoch-Schonlein purpura in 1 patient, Drash syndrome in 1 patient, and unknown in 1 patient.

All peritoneal dialysis was performed at night during sleep using dialysate fluid of various dextrose concentrations (Dianeal 1.5%, 2.5%, and 4.25% glucose concentrations) instilled into the peritoneal cavity via a surgically implanted, curled Tenckhoff catheter. The daily CCPD prescription involved using 36.7 ± 0.5 ml/kg per exchange volume with a daily total of 9.3 ± 0.3 cycles in 19 children (6–18 years) and 34.5 ± 0.8 ml/kg per exchange volume with a daily total of 9.6 ± 0.3 cycles in 6 infants (2–24 months). All CCPD patients had an average of 11.3 ± 1 ml/kg of fresh dialysate in their peritoneal cavity (day

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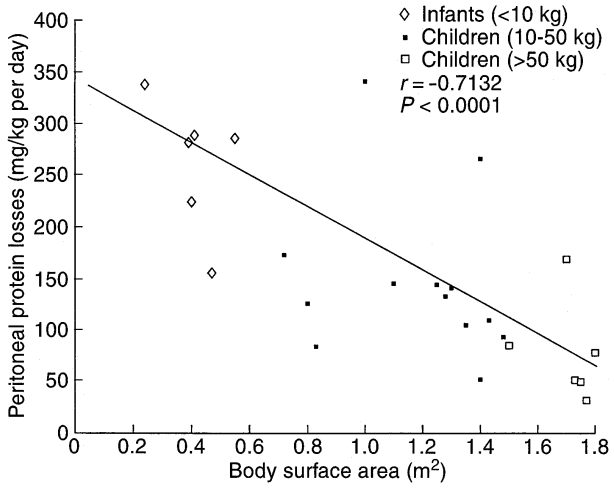

Fig. 1 Peritoneal protein loss (mg/kg per day) versus body surface area. Each point represents the mean of at least two 24 h dialysate fluid collections per patient

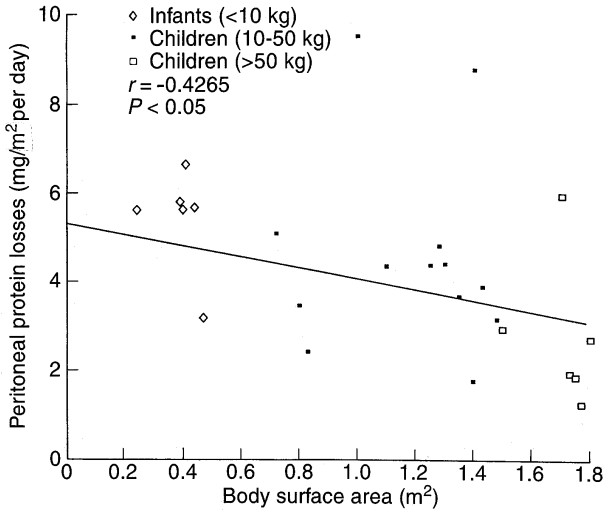

Fig. 2 Peritoneal protein loss (mg/m^2 per day) versus body surface area. Each point represents the mean of at least two 24-h dialysate fluid collections per patient

dwell) during the day until nightly CCPD again. The dialysate dextrose concentration was adjusted individually to keep all patients euvolemic. Patients were on CCPD for a mean of 23.5 months (range 5–96 months).

Total peritoneal protein losses were measured in each patient on the total collected dialysate effluent for 1 day, including the day dwell. Each patient's peritoneal protein losses were measured on at least two separate occasions. Protein measurement was performed in our hospital clinical laboratory (Children's Medical Center of Dallas) using the standard modified biuret method (Ektachem).

Anthropometric measurements were taken by a renal dietician. Mid-arm circumference (MAC) was measured with a cloth tape measure. Triceps skinfold thickness (TSF) was measured in the posterior triceps midway between the acromion and the olecranon using a Lange caliper (Cambridge Scientific Instruments). Mid-arm muscle circumference (AMC) was estimated from the following calculation [17]: AMC=MAC−(TSF×0.314)

Anthropometric measurements were compared with normal values for American children [18]. Using the mean value for normal children, an individual patient's anthropometric measurements were used to calculate a Z score [19]: Z=(patient's measurement - mean of normal values)/SD for measurement.

The mean used was either that for the patient's chronological age or that for the age at which the patient's height was at the 50th percentile (height age). The SD for any measurement was calculated from the difference between the 5th and 95th percentile divided by 3.3 [18,19]. The Z score represents the number of SDs above (+) or below (–) the mean and is a better tool for comparison purposes.

Total caloric and dietary protein intake was calculated from 3-day diet histories obtained from patients and/or their parents. All infant patients received supplemental feeds either through a nasogastric tube or a gastrostomy button. Supplemental feeds consisted of enteral nutrition such as PM 60/40 (Ross), Nepro (Ross), Suplena (Ross), Kindercal (Mead-Johnson), or Pediasure (Ross).

Statistical analysis. All data are reported as the mean ±SEM. Statistical analyses were carried out using the Student's t-test between the Z scores of anthropometric measurements.

Results

Peritoneal protein loss

The degree of protein loss between CCPD patients varied greatly, depending upon the body surface area of the child. As demonstrated in Fig. 1, peritoneal protein loss (expressed as mg/kg per day) was the highest in infants and the lowest in patients who were above 50 kg (277 ± 22 mg/kg per day vs. 91 ± 15 mg/kg per day, $P < 0.0001$). Intermediate degrees of peritoneal protein loss were observed in patients whose weights fell between 10 and 50 kg. We found an inverse linear relationship between peritoneal protein losses, expressed as mg/kg per day and body surface area (Fig. 1, $r = -0.7132$, $P < 0.0001$). We also found a similiar inverse linear relationship between peritoneal protein losses, expressed as mg/m^2 per day and body surface area (Fig. 2, $r = -0.4265$, $P < 0.05$). Although not statistically significant, the average serum albumin in our children over 50 kg (3.5 ± 0.1 g/dl) was slightly higher than that in the infants (3.3 ± 0.2 g/dl).

Dietary intake and anthropometry

Total dietary intake in children over 50 kg averaged 1.2 ± 0.3 g/kg per day of protein and 30 ± 11 calories/kg per day. Dietary intake in infants averaged 2.4 ± 0.8 g/kg per day of protein. Although caloric intake averaged 100 ± 29 calories/kg per day, the total intake varied greatly between infants.

Anthropometric measurements, expressed as Z scores for chronological and height age, are shown in Table 1. As expected, the height growth was most severely retarded in infants. Using chronological age to calculate Z scores, MAC and AMC in infants were greater than in children over 50 kg. There was no statistically significant difference in either the Z scores for TSF or weight between infants and

Table 1. Anthropometric parameter Z scores

	Same chronological age[a]		Same height age[b]	
	Infants	Older children	Infants	Older children
Height	–3.3 ±0.4	–1.6±0.4*		
Weight	–1.1 ±0.4	–0.7±0.3	1.8±0.4	0.8 ±0.3
MAC	1.1 ±0.4	–0.3±0.3*	1.4±0.4	0.6 ±0.4
TSF	–0.04±0.9	0.4±0.7	–0.1±0.7	1.1 ±0.8
AMC	1.6 ±0.3	–0.6±0.2*	–1.3±0.4	–0.04±0.3*

MAC, Mid-arm circumference; TSF, triceps skinfold thickness; AMC, mid-arm muscle circumference

* $P < 0.05$ between infants and older children

[a] Scores were calculated using the mean anthropometric measurement for the same chronological age as our patients

[b] Scores were calculated using the mean anthropometric measurement for the age at which the patients height was at the 50th percentile

children over 50 kg. When height age was used to calculate Z scores, only the AMC of infants was higher than in children over 50 kg.

Discussion

In this study, we demonstrate that peritoneal protein loss in pediatric dialysis patients treated with CCPD is substantial and is highest in the young infants. In contrast, peritoneal protein loss was the lowest in older patients above 50 kg and was similiar to losses previously reported for adults treated with CAPD [9,10,12]. As seen in Figs. 1 and 2, we found an inverse linear relationship between peritoneal protein losses and body surface area. Figure 1 expresses peritoneal protein losses as mg/kg per day, while Fig. 2 expresses it as mg/m^2 per day. Our data are in agreement with those previously reported by Balfe et al. [5] on 12 CAPD patients, where he found children less than 6 years of age lost 300±60 mg/kg per day of peritoneal protein, while children older than 6 years of age lost only 140±20 mg/kg per day. Similiar studies also described an inverse linear relationship between protein loss and body weight in patients on CAPD and CCPD [8,13,14]. In contrast to the above studies, our present study examines patients spanning the pediatric age range, including much younger infants, all less than 2 years of age.

The etiology of the higher degree of peritoneal protein loss in infants is currently unknown. The greater amount of protein loss may, in part, result from a proportionally greater peritoneal surface area in infants compared with older children and adults. However, as seen in Fig. 2, protein losses in infants are still greater than in older children when such losses are analyzed per meter square of body surface area. Thus, both a higher permeability and greater surface area of the infant peritoneal membrane likely allow for greater losses of peritoneal protein. The permeability of the peritoneal membrane likely changes with age and approaches that observed in adults. The observation that dialysate glucose is more rapidly absorbed in many young infants on CCPD may reflect an overall greater permeability of their peritoneal membrane [20]. Recently, Bazzato et al. [21] reported that addition of glycosaminoglycans to dialysate solution decreased peritoneal protein losses. The altered permeability of the infant peritoneal membrane may reflect, among other factors, a different glycosaminoglycan content. It is also interesting that the magnitude of protein loss reported in CAPD is similiar to that found in CCPD. Given the greater number of exchanges and higher total dialysate volumes used in CCPD, greater losses of protein might have been expected. The comparable magnitude of protein loss should make care of CCPD patients no more difficult than that for CAPD patients.

Such losses of protein can contribute to overall protein calorie malnutrition. This problem is exacerbated by suboptimal nutritional intake common to many dialysis patients. Blumenkrantz et al. [10] have reported that in adult CAPD patients peritoneal protein losses alone accounted for nearly 20% of the total body nitrogen loss. The remainder of the nitrogen losses consisted primarily of urea, uric acid, and creatinine. Greater peritoneal protein losses in infants would undoubtedly account for an even higher percentage of total nitrogen losses. Such losses result in poor growth as illustrated by the anthropometric parameters shown in Table 1. Children, and particularly infants, on peritoneal dialysis require aggressive nutritional support and, in many cases, nighttime nasogastric feeds [16,22]. Daily caloric and dietary protein intake should be monitored closely and be in accordance with current recommendations [13,16]. In our infants, nutritional support consisted of dietary protein intake (2.5 gm/kg per day) at the recommended level of 2.5–4.0 g/kg per day, while total caloric intake (100 cal/kg per day) was near the recommended level of 105–115 cal/kg per day. In contrast, for the remainder of our patients (6 years - 18 years), dietary protein intake (1.2 g/kg per day) was below the recommended level of 1.5–2.5 g/kg per day. Similiarly, total caloric intake (30 cal/kg per day) was also below recommended levels of 60 cal/kg per day. Early intervention with aggressive nutritional supplementation, particularly in infants on peritoneal dialysis, is currently the best therapy to overcome peritoneal protein losses and maintain growth. Growth failure in such young infants commonly results in the permanent loss of growth potential [16]. Thus, both early and aggressive nutritional support is vital to maximize growth in infants.

Another reported method of overcoming peritoneal protein losses involves the use of amino acid-containing dialysate solutions. In some studies, such dialysate solutions have been shown to compensate for peritoneal protein losses [23,24]. However, such solutions are costly and routine use is still very controversial.

In summary, pediatric patients lose substantial amounts of peritoneal protein on CCPD. Young infants proportionally lose the most protein and, therefore, are at risk for protein calorie malnutrition. Peritoneal protein losses on CCPD decrease with increasing body size and are comparable to losses occurring on CAPD.

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Literature abstract

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Atypical hemolytic-uremic syndrome: a comparison with postdiarrheal disease

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Objectives: To compare the epidemiologic, laboratory, clinical, and outcome variables of atypical (nondiarrheal) hemolytic-uremic syndrome with those of classic postdiarrheal disease.

Methods: A 24-year retrospective review of 28 episodes of atypical HUS that occurred in 22 children compared with 266 episodes of typical postdiarrheal disease in 265 children treated during the same period.

Results: Of the 294 episodes of HUS, 9.5% were atypical (nondiarrheal), and 18% of the patients in the atypical disease group had recurrences. Prodromal features (other than the presence or absence of diarrhea) were similar between the groups. White blood cell count and serum creatinine concentration on admission to the hospital and most abnormal blood urea nitrogen values during hospitalization were significantly lower ($p = 0.02$) in the patients with atypical HUS. Oliguria, anuria, and the need for dialysis were also less common ($p = 0.02$) in the atypical disease group. There were no deaths in the subset of patients with atypical disease; 3.4% of the patients in the typical disease group died. Although there were no statistically significant differences in the incidence of end-stage renal disease between the atypical and typical disease groups, two of the four patients with atypical disease who had recurrences also had end-stage renal disease. There were no significant differences in chronic renal sequelae between the groups one or more years after HUS.

Conclusions: In contrast to reports from most other regions, patients with atypical disease in our area of the western United States have milder acute nephropathy and, with the exception of those with recurrence, do not experience worse outcomes.