

# Supplements in CKD



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1400/10/14

# Introduction

- Dialysis Outcomes and Practice Patterns Study (DOPPS): **>70% of MHD patients** in the U.S. **take supplements.**
- **Insufficient evidence** whether micronutrients or **multivitamin supplementation is beneficial or detrimental** in this population.

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- Despite most guidelines that recommend multivitamin supplements for dialysis patients, **insufficient evidence to support routine multivitamin use in hemodialysis patients.**

Brenner and Rector's the kidney-2018- ch. 60

# Supplements in CKD

Supplements	
Folic acid	Vitamin E (fat- soluble)
Thiamine	Vitamin K (fat- soluble)
Riboflavin	Zinc
Vitamin B6	Selenium
Vitamin B12	Probiotics
Vitamin C	Ketoanaloges
Vitamin A (fat- soluble)	Omega-3
Vitamin D (fat- soluble)	CoQ10

# FOLIC ACID- vitamin B complex

- **Folic Acid Supplementation for Hyperhomocysteinemia :**  
we recommend **not to routinely supplement folate with or without B-complex** since there is no evidence demonstrating reduction in adverse cardiovascular outcomes (1A).
- **Folic Acid Supplementation for Folic Acid Deficiency and Insufficiency :**  
In adults with CKD 1-5D (2B) or posttransplantation (OPINION), we suggest **prescribing folate, vitamin B12, and/or B-complex** supplement to correct for folate or vitamin B12 deficiency/insufficiency based on **clinical signs and symptoms** (2B).



# Vitamin C

## Vitamin C Supplementation:

- In adults with CKD 1-5D or posttransplantation who are at **risk of vitamin C deficiency**, it is reasonable to consider **supplementation** to meet the recommended intake of **at least 90 mg/d for men and 75 mg/d for women** (OPINION).



# Vitamin D

**Vitamin D Supplementation for Vitamin D Deficiency and Insufficiency:**  
**CKD 1-5D (2C) or posttransplantation** (OPINION), we suggest prescribing vitamin D supplementation in the form of **cholecalciferol or ergocalciferol** to correct 25-hydroxyvitamin D (25(OH)D) deficiency/insufficiency.

## **Vitamin D Supplementation with Proteinuria:**

CKD 1-5 with **nephrotic range proteinuria**, it is reasonable to consider supplementation of **cholecalciferol, ergocalciferol**, or other safe and effective 25(OH)D precursors (OPINION).

**Vitamin D** supplementation had **no effect on calcium or phosphorus levels.**

# Vitamin D





# Vitamins A and E

## **Vitamins A and E Supplementation and Toxicity:**

- High doses of vitamin A causes anemia, abnormalities of lipid and calcium metabolism. Daugirdas JT, handbook of dialysis, 2015
- Vitamin E is a fat-soluble nutrient recognized for **antioxidant properties**.
- There are 8 known forms of vitamin E, but **alpha-tocopherol is the only known form of vitamin E found in plasma**.
- Serum **vitamin E** levels provided **protection to erythrocyte survival** when **exposed to hydrogen peroxide**.

# Vitamins A and E...

## Vitamins A and E Supplementation and Toxicity:

- High doses of vitamin E increase the risk for hemorrhagic stroke and impair platelet aggregation.
- Vitamin E interacts with anticoagulant and antiplatelet medications
- Caution for patients with CKD already receiving these medications.
- Oral doses  $\geq 400$  IU of vitamin E are not recommended without intermittent monitoring of serum vitamin E levels.

# Vitamins A and E..

## Vitamins A and E Supplementation and Toxicity:

- CKD 5D on MHD or on PD, **not routinely supplement vitamin A or E** because of the potential for **vitamin toxicity**.
- If warranted should be monitored for toxicity (OPINION).
- Monitoring and Evaluation:  
**Platelet count**, changes in **medical status**, **medications**, and **nutritional status**.

# Vitamin E, A



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Chronic Kidney Disease (CKD)

**Each Tablet Contains :**

Vitamin B12	6 mcg
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Vitamin B2	1.7 mg
Vitamin B6	10 mg
Vitamin E	50 IU
Vitamin B5	10 mg
Ascorbic Acid	60 mg
Biotin	300 mcg
Zinc (as Zinc Oxide)	25 mg
Niacinamide	20 mg
Folic Acid	500 mcg

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**هر قرص روکشدار حاوی :**

ویتامین ب ۱	۱.۵ میلی گرم
ویتامین ب ۲	۱.۷ میلی گرم
ویتامین ب ۳ (نیاسینامید)	۲۰ میلی گرم
ویتامین ب ۵	۱۰ میلی گرم
ویتامین ب ۶	۱۰ میلی گرم
ویتامین ب ۱۲	۶ میکرو گرم
بیوتین	۳۰۰ میکرو گرم
ویتامین ای	۵۰ میلی گرم
اسید اسکوربیک	۶۰ میلی گرم
زینک	۲۵ میلی گرم
اسید فولیک	۱ میلی گرم

- دارو را در دمای کمتر از ۳۰ درجه سانتیگراد، دور از نور و رطوبت و داخل جعبه اصلی نگهداری نمایید.
- قبل از مصرف، برگه راهنمای درون جعبه را به دقت مطالعه نمایید.
- دارو را دور از دسترس کودکان نگهداری نمایید.
- اثربخشی درمانی این فرآورده به تایید سازمان غذا و دارو نرسیده است.

دستور پزشک:

قیمت برای مصرف کننده:

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مولتی ویتامین CKD (بیماریهای مزمن کلیوی)

مکمل تغذیه ای

بدون قند

۱۰۰ قرص روکش دار

هر قرص روکشدار حاوی

۶ میکرو گرم	ویتامین ب ۱۲
۱/۵ میلی گرم	ویتامین ب ۱
۱/۷ میلی گرم	ویتامین ب ۲
۱۰ میلی گرم	ویتامین ب ۶
۵۰ میلی گرم	ویتامین ای
۱۰ میلی گرم	ویتامین ب ۵
۶۰ میلی گرم	اسید اسکوربیک
۳۰۰ میکرو گرم	بیوتین
۲۵ میلی گرم	زینک (به صورت زینک اکساید)
۲۰ میلی گرم	نیکوتینامید
۵۰۰ میکرو گرم	اسید فولیک

Vitamin A	None
β-carotene	None
Retinol	None
Thiamine (mg)	1.5
Riboflavin (mg)	1.7
Vitamin B6 (mg)	10
Vitamin B12 (mg)	0.006
Niacin (mg)	20
Folic acid (mg)	>1.0
Pantothenic acid (mg)	10
Biotin (mg)	0.3
Vitamin C (mg)	60–100
Vitamin E	None
Vitamin D	See Chapter 36
Vitamin K	See text

Daily dietary recommended for dialysis patients (handbook of dialysis-2015)

# Vitamin K

## Anticoagulant Medication and Vitamin K Supplementation

- **72.1%** of adults with mild to moderate **CKD** (eGFR [CKD-EPI]: 58 mL/min) had vitamin K intake below the recommended adequate intake level.
- In **MHD** patients, **vitamin K intake and serum vitamin K levels** are often **low or undetectable**
- **CKD 1-5D or posttransplantation patients receiving anticoagulant medicines** known to inhibit vitamin K activity (eg, warfarin compounds) **do not receive vitamin K supplements (OPINION).**

# Vitamin K

## Anticoagulant Medication and Vitamin K Supplementation

- Vitamin K also enables normal calcification processes in bone and soft tissues.
- Matrix Gla protein (MGP) is a vitamin K–dependent protein produced by vascular smooth muscle cells that is a powerful inhibitor of vascular calcification
- Patients receiving antibiotics who have poor intake and are at higher risk for bleeding (eg, surgical patients) may be considered for vitamin K supplements, particularly if they have acute kidney injury or CKD



# Vitamin K

- **Anticoagulant Medication and Vitamin K Supplementation**

. Large doses of vitamin E may induce vitamin K deficiency. (Mol Nutr Food Res. 2014;58(8):1590-1600)

- ویتامین K1 یا phytonadione: آمپول 10 و 1 میلیگرم- قرص 10 میلیگرم



# Selenium and Zinc

## Selenium and Zinc Supplementation

- CKD 1-5D, we suggest to **not routinely supplement selenium or zinc** since there is little evidence that it improves **nutritional, inflammatory, or micronutrient** status (2C).
- **Selenium**: trace element, **antioxidant properties**, cofactor for the reduction in antioxidant enzymes such as glutathione peroxidase and thus protects against oxidation.



# Selenium and Zinc ..

## Zinc Supplementation

Zinc is a component of biomembranes.

- Antioxidant and anti-inflammatory effects and prevents free radical–induced injury during inflammation.
- Protect against atherosclerosis by inhibiting the oxidation of LDL-C in animal studies.
- Essential for insulin synthesis, and zinc deficiency has been suggested to impair insulin secretion and decrease leptin levels.
- A high prevalence of zinc deficiency in HD patients.

# Selenium and Zinc..



# KETOANALOGS

- Ketoacids (KAs) used for > 40 years to supplement low protein diets (LPDs) for CKD patients.
- KAs lack the amino group of an amino acid, converted to their respective amino acids without providing additional nitrogen.
- Thus when a person consumes KA analogues of EAAs, increasing the respective EAA.
- KA/EAA-supplemented VLPDs (~ 0.3 to 0.4 g/kg/d) or (~ 20-28 g/d) of protein of miscellaneous biological value generate lesser amounts of metabolic products of nitrogen metabolism

# ketoanalogs

- **Low protein diets** (0.6-0.8 g/kg/day), sometimes supplemented **with non-nitrogen ketoanalogs**, have been associated with **slower GFR decline**.
- Some patients with intakes below 0.8 g/kg/bw/day, even the described minimum level of **0.6 g/kg/day**, develop **protein energy wasting** and **increased mortality**.
- **Animal-based dietary protein** is associated with the production of **high levels of gut-derived substances** which are putative **kidney toxins**.

# Protein restriction plus KA supplement

CKD patients with eGFR < 20 mL/min/1.73 m<sup>2</sup> (without diabetes, not dialysis), **a very LPD (VLPD) 0.28 to 0.43 g protein/kg /day with the addition of KAs** to meet protein requirements **may be recommended.**

# Protein restriction plus KA supplement

## Could

- **Preserve kidney function** in patients with stages 3-5 CKD.
- **Decrease serum phosphate** levels and **improve** some markers of bone metabolism (**calcium and PTH**)
- **Improve serum lipid** profiles.

**No significant effect on serum albumin** levels and **nutritional status** (SGA[Subjective Global Assessment] and anthropometry) were inconclusive.

**An LPD/VLPD plus KA should not be started during a catabolic state** in patients with CKD.



# ketoanalogs

## **Potential benefits of KA/EAA supplemented LPDs:**

1. Enables protein-energy status to be maintained with very low protein diets.
2. Reduces metabolic waste products leading to reduced uremia and ? slower GFR loss.
3. KA of leucine may decrease protein degradation and enhance protein synthesis.
4. LPDs decrease phosphorous and potassium intake
5. Possible phosphate binding by the calcium salt of the KA.
6. Reduced acid load from the lower protein intake.

# ketoanalogs

- Very low protein intake, **0.4 g/kg/day**, **13% reduced risk of progression to ESKD** in the **very low protein intake versus the low protein intake** groups
- **Cost** is the single most obtrusive **barrier to KAs** becoming a consistent strategy of nutritional care in a population that strongly requires fastidious intervention.

عدد 100 = 280.000-370.000



# PROBIOTICS

- **Probiotics:** live microorganisms which when administered in adequate amounts confer a health benefit on the host.
- The probiotics could provide the nutrients for colonic epithelial cells and help to maintain the intestinal microbial balance.
- In CKD: active secretion of uric acid and oxalate into colon.
- Gut microbiota bacteria, plays a vital role in the pathogenesis and metabolic disturbance of CKD.

# Probiotics...

## Microbial analysis of CKD:

1. The heavy **expansion of bacteria possessing urease**, uricase, p-cresol and indole-forming enzymes.
2. **Decreased** production of **beneficial micronutrients**,
3. **Increased** generation of **toxic solutes** and
4. Microbial **dysbiosis** could accelerate the **progression of CKD**.

Probiotics are ineffective or less effective to reduce circulating uremic toxins.

# Dysbiosis

- ***An imbalance between the types of organism present in a person's natural microflora***, especially that of the gut, thought to contribute to a range of conditions of ill health.

# Prebiotics

## Prebiotics: nonliving indigestible fibers

- May stimulate the growth and/or activity of beneficial microorganisms in the gut.
- Favor the proliferation of bacteria such as bifidobacteria and lactobacilli
- In CKD, mitigating the production of colon-derived uremic solutes
- Increasing the production of short-chain fatty acids (SCFAs), which can reduce inflammation.

probiotics with prebiotics named **synbiotics**.

*Nephrology* 24 (2019) 1122–1130

Original Article

## Effects of probiotic supplements on the progression of chronic kidney disease: A meta-analysis

SIBEI TAO,<sup>1</sup> SIYING TAO,<sup>2</sup> YIMING CHENG,<sup>1</sup> JING LIU,<sup>1</sup> LIANG MA<sup>1</sup> and PING FU<sup>1</sup>

<sup>1</sup>Kidney Research Laboratory, Division of Nephrology, National Clinical Research Center for Geriatrics, West China Hospital of Sichuan University, and <sup>2</sup>State Key Laboratory of Oral Diseases, National Clinical Research Center for Oral Diseases, Department of Cardiology and Endodontics, West China Hospital of Stomatology, Sichuan University, Chengdu, China

- A systematic search, evaluating the effects of probiotic supplements on CKD were included.
- A total of 10 randomized controlled trials in 8 countries were selected.
- In the meta-analysis, **urea level was significantly reduced in probiotics-administrated non-dialysis patients.**

*Nephrology* 24 (2019) 1122–1130

Original Article

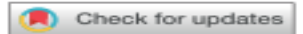
## **Effects of probiotic supplements on the progression of chronic kidney disease: A meta-analysis**

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- **No meaningful impacts** on the reduction of **uric acid**, **C-reactive protein**, **creatinine** and estimated glomerular filtration rate (**eGFR**) preservation of CKD population.



REVIEW



## Probiotics, prebiotics, and synbiotics for the improvement of metabolic profiles in patients with chronic kidney disease: A systematic review and meta-analysis of randomized controlled trials

Hui Juan Zheng<sup>a\*</sup>, Jing Guo<sup>a\*</sup>, Qihong Wang<sup>b\*</sup>, Liansheng Wang<sup>c</sup>, Yahui Wang<sup>a</sup>, Fan Zhang<sup>a</sup>, Wei-Jun Huang<sup>a</sup>, Wenting Zhang<sup>a</sup>, Wei Jing Liu<sup>a</sup>, and Yaoxian Wang<sup>a</sup>

13 RCT were met their inclusion criteria (7 from Iran).

Results: supplementation with **probiotics, prebiotics, and synbiotics** could

- **Decrease pro-inflammatory biomarker (CRP),**
- **Improve the oxidative unbalance,**
- **Ameliorate the lipid profile (TC, HDL, and LDL),** when compared with placebo groups,
- **Did not affect on TG in CKD patients.**



# Omega-3

- Plant-based foods which contain omega 3 polyunsaturated fatty acids, **high intake** of which has been associated **with reduced CKD risk.**

# Long Chain Omega-3 Polyunsaturated Fatty Acids (LC n-3 PUFA)

1. Long chain **omega-3 polyunsaturated fatty acids** (LC n-3 PUFAs) are obtained from **dietary sources** such as **cold-water fish** (ie, fish oil) or **linoleic acid**, which is derived from **flaxseed** or **certain other vegetable oils**.
2. Putative effects on **cardiac membrane stabilization**, leading to possible **reduction of malignant arrhythmias and sudden cardiac death**.
3. CKD have some of the lowest blood levels of LC n-3 PUFAs **in the literature**.

# Long Chain Omega-3 Polyunsaturated Fatty Acids (LC n-3 PUFA)

## 1. Mortality and Cardiovascular Disease:

- **CKD 5D on MHD or posttransplantation**, we suggest **not routinely prescribing LC n-3 PUFA**, to lower risk of mortality (2C) or cardiovascular events (2B).
- **CKD 5D on PD**, it is reasonable **not to routinely prescribe LC n-3 PUFA**, to lower risk of mortality or cardiovascular events (OPINION).

# Long Chain Omega-3 Polyunsaturated Fatty Acids (LC n-3 PUFA)..

## 2. Lipid Profile:

- CKD 5D on MHD, we suggest that **1.3-4 g/d** LC n-3 PUFA may be prescribed to **reduce triglycerides and LDL cholesterol (2C) and raise HDL levels (2D)**.
- CKD 5D on PD, it is reasonable to consider prescribing **1.3-4 g/d LC** n-3 PUFA to **improve the lipid profile (OPINION)**.
- CKD 3-5, we suggest prescribing **~ 2g/d LC** n-3 PUFA to **lower serum triglyceride levels (2C)**.

# Long Chain Omega-3 Polyunsaturated Fatty Acids (LC n-3 PUFA)..

## 3. Arteriovenous (AV) Graft and Fistula Patency:

- CKD 5D on MHD, we suggest **not routinely prescribing fish oil** to improve primary patency rates in patients with AV grafts (2B) or fistulas (2A).

## 4. Kidney Allograft Survival

- CKD posttransplantation adults, we suggest **not routinely prescribing LC n-3 PUFA** to reduce the number of rejection episodes or improve graft survival (2D).

50 عدد = 90.000 تومان



**Omega-3**  
50 Capsules Dietary Supplement

**Mercury free**

Supplement Facts  
Serving Size: 1 Capsule

	Amount Per Serving	% DV*
Fish Oil	1000 mg	**
EPA	180 mg	**
DHA	120 mg	**

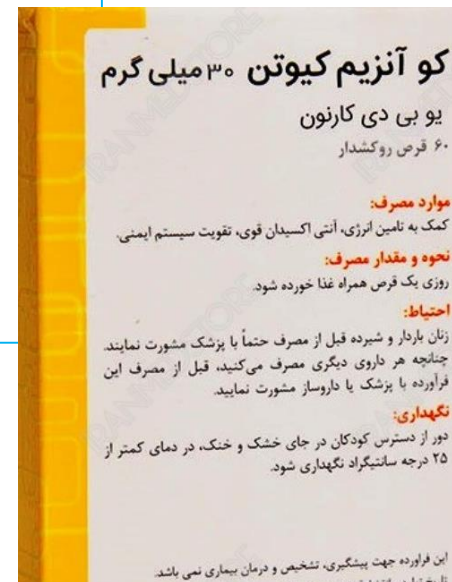
\* Daily Value  
\*\* Daily Value not established

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# Co Q10

- CoQ10, first identified in 1940, is mostly found in meat, fish, and whole grains .
- CoQ10 generate **ATP energy** to cell, most commonly used for an **antioxidant**.
- Improve **cardiovascular** diseases, **heart failure**, **diabetes**, **hypercholesterolemia**, **migraine headache**, related to lower CoQ10 levels.





*Review*

## **Systematic Review of Nutrition Supplements in Chronic Kidney Diseases: A GRADE Approach**

Pei-Chin Lin <sup>1,2</sup> , Chu-Lin Chou <sup>3,4,5</sup>, Shih-Hsiang Ou <sup>6</sup>, Te-Chao Fang <sup>3,5,7,\*</sup>  and Jin-Shuen Chen <sup>1,6,8,\*</sup>

- **No effect** on serum **urea and SCr** and no impact on **kidney function**.
- **Insufficient evidence** to recommend CoQ10 intake **in CKD** patients.

**Co Q10**

## Take home message

1. Folic acid and vitamin B complex recommended based on clinical findings.
2. Vitamin D for nephrotic syndrome or vit. D deficient.
3. Vitamin C low dose 75 -100 mg/d.
4. Vitamin A and E do not routinely prescribe, risk of bleeding and toxicity.
5. Vitamin K if poor intake or taking antibiotics.
6. Selenium and zinc not routinely prescribe.
7. Ketoanalogs in patients with very low protein diet.
8. Probiotics ameliorate lipid profile (LDL, HDL) and reduced serum urea level.
9. Omega-3 improved lipid profile
10. Co Q10 no sufficient evidence to recommend in CKD patients

# Very thanks for your patience

