Ketogenic Diet Therapies for Epilepsy

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Parent Link
Ketogenic Diet Therapies for Epilepsy:

For the New Patient (Robyn)

For the Experienced Patient (Wes)
Ketogenic Diet Centers (2017), author: Eric Kossoff, MD
Lurie Children’s Ketogenic Diet Program

• 2 Full time dietitians for the Epilepsy Center (Wes & Robyn)
• Current caseload for KD-205 pts MAD-30 pts
• The Keto Team
  Nurse Practitioners (4)
  Social Worker (Josephine DeLira)
  Registered Dietitians (2)
• Diet therapy for epilepsy is a choice in treatment
• It is our passion to help families be successful on the diet by supporting them prior to the start of the diet, during the initiation of the diet and the day to day happenings in the future.
Who benefits from the KD?

- Medically resistant epilepsy
- Metabolic deficiencies / Pathogenic variants in genetics
- Glucose transporter protein defect (GLUT-1)
- Pyruvate dehydrogenase deficiency (PDHD)
- Refractory infantile spasms (West syndrome)
- Myoclonic epilepsies (Doose-MAE, Dravet syndrome)
- Nonspecific epilepsy diagnoses
- Infants to children of all ages and abilities
Types of Diet Therapies

• Ketogenic Diet (KD)
  – Classic (hospital initiation with ratio of Fat : Non-Fat, use of gram scale)
  – What you see on the internet (carb counting with added fat)

• Modified Atkins Diet (MAD)

• Low-Glycemic Index Treatment (LGIT)
THE KETOGENIC DIET

A HIGH FAT, LOW CARBOHYDRATE DIET THAT CAUSES THE BODY TO USE FAT AS THE MAIN ENERGY SOURCE, THEREBY PRODUCING KETONES.
KETOGENIC DIETS: METHODS OF ADMINISTRATION
FORMULA FEEDING

TUBE FEEDING

BOTTLE FEEDING

OPEN CUP
BLENDERIZED FEEDING

PUREES FED BY MOUTH

MEALS FED BY TUBE
SOLIDS FEEDING

MEALS AND SNACKS BY MOUTH
• PROTEIN, FRUIT/VEGETABLE, BUTTER/OIL, CREAM.
NUTRITION IMPLICATIONS OF MEDICINES AND DIET

BODY WEIGHT

MEDICATIONS THAT COULD AFFECT BODY WEIGHT

• POTENTIAL WEIGHT GAIN
  – VALPROATE (DEPAKOTE), CARBAMAZEPINE, GABAPENTIN (NEURONTIN), STEROIDS.

• POTENTIAL WEIGHT LOSS
  – FELBAMATE, TOPIRAMATE (TOPAMAX), CBD OIL?.

CONSIDERATIONS TO MAKE

• COMBATTING WEIGHT GAIN
  – DRINK MORE WATER, EAT MORE HIGH WATER FOODS (LOW CALORIE FRUITS AND VEGETABLES)

• COMBATTING WEIGHT LOSS
  – EATING SMALLER MEALS MORE FREQUENTLY, CONCENTRATING CALORIES THROUGH THE USE OF HIGH FAT FOODS (OIL, BUTTER, CREAM, KETO FOODS!)
ACIDOSIS

MEDICATIONS THAT COULD CAUSE ACIDOSIS

• TOPIRAMATE (TOPAMAX)
• ZONISAMIDE (ZONEGRAN)
• ACETAZOLAMIDE (DIAMOX)
• KETOGENIC DIET

CONSIDERATIONS TO MAKE

• BLOODWORK MONITORING (CARBON DIOXIDE)
• ADDITION OF A BASE TO NEUTRALIZE ACIDIC CONDITIONS (BAKING SODA, SODIUM BICARBONATE, POTASSIUM CITRATE)
BONE HEALTH

MEDICATIONS THAT COULD AFFECT BONE HEALTH

• PHENYTOIN (DILANTIN)
• PHENOBARBITAL (PHENOBARBITAL)
• CARBAMAZEPINE (TEGRETOL)
• VALPROATE (DEPAKOTE)

CONSIDERATIONS TO MAKE

• CALCIUM AND VITAMIN D SUPPLEMENTATION (MAY BE ADEQUATE FOR SOME FORMULA FED PATIENTS)
• BLOODWORK MONITORING
• BONE HEALTH CLINIC REFERRALS
KIDNEY STONES

MEDICATIONS THAT COULD CAUSE KIDNEY STONES

• TOPIRAMATE (TOPAMAX)
• ZONISAMIDE (ZONEGRAN)
• ACETAZOLAMIDE (DIAMOX)
• KETOGENIC DIET

CONSIDERATIONS TO MAKE

• BLOODWORK MONITORING (CARBON DIOXIDE) TO PREVENT DEVELOPMENT OF STONES
• ADDITION OF A BASE TO NEUTRALIZE ACIDIC CONDITIONS (BAKING SODA, SODIUM BICARBONATE, POTASSIUM CITRATE)
• INCREASED WATER INTAKE TO FLUSH KIDNEYS
## ADDITIONAL POTENTIAL SIDE EFFECTS OF THE KETOGENIC DIET

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<tr>
<th>CARNITINE DEFICIENCY</th>
<th>CONSIDERATIONS TO MAKE</th>
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<tbody>
<tr>
<td>• Used by the body to metabolize fats. Often depleted when on a ketogenic diet. Potential with Depakote.</td>
<td>• Bloodwork monitoring (Carnitine)</td>
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<td>• Addition of a Carnitine supplement as needed.</td>
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<th>CONSTIPATION</th>
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<td>• Fat slows the movement of food through the body which causes constipation.</td>
<td>• Increased water intake to keep food moving through the body.</td>
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<td>• Increased physical activity when possible (physical therapy, too).</td>
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<td>• Laxatives (Miralax, Senna, suppositories).</td>
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<th>VITAMIN INSUFFICIENCY</th>
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<td>• Daily multivitamin if not taking formula.</td>
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SPECIALTY FOODS

NAME SOME SPECIALTY FOODS OR INGREDIENTS THAT YOU’VE FOUND USEFUL FOR THE KETOGENIC DIET...

- Avocado
- Macadamia nuts
- Almond flour
- Miracle noodles
NAME SOME WEBSITES THAT YOU’VE FOUND USEFUL FOR THE KETOGENIC DIET...

https://www.charliefoundation.org/

https://ketocook.com/

http://www.matthewsfriends.org/
NAME SOME SPECIALTY KITCHEN TOOLS THAT YOU’VE FOUND USEFUL FOR THE KETOGENIC DIET...

Zoodlers:  
https://www.oxo.com/products/preparing/fruit-vegetable-tools/hand-held-spiralizer

Stick blenders:  

Cream whippers:  
Decreased health care utilization and health care costs in the inpatient and emergency department setting following initiation of ketogenic diet in pediatric patients: The experience in Ontario, Canada

“Children on the KD experienced a mean decrease in ED visits of 2.5 visits per person per year [95% CI (1.5–3.4)], and a mean decrease of 0.8 inpatient visits per person per year [95% CI (0.3–1.3)], following diet initiation.”

Neuronal inhibition and seizure suppression by acetoacetate and its analog, 2-phenylbutyrate.

• The diet treatment markedly increases ketone bodies (acetoacetate and β-hydroxybutyrate). We investigated effects of acetoacetate on voltage-dependent Ca\(^{2+}\) channels (VDCCs) in pyramidal cells of the hippocampus of mice. We further explored an acetoacetate analog that inhibited VDCCs in pyramidal cells, reduced excitatory postsynaptic currents (EPSCs), and suppressed seizures in vivo.

• These results demonstrate that 2-phenylbutyrate (an acetoacetate analog) inhibits VDCCs and EPSCs in pyramidal cells, suppresses hippocampal seizures in vivo, and has brain penetration ability. Thus 2-phenylbutyrate provides a useful chemical structure as a lead compound to develop new antiseizure drugs originating from ketone bodies.

Hypothetical pathways leading to the anticonvulsant effects of the ketogenic diet:

EXPLAINED:

• Elevated free fatty acids (FFA) lead to chronic ketosis and increased concentrations of polyunsaturated fatty acids (PUFAs) in the brain. Chronic ketosis is predicted to lead to increased levels of acetone; this might activate K<sub>ATP</sub> channels to hyperpolarize neurons and limit neuronal excitability. Chronic ketosis is also anticipated to modify the tricarboxylic acid (TCA) cycle, as would the presence of anaplerotic substrates such as triheptanoin. This would increase glutamate and, subsequently, GABA synthesis in brain. Among several direct inhibitory actions, PUFAs boost the activity of brain-specific uncoupling proteins (UCPs). This is expected to limit ROS generation, neuronal dysfunction, and resultant neurodegeneration. Acting via the nuclear transcription factor peroxisome proliferator-activated receptor-α (PPARα) and its co-activator peroxisome proliferator-activated receptor γ coactivator-1 (PGC-1α), PUFAs would induce the expression of UCPs and coordinately up-regulate several dozen genes related to oxidative energy metabolism. PPARγ expression is inversely correlated with IL-1β cytokine expression; given the role of IL-1β in hyperexcitability and seizure generation, diminished expression of IL-1β cytokines during KD treatment could lead to improved seizure control. Ultimately, PUFAs would stimulate mitochondrial biogenesis. Mitochondrial biogenesis is predicted to increase ATP production capacity and enhance energy reserves, leading to stabilized synaptic function and improved seizure control. In particular, an elevated phosphocreatine:creatine (PCr:Cr) energy-reserve ratio is predicted to enhance GABAergic output, perhaps in conjunction with the ketosis-induced elevated ketones produced, leading to diminished hyperexcitability. Reduced glucose coupled with elevated free fatty acids are proposed to reduce glycolytic flux during KD, which would then feedback inhibit mitochondrial concentrations of citrate and ATP produced during KD treatment. This would activate metabolic K<sub>ATP</sub> channels. Ketones may also directly activate K<sub>ATP</sub> channels. Reduced glucose alone under conditions of adequate or enhanced energy levels activate pannexin hemi-channels on CA3 pyramidal neurons, releasing ATP into the extracellular space; ATP is converted via ectonucleotidases to adenosine which subsequently activates adenosine receptors (A<sub>1</sub>R). A<sub>1</sub>R activation is also coupled to K<sub>ATP</sub> channels. Ultimately, opening of K<sub>ATP</sub> channels would hyperpolarize neurons and diminish neuronal excitability to contribute to the anticonvulsant (and perhaps neuroprotective actions of the KD). Increased leptin, seen with KD treatment, can reduce glucose levels and inhibit AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptor-mediated synaptic excitation. Reduced glucose is also expected to down-regulate brain-derived neurotrophic factor (BDNF) and TrkB signaling in brain. As activation of TrkB pathways by BDNF have been shown to promote hyperexcitability and kindling, these potential KD-induced effects would be expected to limit the symptom (seizures) as well as epileptogenesis. Boxed variables depict findings described from KD studies; up (↑) or down (↓) arrows indicate the direction of the relationship between variables as a result of KD treatment. Dashed lines are used to clarify linkages and are not meant to suggest either magnitude or relative importance compared to solid lines. Adapted with permission from reference 40.
REFERENCES


Thank you!