Dialysis Nutrient Losses and Malnutrition

Annual Dialysis Conference, March 2023

Laura Quenneville, RD

CHEO

Objectives

Review:

- Clearance of key water-soluble and trace elements during dialysis
- Signs and risk for deficiency
- Recommended dosage for supplementation (maintenance & repletion)
- Risk of malnutrition in dialysis patient

Children's Hospital of Eastern Ontario Ottawa, Canada

Important Facts

- Most studies have been done on CRRT patients when looking at dialysis population
- Absence of data on ideal vitamin and trace element intakes in infants/children with advance renal disease
- NKF-KDOQI clinical practice guidelines for nutrition in children with CKD detail daily vitamin and trace element needs based on general pediatric population
- Pediatric Renal Nutrition Taskforce: Clinical Practice Recommendations

Dialysis Definitions:

- “A procedure to remove waste products and excess fluid from the blood when the kidneys stop working properly”
- “Process of removing excess water, solutes, and toxins from the blood”
- “Separation of particles in a liquid on the basis of differences in their ability to pass through a membrane”
- “Clinical purification of blood by dialysis, as a substitute for the normal function of the kidney”

- **Filtration-based technique that removes waste BUT also other substances that may not be present within the dialysate like water-soluble vitamins and trace elements.**

Pediatr Nephrol. Author manuscript; available in PMC 2019 Jul 1.
Published in final edited form as:
Pediatr Nephrol. 2018 Jul; 33(7): 1133–1143.
Published online 2017 Jul 27. doi: 10.1007/s00467-017-3751-z

PMCID: PMC5787050
NIHMSID: NIHMS896118
PMID: 28752387

Vitamin and trace element deficiencies in the pediatric dialysis patient

Lyndsay A. Harshman, Kathy Lee-Son, and Jennifer G. Jetton

Curr Opin Crit Care. 2021 Aug; 27(4): 367–377.
Published online 2021 May 25. doi: 10.1097/MCC.0000000000000851

PMCID: PMC8270509
PMID: 34039873

Nutrients and micronutrients at risk during renal replacement therapy: a scoping review

Mette M. Berger,[a] Marcus Broman,[b] Lui Forni,[c] Marlies Ostermann,[d] Elisabeth De Waele,[e] and Paul E. Wischmeyer[f]

Clearance of Key Nutrients During : Chronic Hemodialysis

Vitamins

- **Thiamine (B1), Pyridoxine (B6), Folate (B9),**
  - Small to middle range molecule, cleared easily by dialysis.
  - B6: necessary for EPO → RBC formation
  - Folic acid = > risk of deficiency if using high flux membrane

- **Vitamin C**
  - >100 mg removed per HD session
  - ↓ plasma level (30-50%)

Clearance of Key Nutrients During : Chronic Hemodialysis

Trace elements

- **Zinc**
  - Decreased intake with prog of CKD + losses with HD = > risk of deficiency
  - Lack of protein-binding→ removed at higher rate than other trace elements but can be falsely low if albumin is low
- **Selenium**
  - Deficiency not as clear if caused by poor nutritional intake and/or increased inflammatory process rather than increased clearance
  - A recent scoping review : selenium is high risk for depletion*
- **Magnesium**: tends to be normal (to mildly high)

Clearance of Key Nutrients During : Peritoneal Dialysis

Vitamins

- Pyridoxine (B6), Folic Acid (B9)
- Thiamine (B1): CAPD Less Clearance
- Vitamin C
  - Adults: High Clearance
  - More Dialysis = > Losses

Trace elements

- Less information when compared to water-soluble vitamins
- Selenium and zinc losses on PD does not appear to be significant

Clearance of Key Nutrients During : CRRT

Vitamins

- Adult studies, losses estimated to:
  - Vitamin C: 70 mg/d (DRI: 15-25 mg/45-90 mg/75-90 mg)
  - Folic acid: 290 mcg/d (DRI: 150-200 mcg/300-400 mcg/400 mcg)
  - Thiamine: 4 mg/d *if prolonged CRRT in critically ill – significant losses (DRI: 0.5 mg/0.9 mg/1.1-1.2 mg)

Trace elements

- Selenium: risk of depletion
  - May need more in TPN

Vitamin and trace element deficiencies in the pediatric dialysis patient. *Pediatr Nephrol* 33, 1133–1143 (2018)

Fat-soluble vitamins?

- Vitamin A
  - Not removed by dialysis
  - Serum levels are 2-5 times higher in dialysis patients
  - Symptoms of toxicity: hypercalcemia, anemia, hyper TG and ↑Alk Phos
  - Supplementation not recommended + not to exceed DRI
- Vitamin E
  - Not removed by dialysis
  - Not to exceed DRI
- Vitamin K
  - Deficiency is rare and dialysis patients are usually not deficient

Kidney Int. 2012 Sep;82(5):605-10. doi: 10.1038/ki.2012.191. Epub 2012 May 30.

Vitamin K intake and status are low in hemodialysis patients

Ellen C M Cranenburg [1], Leon J Schurgers, Herma H Uiterwijk, Joline W J Beulens, Gerdien W Dalmeijer, Ralf Westerhuis, Elke J Magdeleyns, Marjolein Herfs, Cees Vermeer, Gozewijn D Laverman

Abstract

Vitamin K is essential for the activity of γ-carboxyglutamate (Gla)-proteins including matrix Gla28 protein and osteocalcin; an inhibitor of vascular calcification and a bone matrix protein, respectively. Insufficient vitamin K intake leads to the production of non-carboxylated, inactive proteins and this could contribute to the high risk of vascular calcification in hemodialysis patients. To help resolve this, we measured vitamin K(1) and K(2) intake (4-day food record), and the vitamin K status in 40 hemodialysis patients. The intake was low in these patients (median 140 µg/day), especially on days of dialysis and the weekend as compared to intakes reported in a reference population of healthy adults (mean K(1) and K(2) intake 200 µg/day and 31 µg/day, respectively). Non-carboxylated bone and coagulation proteins were found to be elevated in 33 hemodialysis patients, indicating subclinical hepatic vitamin K deficiency. Additionally, very high non-carboxylated matrix Gla28 protein levels, endemic to all patients, suggest vascular vitamin K deficiency. Thus, compared to healthy individuals, hemodialysis patients have a poor overall vitamin K status due to low intake. A randomized controlled trial is needed to test whether vitamin K supplementation reduces the risk of arterial calcification and mortality in hemodialysis patients.

Functional deficiency of vitamin K in hemodialysis patients in Upper Silesia in Poland.

Wyskida K, Żak-Gołąb A, Wajda J, Klein D, Witkowicz J, Ficek R, Rotkegel S, Spiechowicz U, Kocemba Dyczek J, Ciepał J, Olszanecka-Glinianowicz M, Więcek A, Chudek J.

Int Urol Nephrol. 2016 May;48(5):765-71. doi: 10.1007/s11255-016-1255-6. Epub 2016 Mar 21.

PMID: 27000106 **Free PMC article.**

Low vitamin K1 intake in haemodialysis patients.

Fusaro M, D'Alessandro C, Noale M, Tripepi G, Plebani M, Veronese N, Iervasi G, Giannini S, Rossini M, Tarroni G, Lucatello S, Vianello A, Santinello I, Bonfante L, Fabris F, Sella S, Piccoli A, Naso A, Ciurlino D, Aghi A, Gallieni M, Cupisti A.

Clin Nutr. 2017 Apr;36(2):601-607. doi: 10.1016/j.clnu.2016.04.024. Epub 2016 Apr 28.

PMID: 27234935

New Therapeutics Targeting Arterial Media Calcification: Friend or Foe for Bone Mineralization?

Van den Branden A, Verhulst A, D'Haese PC, Opdebeeck B.

Metabolites. 2022 Apr 5;12(4):327. doi: 10.3390/metabo12040327.

PMID: 35448514 **Free PMC article.** Review.

Review > Curr Opin Nephrol Hypertens. 2021 Jul 1;30(4):430-436.

doi: 10.1097/MNH.0000000000000712.

Vitamin K and vascular calcification

Jennifer S Lees [1], Patrick B Mark [1], Miles D Witham [2]

Treatment of Vitamin K Deficiency in Hemodialysis Patients - A Pilot Study Comparing Menaquinone-7 Tablets and a Vitamin K Rich Diet.

Lentz KA, Vahlgren J, Hansen D, Plebani M, Fusaro M, Rasmussen LM, Jakobsen J, Sloth JJ, Post Hansen H, Andersen JR.

Int J Nephrol Renovasc Dis. 2022 Oct 17;15:267-276. doi: 10.2147/IJNRD.S365912. eCollection 2022.

In Summary

- Thiamine (B1) cleared more readily by HD than PD
- Risk of thiamine (B1) deficiency is higher in critically ill dialysis pts (HD or CRRT) especially if pre-existent malnutrition and long term high CHO TPN
- Vitamin C cleared by HD and PD
  - Adult studies showed lower vitamin C levels in HD
  - Pediatric data showed pts with ESRD with normal C levels if adequate intake from well tolerated EN + supplemented with water soluble vitamins
- Zinc levels are more likely to be lower in maintenance HD
- Selenium: HD and CRRT patients at higher risk for deficiency

Symptoms of deficiency
&
Nutritional sources

3a - Overview of water soluble vitamin and trace minerals at risk for deficiency in the pediatric dialysis population

Nutrient	Symptoms of Deficiency	Dietary Sources	Diagnostic Tests
Thiamine (B1)	"Wernicke encephalopathy" – peripheral neuropathy, ophthalmoplegia, nystagmus, ataxia, edema	dairy, nuts, legumes, fruits, egg, unrefined grains, pork, vegetables	Thiamine pyrophosphate level, whole blood/red blood cell transketolase activation test
Pyridoxine (B6)	Facial seborrhea, glossitis, angular stomatitis, cheilosis, mental status changes	Fortified cereals	Pyridoxal 5′-phosphate 4-pyridoxic acid
Folate (B9)	Abdominal cramps, nausea, diarrhea, irritability, poor sleep, seizures, megaloblastic anemia	Green vegetables, liver, grains, some fruits	Acute deficiency – low serum folate Chronic deficiency – low red blood cell folate
Vitamin C (ascorbic acid)	"Scurvy" – osmotic diarrhea, gingival bleeding, perifollicular hemorrhage, long-bone changes (arthropathy)	Citrus fruits	White blood cell ascorbate concentration, radiographic evidence of long bone widening

1. Vitamin and trace element deficiencies in the pediatric dialysis patient, Harshman, Lee-Son, Jetton, Pediatr Nephrol. 2018

Zinc	Clinical phenotype of "Acrodermatitis enteropathica" – anorexia, hypogeusia, growth retardation, diffuse skin lesions with impaired wound healing	Meat, dairy, legumes, whole grains, oysters	Blood zinc level
Selenium	"Keshan disease" – progressive cardiomyopathy, cardiovascular disease with thyroid disease, also with myositis	Meats, seafood, nuts	Blood selenium level

1. Vitamin and trace element deficiencies in the pediatric dialysis patient, Harshman, Lee-Son, Jetton, Pediatr Nephrol. 2018

Dosing of vitamins and minerals

3b – Repletion dosing for vitamin and trace mineral deficiencies in the general pediatric population^^	
Thiamine (B1)	Children:10–25 mg/day parenterally x 1–2 wk, followed by 5 mg PO for 6 weeks [90]
Pyridoxine (B6)	5–25 mg/day of oral pyridoxine x 3 weeks, followed by 2.5–5 mg/day orally via multivitamin
Folate (B9)	Deficiency in infants: 0.1 mg/kg/day oral administration daily Deficiency in children: 1.0 mg oral administration daily, followed by 0.1 to 0.5 mg daily maintenance dosing.
Vitamin C	100 mg orally, intramuscularly, or intravenously 3x per day x 1 week, followed by 100 mg daily [91]
Zinc	Supplementation trial with 1 mg/kg; can increase to 2 mg/kg BID-TID [92]
Selenium	2 mcg/kg/day IV selenium for repletion followed by 1 mcg/kg/day as maintenance therapy for goal of serum level of 50–150 mcg/L [93]

1. Vitamin and trace element deficiencies in the pediatric dialysis patient, Harshman, Lee-Son, Jetton, Pediatr Nephrol. 2018

ADULTS		
	Interesting Facts	Dose
Thiamine (B1)		5-10 mg TID (when deficient)
Pyridoxine (B6)	• ↑needs with ↑ protein intake, hepatic disease, cancer and HIV/AIDS	10 mg/day (to replace dialysis losses)
Folate (B9)	• B12, Vitamin C, Fe deficiency inhibits folate metabolism • Long term use of folic acid can deplete zinc and Vitamin B12 levels	1 mg/day (for all dialysis patients)
Cyanocobalamin (B12)	• Use of supplemental folic acid can mask Vitamin B12 deficiency • Renal MVI does not contain adequate B12 to treat deficiency	250-1200 mcg/day (Pernicious anemia and B12 Deficiency)
Vitamin C	• May be contraindicated if history oxalate kidney stones	60-100 mg/day
Zinc	• 40 mg/day supp can cause copper depletion > 50-100 mg/day can increase LDL	25-40 mg zinc for 10 days to 6 weeks for wound healing when zinc deficiency is suspected
Selenium	• Dosages of 75 mcg were not enough to correct blood concentrations in deficient dialysis patients	DRI: 40-55 mcg/day (adults) *DRI: 20-40 mcg/day (children)*

Suggested Blood Work Protocol

- Initial
  - Depending on patients nutritional history and risk of malnutrition
  - B12, Folate, *other B & fat soluble*
  - Trace elements: selenium, copper and zinc
- Monthly
  - Iron, Ferritin, Mag
  - Could move to Q6Months:
    - Full lipid panel, vitamin D
- Q6 months
  - Lipid panel
  - Vitamin D
  - B12 and Folate
- Q12 months (pt's' birthday?)
  - Water-soluble: C
  - Fat-soluble: A, E, K
  - Trace elements: selenium, copper, zinc
- As needed
  - If suspected deficiency
  - Can be ordered by Md, RN or RD (medical directive)

High Risk For Nutritional Deficiencies

- Dialysis: removing more than accumulated waste products

- Multiple food restrictions can lead to deficiencies
  - Low potassium = higher chances of vitamin C deficiencies, less fiber
  - Limited protein intake = lower intake of minerals such as iron, zinc and selenium
  - Low phosphate = poor calcium and vitamin D intake

- Other impacts of nutritional restrictions:
  - Meals are not as appetizing, less interest towards food, lack of variety
  - Poor growth and higher risk of malnutrition

- And what if we have a selective or picky eater ?

Malnutrition

- WHO: “Inadequate or excessive intake of protein, energy and micronutrients such as vitamins, and the frequent infections and disorders that results”

- Malnutrition assessment should include:
  - Medical conditions history and symptoms
  - Diet history: dietary prescription adherence, food intolerances/allergies
  - Medication/supplements that could impact absorption of nutrients
  - Physical exam (weight/height/BMI, skin, hair, nails, mouth, etc)

- Challenging diagnosis: between true malnutrition & inflammation
  - Both can coexist in same patient
  - Chronic inflammation can lead to protein depletion in muscle, fat wasting, hypoalbuminemia and hypercatabolism.

Malnutrition

	Protein-Calorie Malnutrition	Inflammatory Wasting
Weight loss	+++	+ to +++
Physical signs of loss of lean mass	+++	+/- to +++
↓ serum albumin	+/-	+++
Improvement with proper feeding	+++	+/-

Adapted from “Medical management of the dialysis patient: Nutritional Assessment and Support”, Friedman, Nephrology Hypertension

Malnutrition in Dialysis Population?

- Predisposition of dialysis population to malnutrition
  - Depends on socioeconomic factors
  - Effect of uremia, endocrine and GI disorders
  - The origin of protein-energy malnutrition (PEM) appears to precede dialysis
    - Decreased appetite + multiple food restrictions
  - Effect of dialysis
    - Leading to protein breakdown/muscle protein loss
    - Increased requirements if peritonitis

Assessment: What, How and When?

WHAT	HOW	WHEN
Food Recall	3-5 days (short: 24 hr)	Minimally Q2-6 months
MUAC	Non dominant, same side	Q6 months
SGA	Dialysis-centric version?	PRN?
BIA	Pre-HD treatment	As per clinical judgment - Limiting factors*
BMI Dry weight	Weight/height - Trend Trend	Monthly or often if needed
nPCR	Various calculator available/look at trend!	Monthly
Laboratory Values		
Nutritional Supplements	PO or EN	
IV	IDPN or TPN	
Appetite Stimulant	Not typically used	Consider more liberal diet before

What about Carnitine?

The role of carnitine in maintenance dialysis therapy

Heather A. Morgans, Vimal Chadha & Bradley A. Warady

Pediatric Nephrology **36**, 2545–2551 (2021) | Cite this article

- "Current literature in the adult and pediatric dialysis populations suggest a high prevalence of carnitine deficiency, which may lead to erythropoietin-resistant anemia, cardiomyopathy, and muscle weakness"

Elizabeth Harvey Carnitine poster – PDF

Carnitine supplementation in dialysis patients protocol draft - PDF

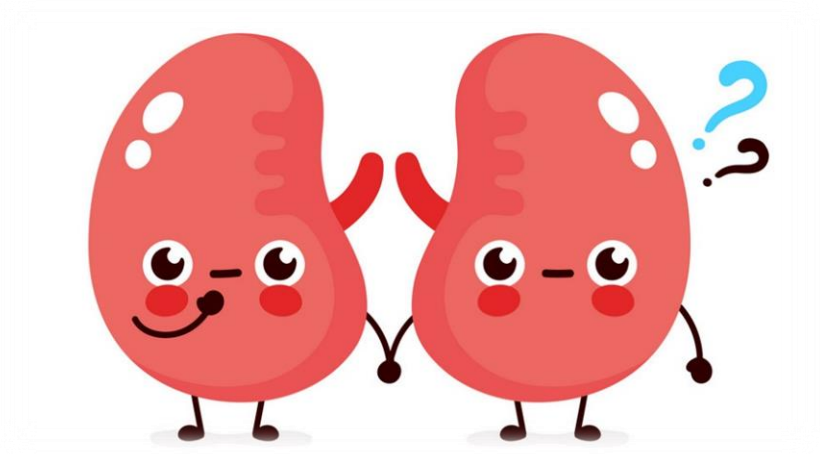
Conclusion

- Malnutrition in CKD: Protein Energy Wasting and Micronutrient Deficiency
- Early screening for malnutrition to be done prior to dialysis start
- Initial blood work as per “protocol” established in your center
- Renal Multivitamin
  - **To be considered** if inadequate nutrition intake pre dialysis
  - **May be recommended** to replace water-soluble vitamins loss during dialysis

- Ideal situation – if you have enough FTE and funding:
  - Malnutrition Assessment Tool: Subjective Global Assessment questionnaire
  - Regular follow ups with dietitians (including nutrition-focus physical exam)
  - Budget for cooking activities – food insecurity

References

- Harshman, L.A., Lee-Son, K. & Jetton, J.G. Vitamin and trace element deficiencies in the pediatric dialysis patient. *Pediatr Nephrol* 33, 1133–1143 (2018). https://doi.org/10.1007/s00467-017-3751-z
- Resty Varia Tutupoho, Ninik Asmaningsih and Risky Vitria Prasetyo , Association of malnutrition with renal function in children with kidney disease, GSC biological and pharmaceutical sciences, 17 (03), 100-106 (2021)
- CAND, The Essential Guide for Renal Dietitians, 4th edition (2020)
- Allon Friedman, Medical management of the dialysis patient Nutritional assessment and support, Renal & Urology News (2019)
- Kamyar Kalantar-Zadeh and Joel D. Kopple, Trace Elements and Vitamins in Maintenance Dialysis Patients, Advances in Renal Replacement Therapy, Vol 10, No 3 (July): pp 170-182 (2003)
- Byham-Gray, Laura, D-Burrowes, Jerrilynn and M.Chertow, Glenn, Nutrition in Kidney Disease, Nutrition and Health (2008)
- Mette M.Berger, Marcus Broman, Lui Forni, Marlies Ostermann, Elisabteh De Waele and Paul E. Wishchmeyer, Nutrients and micronutrients at risk during renal replacement therapy: a scoping review, Current Opinion critical care (2021)
- Morgans, H.A., Chadha, V. & Warady, B.A. The role of carnitine in maintenance dialysis therapy. *Pediatr Nephrol* 36, 2545–2551 (2021)
- https://www.albertahealthservices.ca/assets/info/nutrition/if-nfs-ng-renal.pdf
- http://www.bcrenal.ca/resource-gallery/Documents/CKDreplavite_updated_Nov_2011%20(1).pdf



Questions & Comments?

CHEO