



Achieving Optimal Vitamin and Mineral Supplementation for Patients on the Medical Ketogenic Diet for Epilepsy

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Disclosures

Consultant – Nutricia North America as a Keto Ambassador

Please note: references made to particular supplements in this presentation are ones that I use in my clinic as it helps to meet nutrient needs of my patients and they are low carbohydrate. Choose the supplement that works best for your patient based on their lab values, medical condition and nutrient needs. They are not an endorsement of that brand and are not affiliated with Nutricia North America.

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Objectives



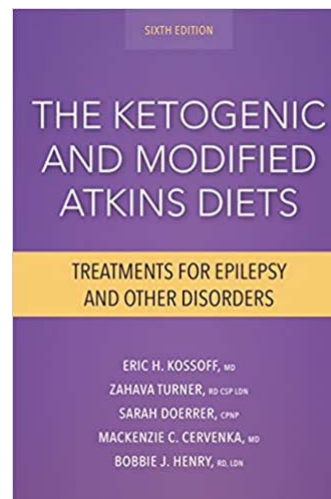
1. Identify common vitamin and mineral concerns including mechanism of action (MOA), symptomology and physical exam findings for patients on the medical ketogenic diet.
2. Describe requirements (DRIs) and suggested supplementation for patients on the diet.
3. Suggest lab work relating to vitamin and mineral deficiencies of patients on the medical ketogenic diet.

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Clinical Data

Kossoff et al (2008)

“...Ketogenic diet can be deficient in vitamins and minerals due to the limited intake of foods with carbohydrate and protein...”



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Clinical Data



Zupec-Kania and Zupanc (2008)

“...analyzed the micronutrients of menus for 3 days of four KD ratios(4:1, 3:1, 2:1, 1:1) revealing the 4:1 meeting only 3 of 28 DRI's and 1:1 meeting 12 of 28...”

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Common vitamins/minerals not meeting DRI for KD



Vitamin D

Calcium

Zinc

Selenium

Potassium

Phosphorus

Iron



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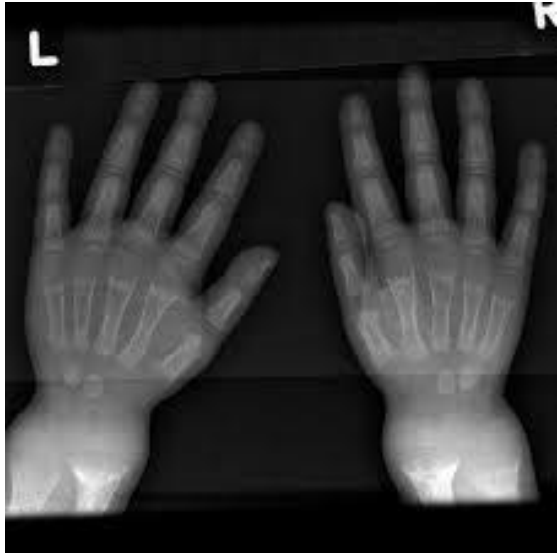
Vitamin D

Vitamin D



- MOA - promotes bone formation, regulates Ca/Phos concentrations
- Potential cause of deficiency - no direct sunlight, diet
- Sources – sunlight, dairy, fortified foods
- Nutrition-Focused Physical Exam (NFPE) – gingivitis, dental caries, bone demineralization, epiphyseal enlargement of wrists, legs, and knees, rickets, weakness, twitching, muscle cramps, muscle pain, memory impairment, behavioral disturbances

Rickets



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Vitamin D



- Labs -25(OH)D test

Status	Amount
Normal	>30 ng/mL
Insufficient	20-30 ng/mL
Deficient	<20 ng/mL

- **Correction of deficiency** – Supplementation D3 (most potent), Ca/Phos deficiency correction.
Dosing for infants/children for levels <20 = 1000-5000 IU/day
- **Suggested supplements** - D3 drops (various brands)
Nature's Bounty® 500 mg Ca with 400 IU Vit D3 tabs

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Calcium



- MOA - promotes bone health, heart rate, muscles
- Potential cause of deficiency - diet, parathyroid gland, kidney disorder, drugs (phenytoin, phenobarbital), Vit D deficiency
- Sources - dairy, dark greens, fortified foods, supplements
- NFPE - Beau's lines, bone demineralization, muscle twitching, tetany

Calcium



- Labs - total calcium, albumin level (calcium bound to albumin).
Also check kidney function tests, magnesium, phosphorus, PTH, Vitamin D
- **Correction of deficiency** - supplements (can cause gas and constipation - balance w/ magnesium)
- **Suggested supplements** - Calcium Citrate and Calcium Carbonate
- **DRI ranges**

Age	Calcium amount
1-3 years	500 mg
4-8 years	800 mg
9-13 years	1100 mg
Adolescent males	1100 mg
Adolescent females	1100 mg

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Zinc



- MOA - cofactor for enzyme system, increases tissue growth and healing, testicular hormones, may inhibit copper absorption
- Potential cause of deficiency - dietary intake
- Sources - meat, seafood, milk, some grains, nuts, seeds
- NFPE- alopecia, angular blepharitis, hypogeusia, dysgeusia, gingivitis, Beau's lines, slow wound healing, eczema, memory impairment, behavioral disturbances

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MOA = Mechanism of Action; NFPE = Nutrition Focused Physical Exam

Zinc



- Labs - Plasma Zinc
**Note: low in patients with hypoalbuminemia, can be measured in neutrophils and lymphocytes (sensitive)
- Low serum Alk Phos levels for age (indicator)
- Correction of deficiency - Dose 1-2 mg/kg/day of elemental zinc (caution: may experience diarrhea)
- Suggested supplement - Nature Made® 30mg Tablets
- DRI range - 6-12 mo-18 years = 2.5-8.5 mg/day

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Zinc Deficiency Acrodermatitis



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Selenium



Selenium



- MOA - converts thyroid hormone (T4)
- Potential cause of deficiency - diet, poor intestinal function, food grown in selenium deficient soil (China, Finland)
- Sources - organ meats, cereal/grains, dairy, brazil nuts (1 nut is 68-91 mcg)
- NFPE – deficiency: hair color changes (darker), depigmentation
toxicity: brittle, soft, dry nails

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MOA = Mechanism of Action; NFPE = Nutrition Focused Physical Exam

Selenium



- Lab - Serum selenium, glutathione peroxidase, selenoprotein P, hair/skin analyses
- Correction of deficiency – supplement 50-200 mcg/day
- Suggested supplement :
 - GNC® 100 mcg tablets
 - Nature's Bounty® 200 mcg tablets
 - Brazil nut - 1/2 to 1/day (1 nut contains up to 91 mcg)
- DRI Range
17 to 45 mcg/day (for 1-18 year olds)

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Phosphorus



- MOA - energy storage, bone formation, muscle and nerve functions
- Potential cause of deficiency – diet
- Sources - dairy, nuts, pumpkin seeds, peanut butter
- NFPE- ophthalmoplegia, bone demineralization, muscle weakness, peripheral neuropathy

Phosphorus



- Labs – Serum Phosphorus level
- Correction of deficiency* - food intake or supplements (RX) such as K-Phos® Neutral, Phospha™ 250 Neutral
- DRI - 1-3Y to 18Y is 380-1055 mg/day

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Iron



Iron



- MOA - Iron important to make hemoglobin for RBC's
- Potential cause of deficiency - blood loss, poor absorption, diet
- NFPE
 - deficiency: alopecia, angular palpebritis, pallor, angular stomatitis or cheilitis, glossitis, pale tongue, koilonychias, nail ridges,
 - toxicity: fatigue, joint/abdominal pain, liver disease, heart attack/heart failure, skin color changes

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MOA = Mechanism of Action; NFPE = Nutrition Focused Physical Exam

Iron



- Labs - CBC, Iron Profile
- Correction of deficiency - Ferrous Sulfate 3-5mg/kg

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Potassium



- MOA: Important for nerve transmission
- Potential cause of deficiency - diet
- Sources - fruits/veggies, meat, fish, avocados, almonds, pistachios
- NFPE- muscle weakness, muscle cramps

Potassium



- Labs - Plasma potassium (BMP)
- Suggested supplements – Rx (dissolve in water), Morton's® Lite Salt, NOW® foods KCl - powder

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Supplementation



Oral Supplementation



Supplement at **100% of DRI's** (not including intake)

Most will need a **multivitamin/mineral** and a **Calcium/Vitamin D**.
In addition some may require **phosphorus and potassium**.

Use the lowest carbohydrate form - usually tablets

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Tube Feeding Ketogenic Diet Supplementation



Evaluate intake from tube feeding formula and supplement individual deficiencies to meet DRI's.

Most tube-feeding patients will need additional Vitamin D and Calcium and sometimes electrolytes. (Potassium, Sodium and Chloride)

Tablets can be crushed or powder forms of vitamins and minerals can be used

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Table Salt, Lite Salt and Salt Substitute



Table Salt
(Sodium Chloride)

Lite Salt
(Potassium Chloride)

Salt Substitute
(Potassium Chloride with some sodium)

➡ All can be added to formula recipes to meet sodium, potassium, iodine and chloride needs.

➡ Oral patients can sprinkle these products on their food.

1.5 grams table salt = ¼ tsp

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Lowest Carbohydrate Supplements



- Powder forms of vitamins/minerals are available to drink or put through feeding tubes
 - Phlexy-Vits (Nutricia)
 - Nano VM® (Solace)
 - FruitiVits™ (Nestlé)
 - Calcium powder
- Others forms of vitamins/minerals.
 - Renzo's Picky Eater Multi (Renzo's Vitamins) dissolvable
 - SuperMini-Multi Capsules Children's Multivitamin (Wellness Resources®)
- Some liquids are allowed on the ketogenic diet (e.g. Carnitine suspension)

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Re-evaluating Supplementation

Re-evaluate during follow up visits since DRI's change with age



DRI Age Ranges



*males and females separates

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Other Supplementation - Carnitine

1. Check serum carnitine levels at diet initiation*



2. Monitor free carnitine, Goal ≥ 24 mcumol/L



3. Start 25-50 mg/kg/day divided into 2 to 3 doses, **if needed**. Use RX carnitine – Carnitor® 330 mg tabs or oral solutions (regular and sugar free) 100mg/mL*



4. Check carnitine levels **every 3-6 months**

May be needed for patients on Depakote® or valproic acid

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Other Supplementation- Baking Soda/ Sodium Bicarbonate



Often used for kidney stone prevention or to manage acidosis

- Dosing for kidney stone prevention*:
 - **Baking Soda** – dose 0.5-2 mEq/kg/day, but can go higher (54.7 mEq /tsp). Combine with 30% of the DRI of K⁺ and possibly phosphorus to prevent mobilization of calcium from bones
 - **¼ tsp Baking Soda** = little less than 1 packet Cytra-K[®]
 - **Potassium Citrate**– dose 1-2 mEq/kg/day
(Cytra-K Crystals 30 mEq/packet, solution 2mEq/ml- white bottle, other- Urocit-K[®])

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*This is a recommendation for the supplementation that I use in my clinic as it helps to meet nutrient needs and is low carbohydrate.

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Acidosis



Can load or dose sodium bicarbonate 0.5 mEq/kg to 4 mEq/kg

- Sodium bicarbonate tablets* (325mg or 650mg)
 - 325mg tab= 3.9 mEq
 - 650mg tab= 7.7 mEq

*This is a recommendation for the supplementation that I use in my clinic as it helps to meet nutrient needs and is low carbohydrate.

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Other Supplementation – Pancreatic Enzymes



Manage symptoms of malabsorption and may be helpful with fat metabolism

- Common Brands- all porcine based
 - Viokace®- 10,440 and 20,880 tabs, dosed 1000 to 4000 units/gram of fat, can crush (no encapsulation)
 - Creon®- dose based on kg – lipase, encapsulated
 - Pancreatic Enzyme -Pure Encapsulations® brand - lipase, amylase (OTC/online)
 - Pertzye®

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Other Supplementation – Fiber, Fish oils



- Fiber - most have carbohydrate but can use Senokot® tablets to help bulk stool
- Adequate fluid intake is imperative
- Also consider: supplemental flax seed meal/oil, aloe vera juice (unsweetened), chia seeds, senna tea and avocado. (depends on MD and age/patient status)
- Fish oils – Good for lipid profile, often use Nordic Naturals® liquids (specifically Ultimate Omega®)

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Other Supplementation - Probiotics



Used to support gut health

- Use a low-carbohydrate brand such as Culturelle®, Florajen®, VSL #3 The Living Shield®
- Can incorporate pre and probiotic foods into the meal plan

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“Optional” Supplementation



- Some parents or patients elect to supplement their diets with extra vitamin/minerals and sometimes herbs and other products.
Examples: CBD oil, elderberry
- Imperative to know if families are using these additional supplements because they may contain hidden carbohydrates
- All carbohydrates should be taken into account for these products.

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How often should labs be drawn?



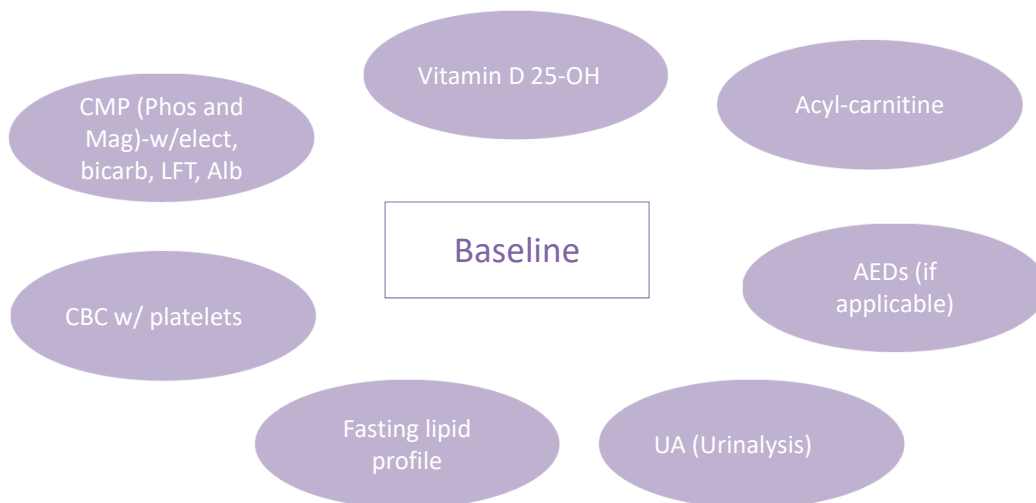
Baseline
(Pre-diet or onset of diet start)

1 month post-diet initiation

Every 3 months for the first year

Every 6 months thereafter

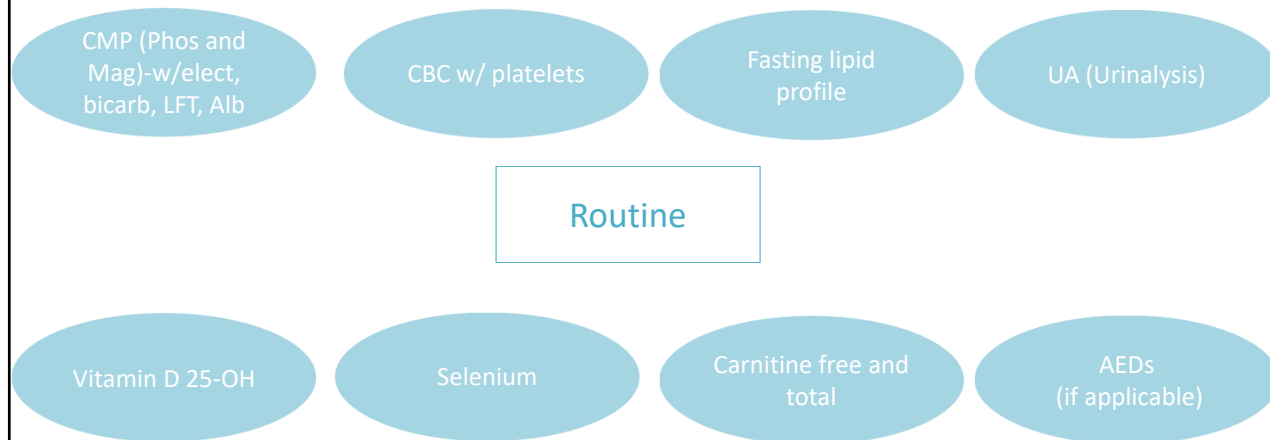
What labs should be done baseline?



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Kossoff, et al. Epilepsia Open. 2018;3:175-92.

What should be monitored routinely*?

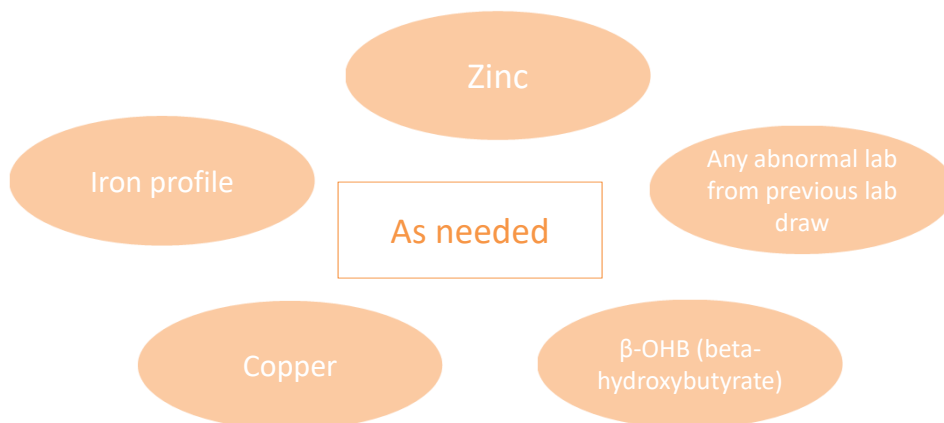


*Routine is every 1, 3, 6, 9, 12 months for the first year on the KD and then every 6 months thereafter. More frequent visits may be necessary to follow-up on lab values or supplementation, or for patients at high nutrition risk.

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Kossoff, et al. Epilepsia Open. 2018;3:175-92.

What should be monitored as needed?



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Lab and Side Effect Monitoring



	Every 3 Months	Annually
General monitoring	CBC with differential CMP Hepatic function tests β-OHB level	
Hyperlipidemia	Lipid panel	
Cardiac disease		Selenium (or q 6 months) EKG (as needed)
Growth failure	Height and weight Prealbumin/albumin	
Nephrolithiasis	Urine Ca/Cr ratio	Urine analysis / culture (as needed)
GI disorders	Hepatic function tests	
Osteopenia		Vitamin D (annually or q 6 months) DEXA
Vitamin/Mineral Deficiencies	CMP Mg, phosphorus	Vitamin D (annually or q 6 months) Selenium

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Adapted from Bergqvist. Epilepsy Res. 2012;100:261-6

Carbon Dioxide (CO₂)



Those in ketosis can have lower CO₂ levels creating a **“new normal”** range.

- **Normal range:** ≥ 18 mEq/L
- **Less than 18 mEq/L** may be treated for metabolic acidosis

➡ If CO₂ levels are low and patient is symptomatic, consider treatment.

➡ Management options:

- Carb-free citrate
- Baking soda
- Sodium bicarbonate tablets

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Lipid Levels



Total Cholesterol

Triglycerides

HDL

LDL

➡ Expect an increase in lipids after KD start.

➡ Obtain fasting labs for more accurate assessment

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Ketones



➡ **β -OHB – Beta-hydroxybutyrate- blood ketone levels**

- >3 mmol/L is usually good ketosis
- 4 to 7 mmol/L is often considered therapeutic
- Use seizure control as assessment for diet efficacy and not levels of BHB independently

➡ **Acetoacetate – Urine ketone levels**

- Goal >80
- Crude and can be effected by age, hydration and length of time on the diet

➡ **Acetone – breath ketones**

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Seeing Patients with Deficiencies



➡ **Look for physical signs of deficiency**

- skin
- hair
- nails

➡ **Be aware of medical signs of deficiency**

- numbness
- confusion
- lethargy

➡ **Altered lab values – Consider lab results but evaluate symptoms**

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Summary



Almost all patients on any form of the KD will require supplementation at some point.

There are many supplements available to meet patients needs including ones that are low in carbohydrate.

All recommendations should be individualized and follow the RD and MD's protocols.

Remember to weigh symptomology with lab values when managing deficiencies.

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