Published in final edited form as:

J Ren Care. 2018 March ; 44(1): 38–43. doi:10.1111/jorc.12226.

Children Tolerate Intradialytic Oral Nutrition

Andrew M. South, MD, MS^{1,2}, Bonnie Fainman, RD, CSP³, Scott M. Sutherland, MD⁴, and Cynthia J. Wong, MD⁴

¹Assistant Professor, Section of Nephrology, Department of Pediatrics, Wake Forest School of Medicine

²Cardiovascular Sciences Center, Wake Forest School of Medicine, Winston Salem, North Carolina

³Patient Access Manager, Raptor Pharmaceuticals, Novato, California

⁴Clinical Associate Professor, Division of Nephrology, Department of Pediatrics, Stanford University School of Medicine, Palo Alto, California, USA

Abstract

Background—Haemodialysis (HD) patients have poor nutrition, which contributes to worse outcomes. Inadequate nutrition has a particularly deleterious effect on growth and neurocognitive development, as well as mortality, in children and adolescents. Nutritional supplementation can improve outcomes but can be difficult to administer.

Objective—Determine the tolerability of intradialytic oral nutrition in paediatric patients.

Design—Cross-sectional quality improvement study in an outpatient paediatric HD unit. Intervention was intradialytic oral nutritional supplementation provided as protein bars and/or meals.

Subjects—Children and adolescents on outpatient HD who were able to participate in surveys and eat by mouth.

Measurements—Adverse effects and symptoms on nurse- and patient-reported surveys, respectively. Relationships between the predictor variables and the outcomes were assessed using generalized estimating equations.

Results—The majority of children felt better after eating on dialysis (72%) with no adverse effects (80%). On unadjusted analyses and confirmed with generalized estimating equation

Corresponding Author: Andrew M. South, MD, MS, Section of Nephrology, Department of Pediatrics, Wake Forest School of Medicine, One Medical Center Boulevard, Winston Salem, NC 27157, Phone (336) 716-9640, Fax (336) 716-9229, asouth@wakehealth.edu.

AMS: Principal Project Leader, participated in design and coordination, analyzed and interpreted the data, helped to draft manuscript, and read and approved the final manuscript.

BF: Participated in coordination, helped interpret the data, helped to draft manuscript, and read and approved the final manuscript.

SMS: Participated in the interpretation of the data, helped to draft manuscript, and read and approved the final manuscript.

CJW: Conceived study, participated in design and coordination, helped to interpret the data, helped to draft manuscript, and read and approved the final manuscript.

Financial Disclosure: The authors have no financial relationships relevant to this article to disclose.

Potential Conflicts of Interest: No conflict of interest has been declared by the authors.

modelling, children who reported being hungry felt better after eating on dialysis (OR 4.58, 95% CI 1.5 to 13.92, $p = 0.007$), despite being more likely to have adverse effects (2.42, 1.0 to 5.87, $p = 0.05$).

Conclusion—The study demonstrates that our paediatric HD patients feel better after eating on HD with minimal adverse effects. The finding that hungry patients are more likely to feel better despite having a higher likelihood of an adverse effect demonstrates the tolerability of eating on HD. Intradialytic oral nutrition could be a safe and well-tolerated opportunity to provide supplemental nutrition to paediatric HD patients and improve outcomes.

Keywords

End stage renal disease; haemodialysis; intradialytic oral nutrition; paediatrics

Introduction

End stage renal disease is a highly-catabolic state. Haemodialysis (HD) patients frequently have a decreased nutritional status, contributing to poor patient outcomes (Fouque *et al.* 2007; Feroze *et al.* 2011). Inadequate nutrition can have a critical effect on growth and neurocognitive development in children (Paglialonga & Edefonti 2009). Enhanced nutrition can improve patient outcomes and quality of life (Weiner *et al.* 2014; Lacson Jr *et al.* 2012; Scott *et al.* 2009). Paediatric dialysis patients frequently require supplemental food to improve their nutritional status (Zioni 2007; Kaur & Davenport 2014; KDOQI Clinical Practice Guideline for Nutrition in Children with CKD: 2008 Update 2009). Sufficient nutrition is difficult for paediatric HD patients to obtain. Providing additional food to patients while on HD could be an efficient and practical way to improve the nutritional state of paediatric dialysis patients.

However opportunities to eat while on HD vary by region and centre (Benner *et al.* 2012; Christner & Riley 2008). Historically, patients were restricted from eating on HD given the theoretical risks of adverse effects related to differential blood flow away from the splanchnic blood vessels, decreased dialysis efficiency, and an increased risk of choking/aspiration (Kistler *et al.* 2014; Christner & Riley 2008; Kistler *et al.* 2015). This is especially true in children on dialysis (Kaur & Davenport 2014). However this clinical practice arose from anecdotal reports, and the actual prevalence of these adverse effects is quite low (Christner & Riley 2008; Kistler *et al.* 2015). There are scant data regarding the safety and tolerability of intradialytic oral nutrition in children and adolescents, and paediatric clinical practice varies by centre. Our hypothesis was that paediatric HD patients are more likely than not to tolerate intradialytic oral nutrition. Our aims were to evaluate the development of adverse effects and self-reported patient outcomes after eating on HD.

Literature Review

The above review of the relevant literature occurred through an online search using PubMed®. The main search function was used to search for the key words 'paediatric', 'haemodialysis', and 'nutrition'. Searches occurred from November 2016 to March 2017.

Methods

Study Design

Cross-sectional quality improvement study of children on HD treated at the paediatric outpatient HD unit of Lucile Packard Children's Hospital at Stanford in Palo Alto, CA, which on average dialyses 15 children with ages ranging from toddlers to teenagers and includes a variety of aetiologies of end stage renal disease such as IgA nephropathy, nephrotic syndrome, obstructive uropathy, and lupus nephritis. Chronic HD patients who receive HD in the unit were eligible to participate and were included if they completed more than one survey. Exclusion criteria included inability to complete an electronic survey and contraindication to eat by mouth during HD. The children received intradialytic oral nutrition consisting of protein bars and/or food prepared through patient-oriented cooking projects, in keeping with prescribed renal dietary restrictions. Examples of prepared food included pies, sandwich wraps, trail mix, and pizza. They received HD per standard of care and were monitored per institutional protocol. The Institutional Review Board exempted the study due to its quality improvement design, so written informed consent and assent was not required.

Data Collection

All data were collected via pre-dialysis and post-dialysis patient surveys administered to each child, and post-dialysis surveys completed by dialysis nurses. Each child was assigned a unique, de-identified study number. Due to the quality improvement study design with a small sample size at a single institution, no demographic information was collected in the surveys.

Each child recorded which meals they ate prior to HD (breakfast, lunch, snack, or did not eat) and when the most recent meal was (<1 hour, 1–2 hours, or >2 hours prior to HD). They noted if they are hungry before HD. After eating on HD, the children reported if they feel better, the same, or worse. The dialysis nurses recorded if a given subject experienced an adverse effect, defined as hypotension, nausea, or cramping, and when the adverse effect occurred (HD hours 1 – 4).

Statistical Analyses

Survey results were summarized with frequency distributions for categorical variables and median with interquartile range [IQR] for continuous variables. Between-group differences were analysed with McNemar's exact test given the correlated nature of the data, as each patient completed multiple surveys. The predictor variables included all meals eaten prior to dialysis, timing of the most recent meal, and whether the child is hungry before dialysis. The primary outcome measure was development of an adverse effect (hypotension, nausea, or cramping) recorded on the post-HD nurse survey. The secondary outcome measure was a child's self-reported status on the post-HD survey (feel better, feel the same, or feel worse). Generalized estimating equation modelling with a logit link function was used to assess the relationships between the predictors and the outcome measures. Predictors were retained in the model if they remained significant at the $p < 0.05$ level. Statistical analyses were

completed using Enterprise Guide software, Version 7.11 of the SAS System for Windows (SAS Institute Inc., Cary, NC, USA).

Results

Eight children consecutively completed the study for a total of 93 HD sessions and a median of 12.5 surveys per patient [IQR 8.0, 15.0]. The majority of patient surveys (90%) reported eating at least one meal before each dialysis session, with breakfast (60%) being the most common meal (Table 1). Most patient surveys (68%) noted eating 1 or more hours prior to dialysis, and half (52%) stated they were hungry before dialysis.

The majority of HD sessions (80%) had no nurse-reported adverse effects (Figure 1). Hypotension and cramping were the most commonly-experienced adverse effects (8% each). Seventy-four percent of adverse effects occurred during the 3rd hour of dialysis. Pre-HD factors associated with having an adverse effect included feeling hungry (68% vs 47%, $p < 0.001$), eating breakfast (63% vs 59%, $p < 0.001$), and eating 1 hour prior to HD (79% vs 66%, $p < 0.001$), according to bivariate analyses. Only 2% of patient surveys reported feeling worse after eating on HD; all children that reported feeling worse also experienced adverse effects. The majority of patient surveys (72%) reported feeling better after eating on HD, and the likelihood of feeling better did not vary by having an adverse effect (Figure 2). Eating breakfast (100% vs 59%, $p < 0.001$) was associated with feeling worse by bivariate analysis.

Multivariable modelling with generalized estimating equations revealed that feeling hungry before HD was associated with the outcome measures (Table 2). Children who feel hungry before HD were more likely to feel better after eating on HD (OR 4.58, 95% CI 1.5 to 13.92, $p = 0.007$), after controlling for eating lunch before HD. This was despite the fact that those children who feel hungry were more likely to have an adverse effect (2.42, 1.0 to 5.87, $p = 0.05$).

Discussion

The paediatric HD patients in our study tolerate intradialytic oral nutrition without clinically-significant adverse effects. Seventy-two percent of patient surveys report feeling better after eating, while only 2% report feeling worse. The most significant factor associated with feeling better after eating on HD is feeling hungry before HD. This was despite the fact that there was a trend to feeling hungry being associated with having an adverse effect. This finding demonstrates that the adverse effects experienced in our study were well tolerated by our children and did not preclude the utilization of intradialytic oral nutrition.

The reasons for the association between hunger and having an adverse effect are unclear but could be due in part to a child eating a larger amount of food when they are hungry, eating particular foods, or not drinking enough fluid before dialysis (Luciano *et al.* 2010; Jansen *et al.* 1990; Puvi-Rajasingham & Mathias 1996). This association could be mitigated by providing standardized intradialytic oral nutrition or educating patients on what food to eat

before HD. Eating on HD is safe in our population and offers an avenue to provide supplemental nutrition to improve patient outcomes and quality of life.

Hypotension and cramping are the most commonly-reported adverse effects in our study (8% for each), but their clinical significance is quite low, which is consistent with the literature (Weiner *et al.* 2014; Benaroya & Iliescu 2008). As HD became more efficient with more rapid solute and volume removal, hypotension became more common, and was thought in part to be caused by a postprandial fall in systemic vascular resistance (Sherman *et al.* 1988; Blagg 2007). Eating on HD was therefore commonly stopped, especially in centres in the United States. Recently, because of the nutritional benefits and low rate of complications, HD centres are increasingly allowing patients to eat during dialysis (Benner *et al.* 2016). Intradialytic oral nutrition has been shown to improve nutritional markers and outcomes despite adverse effects like hypotension and cramping, including amino acid delivery to muscle, a higher quality of life, and improved mortality (Pupim *et al.* 2006; Vilay & Mueller 2013; Weiner *et al.* 2014). Indeed, intradialytic oral nutrition administration is becoming a routine and first-choice option for HD patients with protein-energy wasting (Kalantar-Zadeh & Ikizler 2013).

Poor growth is an independent risk factor of death in paediatric dialysis patients in particular (Furth *et al.* 2002; Wong *et al.* 2000). Thus paediatric patients stand to benefit the most from a maximized nutritional state. Data are lacking regarding intradialytic oral nutritional supplementation in paediatric HD patients, who are especially at risk for malnutrition (Kaur & Davenport 2014; Kopple 1999). Most studies investigated the use of intradialytic parenteral nutrition, wherein adverse effects such as emesis are uncommon (Krause *et al.* 2002). The present study demonstrates that children on HD feel better with intradialytic oral nutrition with minimal and clinically-insignificant adverse effects, supporting the burgeoning use of routine oral intradialytic nutrition to improve patients' nutritional status and clinical outcomes (Kalantar-Zadeh & Ikizler 2013). Our findings are consistent with a recent study in adults on HD that employed a similar study design and found a minimal effect of mealtime on intradialytic hypotension and no nausea or emesis (Borzou *et al.* 2016). If there is concern for hypotension, the authors suggested that a patient could eat early in the HD treatment to lessen the impact of hypotension. This is consistent with our finding that most adverse effects occur in the third hour of HD.

The strengths of the study include the cross-sectional design, the paediatric population, a large sample of patient surveys, and both nurse-reported and patient-reported outcomes. Limitations of our study include patients from a single centre, lack of randomization with a control group, no standardized or qualitative approach to how food is provided, a lack of measurable nutritional status markers, no demographic or clinical information, and inability to control for potentially-confounding factors. While our patient sample size is small and thus may reduce the ability to generalize our findings, it is representative of a typical large paediatric HD unit.

Application to Practice

Providing meal service in outpatient HD units has the potential to improve the nutritional state of children on HD by ensuring adequate access to a free, nutritionally-balanced meal within the restrictions of a renal diet three to four times a week. Intradialytic meals also promote an improved nutritional state by discouraging skipping meals and by providing opportunities for ongoing nutritional education with children and their families.

Acknowledgments

Funding Source: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Biography

Andrew South is an assistant professor of pediatric nephrology at Wake Forest School of Medicine. His primary research interests are the translational applications of the renin-angiotensin system in renal and cardiovascular disease. His clinical and research interests include quality improvement, dialysis, transplantation, and hypertension.

Abbreviations

HD Haemodialysis

References

- Benaroya M, Iliescu EA. Oral intake during hemodialysis: is there an association with intradialytic hypertension? *Hemodialysis International*. 2008; 12:62–65. [PubMed: 18271843]
- Benner D, Burgess M, Stasios M, et al. In-center nutrition practices of clinics within a large hemodialysis provider in the United States. *Clinical Journal of the American Society of Nephrology*. 2016; 11:770–775. [PubMed: 27084879]
- Benner D, Davis M, Stasios M, et al. Practices and opinions on in-center food consumption across 1,223 facilities in the United States. *Kidney Research and Clinical Practice*. 2012; 31:A60.
- Blagg CR. The early history of dialysis for chronic renal failure in the United States: a view from Seattle. *American Journal of Kidney Diseases*. 2007; 49:482–496. [PubMed: 17336711]
- Borzou SR, Mahdipour F, Oshvandi K, et al. Effect of mealtime during hemodialysis on patients' complications. *Journal of Caring Sciences*. 2016; 5:277–286. [PubMed: 28032072]
- Christner H, Riley M. Should patients eat during hemodialysis treatments? *Nephrology Nursing Journal*. 2008; 35:203–4. [PubMed: 18472688]
- Feroze U, Noori N, Kovesdy CP, et al. Quality-of-life and mortality in hemodialysis patients: roles of race and nutritional status. *Clinical Journal of the American Society of Nephrology*. 2011; 6:1100–1111. [PubMed: 21527646]
- Fouque D, Kalantar-Zadeh K, Kopple J, et al. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. *Kidney International*. 2007; 73:391–398. [PubMed: 18094682]
- Furth LS, Hwang W, Yang C, et al. Growth failure, risk of hospitalization and death for children with end-stage renal disease. *Pediatric Nephrology*. 2002; 17:450–455. [PubMed: 12107811]
- Jansen RWMM, Peeters TL, Van Lier HJJ, et al. The effect of oral glucose, protein, fat and water loading on blood pressure and the gastrointestinal peptides VIP and somatostatin in hypertensive elderly subjects. *European Journal of Clinical Investigation*. 1990; 20:192–198. [PubMed: 1972066]

- Kalantar-Zadeh K, Ikizler TA. Let them eat during dialysis: an overlooked opportunity to improve outcomes in maintenance hemodialysis patients. *Journal of Renal Nutrition*. 2013; 23:157–163. [PubMed: 23313434]
- Kaur A, Davenport A. Hemodialysis for infants, children, and adolescents. *Hemodialysis International*. 2014; 18:573–582. [PubMed: 24725354]
- KDOQI Clinical Practice Guideline for Nutrition in Children with CKD: 2008 Update. *American Journal of Kidney Diseases*. 2009; 53:S11–S104.
- Kistler B, Benner D, Burgess M, et al. To eat or not to eat—international experiences with eating during hemodialysis treatment. *Journal of Renal Nutrition*. 2014; 24:349–352. [PubMed: 25443543]
- Kistler BM, Fitschen PJ, Ikizler TA, et al. Rethinking the restriction on nutrition during hemodialysis treatment. *Journal of Renal Nutrition*. 2015; 25:81–7. [PubMed: 25443693]
- Kopple JD. Pathophysiology of protein-energy wasting in chronic renal failure. *Journal of Nutrition*. 1999; 129:247S–251S. [PubMed: 9915908]
- Krause I, Shamir R, Davidovits M, et al. Intradialytic parenteral nutrition in malnourished children treated with hemodialysis. *Journal of Renal Nutrition*. 2002; 12:55–59. [PubMed: 11823995]
- Lacson E Jr, Wang W, Zebrowski B, et al. Outcomes associated with intradialytic oral nutritional supplements in patients undergoing maintenance hemodialysis: a quality improvement report. *American Journal of Kidney Diseases*. 2012; 60:591–600. [PubMed: 22632807]
- Luciano GL, Brennan MJ, Rothberg MB. Postprandial hypotension. *American Journal of Medicine*. 2010; 123:281.e1–281.e6.
- Paglialonga F, Edefonti A. Nutrition assessment and management in children on peritoneal dialysis. *Pediatric Nephrology*. 2009; 24:721–730. [PubMed: 18253763]
- Pupim LB, Majchrzak KM, Flakoll PJ, et al. Intradialytic oral nutrition improves protein homeostasis in chronic hemodialysis patients with deranged nutritional status. *Journal of the American Society of Nephrology*. 2006; 17:3149–3157. [PubMed: 17021267]
- Puvi-Rajasingham S, Mathias CJ. Effect of meal size on postprandial blood pressure and on postural hypotension in primary autonomic failure. *Clinical Autonomic Research*. 1996; 6:111–114. [PubMed: 8726096]
- Scott MK, Shah NA, Vilay AM, et al. Effects of peridialytic oral supplements on nutritional status and quality of life in chronic hemodialysis patients. *Journal of Renal Nutrition*. 2009; 19:145–52. [PubMed: 19218041]
- Sherman RA, Torres F, Cody RP. Postprandial blood pressure changes during hemodialysis. *American Journal of Kidney Diseases*. 1988; 12:37–9. [PubMed: 3389352]
- Vilay AM, Mueller BA. Intradialytic oral nutritional supplements improve quality of life. *American Journal of Kidney Diseases*. 2013; 61:349.
- Weiner DE, Tighiouart H, Ladik V, et al. Oral intradialytic nutritional supplement use and mortality in hemodialysis patients. *American Journal of Kidney Diseases*. 2014; 63:276–85. [PubMed: 24094606]
- Wong CS, Gipson DS, Gillen DL, et al. Anthropometric measures and risk of death in children with end-stage renal disease. *American Journal of Kidney Diseases*. 2000; 36:811–819. [PubMed: 11007685]
- Zioni N. Improving the nutritional condition of infants and young children undergoing hemodialysis. *Journal of Renal Care*. 2007; 33:11–16. [PubMed: 17695555]

Figure 1.
Nurse-Reported Post-Haemodialysis Adverse Effects

Figure 2.
Patient-Reported Post-Haemodialysis Survey Results by the Presence of Adverse Effects
Percent feeling better, the same, or worse after eating on haemodialysis

Table 1

Patient Pre-HD Survey Results by Adverse Effect

		Adverse Effect 19 (20%)	No Adverse Effect 74 (80%)
Hungry	47 (52%)	13 (68%)*	34 (47%)
Pre-HD Meals			
Breakfast	56 (60%)	12 (63%)*	44 (59%)
Lunch	35 (38%)	5 (26%)	30 (41%)
Snack	15 (16%)	1 (5%)	14 (19%)
Did Not Eat	9 (10%)	4 (21%)	5 (7%)
Last Meal 1 Hour	63 (68%)	15 (79%)*	48 (66%)

N(%). Hemodialysis (HD).

* Significant at $p < 0.05$ by McNemar's exact test.

Table 2

Factors Associated with Adverse Effects and Feeling Better

	OR (95% CI)	p Value
<u>Adverse Effects</u>		
Hungry	2.42 (1.0 to 5.87)	0.05
<u>Feel Better</u> *		
Hungry	4.58 (1.5 to 13.92)	0.007

Generalized estimating equation modelling.

* Controlling for eating lunch before HD.