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DIALYSIS

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# nPCR assessment and IDPN treatment of malnutrition in pediatric hemodialysis patients

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**Abstract** Very few pediatric studies have monitored nutritional status using normalized protein catabolic rate (nPCR) or treating protein-energy malnutrition (PEM) with intradialytic parenteral nutrition (IDPN). The current study compares nPCR with serum albumin as a marker for nutritional status and examines the effectiveness of IDPN treatment in three malnourished adolescent patients receiving chronic hemodialysis in a pediatric dialysis unit. All patients demonstrated reversal of weight loss and initiation of weight gain within 6 weeks of IDPN initiation. Mean values of monthly percentage weight and percentage body mass index (BMI) change were significantly lower in the pre-IDPN era (–0.61±2.70 and –1.3±2.7) versus the IDPN treatment period (1.8±2.1 and 1.3±2.1) ($P$<0.02). Two patients attained ideal body weight and IDPN was discontinued after 5 months. Patients required 150% recommended daily allowance to achieve weight and BMI gain. While mean monthly nPCR was significantly lower in the pre-IDPN period versus the IDPN period (1.05±0.36 versus 1.35±0.37, $P$<0.05), monthly serum albumin levels were no different before and after IDPN was initiated (3.7±0.8 versus 3.8±0.6). The current study demonstrates IDPN to be effective therapy for adolescent hemodialysis patients with PEM not correctable by enteral supplementation. nPCR was superior to serum albumin as a nutritional status marker in these malnourished pediatric patients receiving hemodialysis.

**Keywords** Intradialytic parenteral nutrition · Malnutrition · Normalized protein catabolic rate · Hemodialysis

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## Introduction

Patients receiving chronic hemodialysis who exhibit protein-energy malnutrition (PEM) may be at risk for increased morbidity and mortality. Multiple studies assessing the impact of nutritional status upon mortality have concluded that PEM is an independent risk factor for death in adult patients receiving hemodialysis [1, 2, 3, 4, 5, 6]. Pediatric patients receiving hemodialysis do not exhibit high mortality rates, but PEM likely impairs growth and development in the children with end-stage renal disease (ESRD) [7].

The important relationship between nutritional status and outcome for patients with ESRD prompted the National Kidney Foundation Kidney-Dialysis Outcomes Quality Initiative (NKF-KDOQI) to create guidelines to assess and treat PEM in both children and adults with ESRD [7]. The pediatric K-DOQI guidelines recommend serum albumin, height/length, dry weight, mid-arm circumference, skinfold thickness, fronto-occipital circumference, and height Z-score to monitor nutritional status and intensive *enteral* nutrition to treat PEM. While these measures are essential to monitor and treat PEM, they may not be sufficient in all cases.

Intradialytic parenteral nutrition (IDPN) provides significant amounts of protein and calories to a patient during the hemodialysis treatment. IDPN is effective treatment for adult patients with PEM [8, 9, 10], and adult K-DOQI nutritional guidelines provide recommendations for IDPN use in adults. IDPN therapy has not been extensively studied in malnourished pediatric patients receiving hemodialysis [11, 12, 13] and pediatric K-DOQI nutritional guidelines do not address IDPN therapy.

Many adult outcome studies use normalized protein catabolic rate (nPCR) as an independent marker of nutrition status [14, 15, 16, 17]. nPCR is derived from the interdialytic rise in blood urea nitrogen levels and has been shown to correlate with nutritional status in adult patients receiving hemodialysis. No published pediatric study has used nPCR as a marker of nutritional status. In fact, little investigation into the validity of nPCR has been performed since the rigorous work of Grupe et al. [18] and Harmon et al. [19] 20 years ago, whose seminal studies in children receiving hemodialysis demonstrated a positive correlation between dietary protein intake and nPCR. They were the first to suggest that positive nitrogen balance, which is essential for growth, could be achieved with moderate protein intake and without an increase in dialysis requirements.

In our pediatric dialysis unit over the past 18 months, we have treated three severely malnourished adolescent patients with IDPN. We have routinely determined monthly nPCR values for the last 4 years in all of our pediatric hemodialysis patients. The aims of the current study are to investigate the effectiveness of IDPN for treating PEM and to compare the sensitivity of serum albumin versus nPCR for monitoring nutritional status in malnourished pediatric patients receiving hemodialysis.

## Materials and methods

### Patient population

Three patients received IDPN for treatment of PEM during January 1999 through May 2001 in the Texas Children's Hospital Renal Dialysis Unit. The lowest weight for each patient ranged from 35.9 to 45 kg. Patient ages were 17, 18, and 25 years and their height ages were 14 years 1 month, 11 years 4 months, and 11 years 11 months, respectively. All patients had completed their growth and demonstrated Tanner stage V sexual maturation.

To qualify for IDPN by our unit protocol, patients had to exhibit a ≥10% weight loss over a 3-month time span and have a gastrointestinal illness that precluded administration of sufficient enteral calories to achieve anabolism. The gastrointestinal causes of PEM in these patients were (1) chronic recurrent pancreatitis and malabsorption, (2) acute pancreatitis with an infected pancreatic pseudocyst and colonic perforation, and (3) severe gastritis, duodenal stricture, and abdominal wall abscess.

### IDPN prescription

IDPN is comprised of three components: dextrose, amino acids, and lipids. The dextrose component was delivered as a 70% solution to provide 5–9 mg/kg per min of carbohydrate. The purpose of the IDPN carbohydrate component is to prevent catabolism and maximize utilization of the IDPN protein component. Serum glucose levels were monitored at the beginning, in the middle of, and immediately after IDPN administration during the 1st week of IDPN treatment or after any change in the dextrose rate. Patients with serum glucose levels >300 mg/ml received regular insulin in the IDPN preparation bag to maintain serum glucose <200 mg/dl.

The amino acid component (Novamine) was delivered as a 15% solution to provide 1.3 g/kg per treatment of protein [20]. The amino acid component was prepared and combined with the carbohydrate component in our outpatient pharmacy on the day of administration.

The lipid component of IDPN was provided as a 20% solution and delivered via a separate bottle. The lipid component is egg based, and is withheld from patients with a history of egg allergy. Patient serum triglyceride levels were checked before and after the first IDPN treatment. A 50% rise above baseline levels after lipid administration was indicative of lipid intolerance and resulted in discontinuation of future lipid administration for a particular patient.

The prescribed volume of IDPN was infused continuously over the entire course of the hemodialysis treatment. To minimize dialyzer clearance of amino acids, IDPN was administered via the venous limb of the hemodialysis circuit (i.e., post dialyzer). The total fluid volume of IDPN was based on the volume needed to deliver the carbohydrate and protein doses described above. The total volume associated with IDPN administration was removed via ultrafiltration over the course of the hemodialysis treatment.

### Nutritional status monitoring

Mid-week monthly nutritional laboratory assessment included serum albumin and nPCR levels. Single-pool Kt/V and nPCR were calculated by single-pool urea kinetic modeling [21]. Post-dialysis patient weight and body mass index [BMI=wt(kg)/ht$^2$(m)] were obtained on the date of serum albumin and nPCR assessment. Month-to-month percentage of weight change and BMI change were used as outcome measures for IDPN therapy. In order to minimize the potential for observed weight gain to be the result of fluid accumulation and not true weight gain, all patients received ultrafiltration guided by non-invasive monitoring of hematocrit (Crit-line, Hemametrics, Salt Lake City, Utah, USA) during each dialysis session. We have previously demonstrated this to be effective in achievement of patient target dry weight with minimal patient symptomatology [22, 23].

### Statistical analysis

To standardize assessment between the three patients, monthly data from the 4 months immediately prior to IDPN treatment were compared with data from the first 5 months of IDPN treatment. Mean values for serum albumin, nPCR, percentage weight change, percentage BMI change, and spKt/V from the pre-IDPN months and the IDPN months were compared using the paired *t*-test. A $P$ value $<0.05$ was considered significant.

## Results

The three adolescent patients reported in this study were the only patients in our unit who exhibited severe PEM (≥10% weight loss over a 3-month time span) that could not be adequately treated with enteral supplementation alone. One patient received dialysis via an arteriovenous graft, one via an arteriovenous fistula, and one patient received dialysis via an indwelling catheter. None of the infants and children within our unit suffered from a significant gastrointestinal disorder that precluded successful enteral supplementation.

All three patients tolerated IDPN administration without adverse events. Total IDPN volume ranged from 478 ml to 597 ml depending on patient weight. One patient demonstrated lipid intolerance (50% increase in triglyceride level above baseline) and did not receive lipids after his first dose of IDPN. Another patient with acute pancreatitis developed transient insulin-dependent diabetes mellitus and required 6 units of regular insulin added to the IDPN preparation to keep serum glucose levels be-

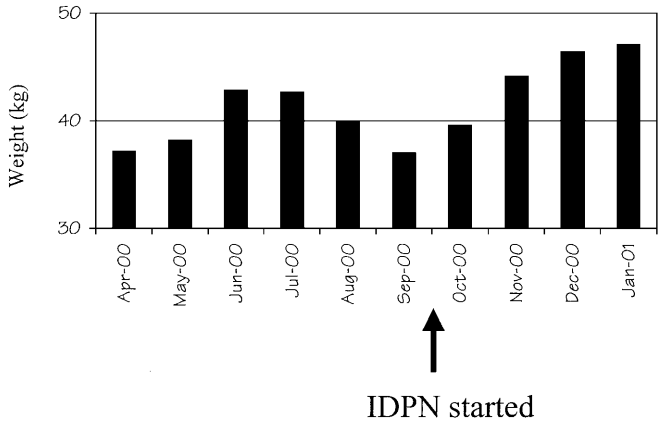


**Fig. 1** Monthly weight graph for a patient receiving chronic hemodialysis before and during intradialytic parenteral nutrition (*IDPN*) for protein-energy malnutrition

**Table 1.** Nutrition and hemodialysis adequacy parameters before and during intradialytic parenteral nutrition (IDPN) (*BMI* body mass index, *nPCR* normalized protein catabolic rate)[a]

| | Pre IDPN | IDPN | *P* |
|---|---|---|---|
| % Weight change | –0.6±2.70 | 1.8±2.1 | <0.02 |
| % BMI change | –1.3±2.7 | 1.3±2.1 | <0.02 |
| nPCR (g/kg per day) | 1.05±0.36 | 1.35±0.37 | <0.05 |
| Serum albumin (g/dl) | 3.7±0.8 | 3.8±0.6 | NS |
| spKt/V | 1.49±0.29 | 1.43±0.18 | NS |

[a] All values mean monthly±SD

low 200 mg/dl. IDPN provided 37%–42% of each patient's weekly protein intake.

All three patients demonstrated reversal of weight loss and initiation of weight gain within 6 weeks of IDPN initiation. A monthly weight chart from one patient is provided in Fig. 1. Examination of patient food diary and IDPN administration records revealed that patients required 150% of the recommended daily allowance for calories and protein to exhibit weight gain. Since all patients in the current study had normal blood pressure parameters and were not receiving concurrent anti-hypertensive medications, the observed weight and BMI gain were not likely secondary to fluid overload.

Two patients attained ideal body weight after 5 months of IDPN therapy. The third patient attained 90% of ideal body weight after 8 months of therapy. All patients had IDPN discontinued and have maintained ideal body weight without IDPN for 3 months.

Mean monthly percentage weight change and percentage BMI change were negative in the pre-IDPN period and positive in the IDPN treatment period. While mean monthly nPCR was significantly lower in the 4-month period prior to IDPN treatment than in the 5 months of IDPN treatment (1.05±0.36 versus 1.35±0.37, $P<0.05$), mean monthly serum albumin levels did *not* differ between the two periods (3.7±0.8 versus 3.8±0.6). In addition, all patients received adequate dialysis clearance defined by DOQI as spKt/V >1.2 and the delivered dose of dialysis was not different between the pre-IDPN and IDPN periods. Mean pre-IDPN and IDPN treatment data are summarized in Table 1.

## Discussion

Nutritional status impacts outcome in adults and children receiving hemodialysis. While various nutritional status markers and their association with morbidity and mortality have been studied in adult patients with ESRD, few published data have assessed nutritional status and outcome in the pediatric hemodialysis population. Tom et al. [24] correlated increased protein administration and urea clearance with improved growth in well-nourished children receiving hemodialysis, but this study relied on dietary history and prescription for monitoring of nutritional status. Furthermore, while there is some experience with and recommendation for IDPN therapy for malnourished adult patients receiving hemodialysis, no data or recommendations exist to guide IDPN therapy in malnourished children and adolescents. One previous pediatric study showed no improvement in amino acid levels after low-dose (0.25 g/kg) amino acid administration during dialysis [13]. A recent pediatric study found that oral intake improved after short-term IDPN therapy (2–3 months) in malnourished adolescents, but neither patient weight nor serum albumin levels increased while on IDPN therapy [12]. To our knowledge, the current study is the first to evaluate the effectiveness of IDPN therapy and compare the accuracy of nPCR with that of serum albumin as a marker of nutritional status in severely malnourished pediatric patients.

Our data demonstrate that IDPN was effective supplemental therapy in all three of our patients with PEM. All patients exhibited weight and BMI gain within 6 weeks of initiation of IDPN therapy, despite significant gastrointestinal disease. No unexpected adverse effects were noted during the course of IDPN administration. One patient could not tolerate the lipid component and another patient, who had transient diabetes associated with pancreatitis, required regular insulin administration in the IDPN preparation bag. Two patients achieved their ideal body weight and one achieved 90% of ideal body weight during IDPN treatment.

Our data also demonstrate that nPCR was much more sensitive than serum albumin as a marker of PEM. Mean monthly nPCR was significantly lower when patients were losing weight and BMI in the pre-IDPN period compared with the IDPN therapy period, but mean monthly serum albumin levels were no different between the two periods. In a recent study Krause et al. [12] also noted no correlation between serum albumin levels and nutrition when IDPN was used to treat four pediatric patients with PEM. Their study did not assess nPCR. Our data suggest that nPCR may be an earlier indicator of worsening nutritional status in adolescents receiving hemodialysis. Since we only examined patients with PEM,

the current study cannot assess the ability of nPCR or serum albumin to predict impending PEM in a group of better nourished children receiving hemodialysis.

Patient nutritional status was not related to the delivered dose of dialysis over the time course of study, since patients in both the pre-IDPN and IDPN periods received a mean spKt/V>1.4. We do not suggest that spKt/V>1.4 is an optimal or even adequate dose of dialysis, although one pediatric study reported improvement in nPCR and appetite in patients with spKt/V>1.3 compared with patients with spKt/V<1.3 [25]. Nevertheless, the current study demonstrates that hemodialysis patient outcome is dependent on more than just the amount of urea clearance during hemodialysis; delivery of optimal hemodialysis also requires assessment of nutritional status.

Severe PEM not amenable to intensive enteral dietary supplementation was seen only in the adolescent subset of our patient population. To date, infants and children with weight loss and poor nutrition in our unit have been able to tolerate and respond to intensive enteral supplementation. However, none of the infants or younger children treated in our unit has had the extensive gastrointestinal complications exhibited by the IDPN-treated patients in this study. IDPN should be effective PEM treatment for patients of any age who cannot tolerate enteral supplementation.

The results of the current study support the use of IDPN to treat severe PEM in adolescent pediatric patients receiving hemodialysis who cannot tolerate enteral supplementation. IDPN can be recommended as a safe and intensive adjunctive treatment for malnourished adolescents receiving hemodialysis. Further study may be necessary to determine the safety and efficacy of IDPN therapy for treatment of severe PEM in infants and younger children. In addition, our data are the first to suggest that nPCR may be more sensitive than serum albumin as a marker of nutritional status in the pediatric hemodialysis population. Further study in a larger patient population is required to compare the ability of nPCR and serum albumin to predict the development of PEM in better nourished children and adolescents receiving hemodialysis.

## References


1. Chauveau P, Combe C, Laville M, Fouque D, Azar R, Cano N, Canaud B, Roth H, Leverve X, Aparicio M (2001) Factors influencing survival in hemodialysis patients aged older than 75 years: 2.5-year outcome study. Am J Kidney Dis 37: 997–1003
2. Herselman M, Moosa MR, Kotze TJ, Kritzinger M, Wuister S, Mostert D (2000) Protein-energy malnutrition as a risk factor for increased morbidity in long-term hemodialysis patients. Ren Nutr 10:7–15
3. Leavey SF, Strawderman RL, Jones CA, Port FK, Held PJ (1998) Simple nutritional indicators as independent predictors of mortality in hemodialysis patients. Am J Kidney Dis 31: 997–1006
4. Goldwasser P, Mittman N, Antignani A, Burrell D, Michel MA, Collier J, Avram MM (1993) Predictors of mortality in hemodialysis patients. Am Soc Nephrol 3:1613–1622
5. Owen WF Jr, Lew NL, Liu Y, Lowrie EG, Lazarus JM (1993) The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. N Engl J Med 329:1001–1006
6. Soucie JM, McClellan WM (1996) Early death in dialysis patients: risk factors and impact on incidence and mortality rates. J Am Soc Nephrol 7:2169–2175
7. Clinical Practice Guidelines for Nutrition in Chronic Renal Failure (2000) Am J Kidney Dis [Suppl 2] 35:S105–S136
8. Korzets A, Azoulay O, Chagnac A, Weinstein T, Avraham Z, Ori Y, Zevin D, Gafter U (1999) Successful intradialytic parenteral nutrition after abdominal “catastrophes” in chronically hemodialysed patients. J Ren Nutr 9:206–213
9. Smolle KH, Kaufmann P, Holzer H, Druml W (1995) Intradialytic parenteral nutrition in malnourished patients on chronic haemodialysis therapy. Nephrol Dial Transplant 10:1411–1416
10. Chertow GM, Ling J, Lew NL, Lazarus JM, Lowrie EG (1994) The association of intradialytic parenteral nutrition administration with survival in hemodialysis patients. Am J Kidney Dis 24:912–920
11. Brewer ED (1999) Pediatric experience with intradialytic parenteral nutrition and supplemental tube feeding. Am J Kidney Dis 33:205–207
12. Krause I, Shamir R, Davidovits M, Frishman S, Cleper R, Gamzo Z, Poraz I, Eisenstein B (2002) Intradialytic parenteral nutrition in malnourished children treated with hemodialysis. J Ren Nutr 12:55–59
13. Zachwieja J, Duran M, Joles JA, Allers PJ, Hurk D van de, Frankhuisen JJ, Donckerwolcke RA (1994) Amino acid and carnitine supplementation in haemodialysed children. Pediatr Nephrol 8:739–743
14. Combe C, Chauveau P, Laville M, Fouque D, Azar R, Cano N, Canaud B, Roth H, Leverve X, Aparicio M (2001) Influence of nutritional factors and hemodialysis adequacy on the survival of 1,610 French patients. Am J Kidney Dis 37[Suppl 2]: S81–S88
15. Cappy CS, Jablonka J, Schroeder ET (1999) The effects of exercise during hemodialysis on physical performance and nutrition assessment. J Ren Nutr 9:63–70
16. Sobh MA, Sheashaa H, Tantawy AE, Ghoneim MA (1998) Study of effect of optimization of dialysis and protein intake on neuromuscular function in patients under maintenance hemodialysis treatment. Am J Nephrol 18:399–403
17. Maggiore Q, Nigrelli S, Ciccarelli C, Grimaldi C, Rossi GA, Michelassi C (1996) Nutritional and prognostic correlates of bioimpedance indexes in hemodialysis patients. Kidney Int 50: 2103–2108
18. Grupe WE, Harmon WE, Spinozzi NS (1983) Protein and energy requirements in children receiving chronic hemodialysis. Kidney Int [Suppl 1] 15:S6–S10
19. Harmon WE, Spinozzi NS, Sargent JR, Grupe WE (1979) Determination of protein catabolic rate (PCR) in children on hemodialysis by urea kinetic modeling. Pediatr Res 13:513
20. Council of Renal Nutrition of New England (1993) Renal nutrition handbook for renal dieticians. National Kidney Foundation, Massachusetts, pp 85–97
21. Depner TA (1991) Single compartment model. In: Depner TA (ed) Prescribing hemodialysis: a guide to urea modeling. Boston, Kluwer, pp 65–89
22. Jain SR, Smith L, Brewer ED, Goldstein SL (2001) Non-invasive intravascular monitoring in the pediatric hemodialysis population. Pediatr Nephrol 16:15–18
23. Michael M, Brewer ED, Goldstein SL (2001) Non-invasive monitoring of hematocrit (NIVM) optimizes achievement of target weight (wt) without increasing intra- or interdialytic symptoms (sx) in children and adolescents receiving hemodialysis (HD). J Am Soc Nephrol 12:398A
24. Tom A, McCauley L, Bell L, Rodd C, Espinosa P, Yu G, Yu J, Girardin C, Sharma A (1999) Growth during maintenance hemodialysis: impact of enhanced nutrition and clearance. J Pediatr 134:464–471
25. Marsenic O, Peco-Antic A, Jovanovic O (2001) Effect of dialysis dose on nutritional status of children on chronic hemodialysis. Nephron 88:273–275