A prospective multicentre study of the nutritional status in children on chronic peritoneal dialysis

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Abstract

The anthropometry–bioimpedance analysis–nutrition (ABN) score is a recently proposed objective method of assessing malnutrition in children on chronic peritoneal dialysis (CPD) that uses nine parameters based on anthropometry, skinfold thickness and bioimpedance analysis.

The aim of this prospective, cross-sectional study was to apply it to children treated with CPD in seven Italian paediatric nephrology centres, with a score of < 10.33 (the 3rd percentile in a population of 264 healthy children) classifying the children as malnourished. The other considered parameters were age, age at the start of dialysis and duration of dialysis; serum haemoglobin, urea, creatinine, total protein, albumin, transferrin, bicarbonate and C-reactive protein; residual urine output; urinary and peritoneal creatinine clearance; and daily protein and energy intake.

The study enrolled 43 patients (mean age 10.2±4.2 years), 21 of whom (48.8%) had an ABN score of <10.33 (the 3rd percentile in a population of 264 healthy children) classifying the children as malnourished. The other considered parameters were age, age at the start of dialysis and duration of dialysis; serum haemoglobin, urea, creatinine, total protein, albumin, transferrin, bicarbonate and C-reactive protein; residual urine output; urinary and peritoneal creatinine clearance; and daily protein and energy intake.

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In conclusion, protein–calorie malnutrition is common in children receiving CPD. A younger age at the start of dialysis and a longer duration of treatment are clear risk factors, and counterbalance the long-term viability of CPD in paediatric age.

Keywords: anthropometry; bioimpedance analysis; children; chronic peritoneal dialysis; malnutrition; nutritional score

Introduction

Protein–calorie malnutrition is common in children undergoing chronic peritoneal dialysis (CPD) and is a major source of morbidity and mortality [1–4]. Its early detection and further follow-up require accurate and sensitive methods of nutritional assessment [5,6], but although many diagnostic techniques are now available, no single method can clearly identify malnutrition or reliably predict its risk in clinical practice. Furthermore, the various methods used by different authors have generated variable data and confusion, and so the real prevalence of malnutrition in CPD-treated children is still unknown. At the same time, the factors affecting nutritional status in this population can be hypothesized only on the basis of adult data.

We have recently proposed a new objective, anthropometry–bioimpedance analysis–nutrition (ABN) score that uses nine parameters based on anthropometry and bioimpedance analysis (BIA) to evaluate the nutritional status of children on PD [7]. After finding out that about one-half of a retrospective cohort of children treated with CPD at our centre suffered from various degrees of protein–calorie malnutrition [7], we started this prospective, multicentre, non-interventional study with the aim of assessing the prevalence and main factors associated with malnutrition in children without comorbid conditions undergoing CPD in Italy.
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Patients and methods

Patients

All patients treated with CPD at seven out of 13 Italian paediatric dialysis centres between June 2002 and June 2003, were considered for study enrollment. The permanent exclusion criteria were an age of >18 years and the presence of comorbid conditions which may permanently worsen nutritional status, such as chronic inflammatory diseases, neurological disorders affecting food intake, high level proteinuria (>40 mg/sqm/h), chronic intestinal diseases causing malabsorption, chronic liver insufficiency, and severe pulmonary, cardiac or systemic diseases, (including any kind of) malignancy. Transient exclusion criteria, which caused the temporary withdrawal of the patient from study enrolment, were an age of <1 year, a dialysis duration of <1 month, an unstable clinical condition, episodes of peritonitis in the month preceding study entry, intercurrent illnesses, and major changes in dialysis prescription in the month preceding the study.

Methods

The study was promoted by an ad-hoc Committee of the Italian Registry of Pediatric Chronic Dialysis and, before it started, protocol meetings were organized for the physicians, dieticians and nurses of the participating centres in order to standardize the anthropometric and BIA measurement techniques and dietary assessment. The data collected for each patient were demographic data (age, age at the beginning of CPD, duration of dialysis), anthropometric and BIA parameters, laboratory data, indices of renal function and dialysis efficiency, and dietary intakes.

The anthropometry parameters included two groups of indices: group 1 consisted of height (H), weight (W) and body mass index (BMI), and group 2 of mid-arm muscle circumference (MAMC), arm muscle area (AMA) and arm fat area (AFA) calculated from the measurements of mid-arm circumference, and triceps skinfold thickness according to Frisancho [8]. Height was measured to the nearest 1.0 mm by means of a stadiometre, weight to the nearest 0.05 kg by means of a balance, and triceps skinfold thickness to the nearest 0.2 mm by means of a Holtain skinfold caliper.

Single-frequency BIA was carried out as previously described [4] using a BIA 101S device (Akern lab., Florence, Italy). The simple bioelectrical measures of resistance (R) and reactance (Xc) were used to calculate phase angle (PA) and distance (D) according to the following formulae:

\[
PA = \arctan \left( \frac{Xc}{R} \right) \times \frac{180}{\pi},
\]

and

\[
D = \left( PA \times 10 + Xc \right) / \sqrt{2}.
\]

Resistance itself was not considered a suitable index of nutrition because it only indicates the amount of body fluids. All of the parameters were expressed as standard deviation scores (SDS) using the general formula:

\[
SDS = \frac{x - \bar{x}}{Sd},
\]

where \(x\) is the individual patient value, \(\bar{x}\) the median value for the normal population, and \(Sd\) the SD from the normal value. Tanner et al.’s [9,10] data were used as references for H and W, Rolland-Cachera et al.’s [11] data for BMI, Frisancho’s [8] data for MAMC, AMA and AFA, and De Palo et al.’s [12] data for the BIA indices.

The anthropometric and BIA measurements were made in the morning, when the patients arrived at the hospital after the end of nightly PD, by the same investigator in each dialysis unit.

The nine A and BIA parameters (H, W, BMI, MAMC, AMA, AFA, Xc, PA and D) were given scores of 5 for values of >2 SDS; 4 for values of <0 and >–1 SDS; 3 for values of <–1 and >–2 SDS; 2 for values of <–2 and >–3 SDS; and 1 for values of <–3 SDS. An average score was calculated for each of the A1, A2 and BIA groups, and these were summed to obtain the ABN score, which could therefore vary from 3 (worst) to 15 (best). A dedicated software helped in calculating the anthropometric and BIA parameters and the ABN score. The average time spent to make all the measurements and calculate the ABN score was 10 min in the average.

In order to establish a cut-off value between normal nutritional status and malnutrition, the method was first applied to 264 healthy children of different ages, and the ABN score corresponding to the 3rd percentile (10.33) was considered the limit of normality [7]. In this study, the patients with ABN scores of <10.33 were classified as malnourished, with mild malnutrition being arbitrarily defined as a score of 8–10.33, moderate malnutrition as a score of 6–8, and severe malnutrition as a score of <6.

All of the patients followed the dietary recommendations for children and adolescents on CPD reported in the literature [5,6]. Dietary protein intake (DPI) and energy intake (DEI) were calculated by the same dietician at each centre, who examined a 3 day diary kept by the children’s parents.

A venous blood sample obtained in the morning at the end of the dialysis session was used to determine the levels of haemoglobin, urea, creatinine, total protein, albumin, transferrin, bicarbonate and C-reactive protein.

Spent dialysate and urine were collected over 24 h before the office visits, and used to measure urinary urea, creatinine and protein, and dialysate urea, creatinine and protein and glucose.

Total creatinine clearance (CrCl) was calculated as the sum of dialytic CrCl and residual CrCl; normalized urinary and dialytic urea clearance (Kt/V) were calculated as the ratio between urinary and dialytic urea clearance and total body water volume obtained by means of the Mells–Cheek equation based on sex, height and weight.

Statistical analysis

The data are expressed as mean values±SD, and were statistically analysed using Student’s t-test for continuous variables and the \(x^2\) test for dichotomous variables. A P-value of <0.05 was considered statistically significant.

Results

Seven out of the 13 Italian paediatric dialysis centres participated in the study: 43 patients (24 males, 19 females), all undergoing automated PD, satisfied the selection criteria and were enrolled for the study. Their characteristics are shown in Table 1. The most
frequent causes of end-stage renal disease were glomerular diseases (14 patients), particularly focal segmental glomerulosclerosis (7 cases) and urinary tract malformations (11 patients); the other causes were renal hypoplasia (4), nephronophthisis (4), haemolytic uraemic syndrome (2), congenital nephrotic syndrome (2), autosomal recessive polycystic kidney disease (2), Wilms’ tumour (1), cystinosis (1), hyperuricaemic familial nephropathy (1) and Bardet–Biedl syndrome (1).

All patients were treated with recombinant human erythropoietin (rhEPO), and 13 (30%) with recombinant human growth hormone (rhGH). All patients received spontaneous nutrition, none was being treated with enteral feeding at the time of the investigation, and there were no clear clinical signs of hyperhydration.

Table 2 shows the nutritional status of the children according to the ABN score: 21/43 (48.8%) had a score of <10.33 indicating malnutrition. Most of them (15/21) were only mildly malnourished; only one patient had a score of <6 suggesting severe malnutrition. The mean ABN score of the patients with malnutrition was 8.6±1.3, and that of those with a normal nutritional status was 12.2±1.1. The values of only the BIA parameters considered in the ABN score were significantly lower in the patients with more than 24 months of CPD than in those who had been on dialysis for a shorter period.

In terms of the factors potentially influencing the nutritional status (Table 3), the patients with an ABN score indicating malnutrition started CPD at a younger age (P<0.05) and had been on dialysis longer than those with a normal ABN score (P<0.01). The patients receiving rhGH and rhEPO treatment were equally distributed in the two groups.

Among the analysed biochemical markers, serum albumin, serum creatinine and serum haemoglobin levels were all significantly lower in the patients with ABN scores of <10.33 (Table 4).

There were no significant differences in the indices of residual renal function, dialytic clearance (weekly CrCl and Kt/V), or dietary and protein intake between the two groups of children (Table 5), but there was a significant inverse correlation between the ABN scores and the duration of dialysis (P<0.05). Considering the absolute ABN scores and the prevalence of malnutrition over time (Table 6), there was a significant worsening in nutritional status after the first 12 months of dialysis: 75% of the children who had received CPD for more than 24 months were classified as malnourished, as against 25% of those undergoing dialysis for 6–12 months (P<0.05).

Finally, the values of only the BIA parameters (Xc, PA and D) considered in the ABN score were significantly lower in the patients with more than 24 months of CPD than in those who had been on dialysis for a shorter period.

**Discussion**

Studies of the nutritional status of children on chronic dialysis have so far been limited by the lack of accepted criteria for a diagnosis of malnutrition because, although many methods of evaluation have been proposed, no gold standard has yet been established [5,6]. Consequently, different parameters have been
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**Table 5.** Comparison of patients with malnutrition (ABN score < 10.33) and patients with normal nutritional status (ABN score ≥ 10.33) by indices of dialytic clearance, residual renal function, and dietary energy and protein intake

<table>
<thead>
<tr>
<th>Index</th>
<th>ABN score &lt; 10.33</th>
<th>ABN score ≥ 10.33</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine output (ml/day)</td>
<td>343 ± 412</td>
<td>708 ± 587</td>
<td>NS</td>
</tr>
<tr>
<td>Residual CrCl (l/1.73m²/week)</td>
<td>9.8 ± 16.7</td>
<td>15.7 ± 20.6</td>
<td>NS</td>
</tr>
<tr>
<td>Total CrCl (l/1.73m²/week)</td>
<td>57.8 ± 22.5</td>
<td>56.8 ± 27.4</td>
<td>NS</td>
</tr>
<tr>
<td>Kt/V urea</td>
<td>2.4 ± 0.8</td>
<td>2.6 ± 1.5</td>
<td>NS</td>
</tr>
<tr>
<td>DEI (%RDA)</td>
<td>88 ± 23</td>
<td>75 ± 23</td>
<td>NS</td>
</tr>
<tr>
<td>DPI (%RDA)</td>
<td>180 ± 62</td>
<td>152 ± 65</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = not significant.

**Table 6.** ABN scores and prevalence of malnutrition by duration of dialysis

<table>
<thead>
<tr>
<th>Duration of dialysis</th>
<th>ABN score &lt; 10.33 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months</td>
<td>11.1 ± 1.7</td>
</tr>
<tr>
<td>6–12 months</td>
<td>11.2 ± 1.8*</td>
</tr>
<tr>
<td>12–24 months</td>
<td>10.5 ± 1.8</td>
</tr>
<tr>
<td>&gt;24 months</td>
<td>9.2 ± 1.7*</td>
</tr>
</tbody>
</table>

**x²-test:** P < 0.05.

* t-test: P < 0.05.

used to identify malnourished children and different prevalence rates have been obtained. The only consensus that has been reached is the need to use a combination of nutritional markers when diagnosing malnutrition, but this gives only a fragmented vision of a patient’s nutritional status and does not allow a clear objective diagnosis of malnutrition [5,6]. Moreover, a paediatric version of the subjective global assessment, that is being increasingly used in adults on dialysis, has never been developed for children [13].

The ABN score is a simple method based on objective parameters that are non-invasive, sufficiently reliable, and cheap and easy to measure in both ill and healthy children [7]. Published data have confirmed that its use leads to a more objective assessment of nutritional status as it enhances the information provided by the individual diagnostic methods [7]. The validity of the criteria used to select the nine parameters (the identification of limits of normality in a large population of healthy children and the preliminary use of the score in paediatric patients treated with CPD) suggests that the score can reliably be used to evaluate the nutritional status of children on dialysis.

This is the first study which has been planned to investigate the nutritional status of children on CPD by means of the ABN score: its multicentre design allowed us to enroll a population of 43 children, one of the largest populations ever considered in previously published paediatric studies. Although a major limitation of this study could be possible between-centre differences in measurement techniques, the pre-study protocol meetings for the physicians and dieticians of the participating centres helped to standardize the assessments and decrease inter-centre variability; intra-centre variability was counteracted by always using the same investigator to make the assessments.

The published prevalence rates of malnutrition in children on dialysis vary widely from 15 to 58% [3,4,7,14]. On the basis of their ABN scores of < 10.33, we found that 48.8% of our patients were malnourished: the percentage of patients with scores suggesting severe malnutrition according to our criteria was very low (2.3%), whereas moderate and mild malnutrition were equally distributed. Our data concerning the prevalence of malnutrition are in line with the highest figures reported in the literature for CPD-treated adults and children but, as the aim of the study was to assess the prevalence of malnutrition in otherwise ‘normal’ stable children on CPD with no comorbid factors and/or associated non-renal diseases that could affect their nutritional status (i.e. only uraemia and PD may have done so), the overall prevalence of malnutrition in CPD-treated children could be even higher.

Only a few studies have investigated the effect of long-term dialysis on the nutritional status of children undergoing CPD, the majority focusing on growth, without taking into account other specific nutritional parameters. In a retrospective study of 18 children on CPD, we found that the prevalence of malnutrition as assessed by means of anthropometric parameters (MAMC, AMA, AFA) and BIA indices (Xc, PA and D), was high at the start of dialysis, decreased significantly during the first 6 months of treatment, but increased again after the 12th month [4]. In contrast, Canepa et al.’s [14] study of 35 children on CPD found that the percentage of patients in the lowest percentiles (< 5th, 5–15th) for MAMC, AMA and AFA was lower in those who had been on dialysis for more than 24 months than in those on CPD for 6–12 months; however, this conflicts with the fact that the SDS of weight, height and triceps skinfold thickness by chronological age were lower in these children after 24 months’ dialysis. A number of studies of adult patients have found a gradual improvement in the nutritional status during the first 12 months of dialysis, and a progressive worsening after 18 months [15]. We found a close inverse correlation between the duration of dialysis and ABN scores: in particular, a worsening in nutritional status was clear in those who had been treated with PD for more than 12 months, with the risk of malnutrition being highest in the children dialysed for more than 24 months. However, the cross-sectional design of the study suggests some caution in drawing definite conclusions: only a longitudinal study could confirm the deleterious effect of long-term dialysis on the nutritional status. The BIA parameters (Xc, PA and D) were more sensitive than the anthropometric indices in detecting altered nutritional status during the first 2 years of dialysis.
It is difficult to identify the factors causing the increased prevalence of malnutrition during long-term PD. Some authors suggest that the dialysis dose may significantly influence the nutritional status of patients on dialysis, but others disagree [3,16,17]. Schaefer et al. [16] found a direct correlation between enhanced PD adequacy (Kt/V) and improved dietary protein intake, but Brem et al. [3] showed that dialysis adequacy inversely correlated with serum albumin in children on CPD. The results of our study fail to identify any statistically significant effect of dialysis clearance or residual renal function on the nutritional status of CPD-treated children, but the children whose ABN scores suggested malnutrition had lower urine outputs and residual CrCl levels than those whose ABN scores indicated a normal nutritional status. This finding may be, at least partially, explained by the relatively small number of patients enrolled in the study and their widely ranging residual renal function, as shown by the high SD values.

Various studies of both adult and paediatric patients have investigated the usefulness of biochemical markers in identifying malnutrition. Our patients with abnormal ABN scores had significantly lower serum albumin, creatinine and haemoglobin levels than those with normal ABN scores. Serum albumin is widely used as a nutritional marker and has been found to be a very strong predictor of a poor outcome in adults on dialysis [18]. However, some authors have criticized its use because it seems to be more closely associated with comorbidities than nutritional status per se, and other factors, such as fluid overload and urinary and dialysate losses, may lead to hypoalbuminaemia [19]. Nevertheless, it is interesting to note that, in our selected population without comorbidities or proteinuria, serum albumin significantly correlated with the objective nutritional score based on anthropometry and BIA.

Serum haemoglobin is not used in general as a nutritional marker, but the presence of lower haemoglobin levels in the malnourished children compared with those having a normal nutritional status may suggest such a case. Since the protocol of rhEPO dosage and iron supplementation was identical in the two groups and there was no reason to suspect non-compliance just in children whose ABN score indicated malnutrition, the only possible explanation for this finding is bone marrow toxicity, caused by uraemia per se.

There is increasing published evidence linking chronic inflammation with uraemia and malnutrition, particularly in adult populations [20]. In paediatric CPD patients, Brem et al. [3] found a close inverse correlation between serum albumin and serum ferritin, an acute-phase reactant whose levels increase in line with the inflammatory response, but this is not supported by our finding that CRP levels were not significantly different between the children whose ABN scores indicated malnutrition and those whose scores indicated a normal nutritional status.

In conclusion, mainly mild/moderate protein-calorie malnutrition is a common finding in children treated with CPD. A younger age at the time of starting PD and a longer treatment duration are clear risk factors for the development of malnutrition. Low serum albumin, serum creatinine and serum haemoglobin levels are associated with low ABN scores, and can be used as late biochemical markers of malnutrition.

More studies are needed to clarify the role of residual renal function and dialytic clearance in the impairment of nutritional status during long-term PD, and identify new strategies for preventing and treating malnutrition in paediatric patients.

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