

## 1 **Unlocking Doors: The Keys to Ketogenic Diet**

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 Pharmacy Grand Rounds  
 Drug Information Question 1/14/19  
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## 2 **Disclosure**

- Nothing to disclose.

## 3 **Objectives**

- List recommended therapies for refractory epilepsy
- Review mechanism of ketogenic diet and it's place in treatment of epilepsy
- Evaluate available literature pertaining to ketogenic diet
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## 4 **Patient Introduction**

- JG: 44M
- Lennox-Gastaut seizure disorder, trach and G-tube dependent
  - Admitted to NCCU for refractory seizures despite being on multiple anti-epileptics
    - Clobazam
    - Levetiracetam
    - Lorazepam
    - Perampanel
    - Ethosuximide solution
    - Rufinamide
    - Phenobarbital
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## 5 **Drug Information Question**

With help from pharmacy, the NCCU team would like to optimize JG's seizure medications and start him on a ketogenic diet

## 6 **Seizure**

- Imbalance of inhibitory and excitatory neurotransmitters
  - GABA
  - Glutamate, aspartate, acetylcholine
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## 7 **Epilepsy**

- Syndrome of  $\geq 2$  unprovoked or recurrent seizures on more than one occasion
- Types of epileptic seizures
  - Generalized
  - Partial

8  **Epidemiology**

- 65 million people in the world have epilepsy
- 3.4 million people in the United States have epilepsy
- One-third of people with epilepsy live with uncontrollable seizures because no available treatment works for them

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9  **Goals of Treatment**

- Improve quality of life
  - Elimination or reduction in seizures
  - Minimize adverse effects from therapy
  - Manage comorbidities
    - Underlying conditions contributing to epilepsy
    - Depression, anxiety, pain, sleep disorders

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10  **Pharmaco-refractory Epilepsy**

- Types of epilepsy often refractory to drug treatment
  - Darvet
  - Doose
  - Lennox-Gastaut
  - West

11  **Approach to Refractory Epilepsy**

- Pharmacologic
  - CBD
- Non-pharmacologic
  - Dietary therapy
    - Examples: Ketogenic diet, modified-Atkins diet
  - Avoid triggers
  - Surgical intervention
  - Vagal nerve stimulation

12  **Epilepsy**13  **Epilepsy**14  **KETOGENIC DIET**15  **KD History**16  **Ketogenic Diet**

- Ketogenic diet (KD)

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- Treatment for medically-refractory epilepsy

### 17 **Ketogenic Diet**

- “Classic” KD: Long-chain saturated triglycerides (LCTs)
  - 3:1-4:1 ratio of fats to carbs + protein
- Typical American diet:
  - 50% carbohydrates
  - 30% fat
  - 20% protein

### 18 **Ketogenic Diet**

- Many studies: 50% reduction in seizures
  - Mimic fasting state while providing nutrients for growth/function
  - Monitoring: blood glucose, urine ketones

### 19 **Mechanism**

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### 21 **Ketogenic Diet**

- Optimal seizure protection
  - Days-weeks after development of ketonemia
  - Ketonemia occurs within hours of KD onset
- Sustained ketosis is important factor in raising seizure threshold

### 22 **More than Just Diet**

### 23 **KD Complications**

- Tolerability
- Safety
  - Adverse effects
    - Initiation phase: dehydration, hypoglycemia, vomiting
    - Maintenance phase: constipation, GERD, nephrolithiasis, hypertriglyceridemia, growth/nutrition
  - Contraindications
    - Relative: pts with more curative alternatives, comorbidities
    - Absolute: metabolism deficiencies
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### 24 **Duration**

- Most remain on KD for up to 2 years
  - Then weaned to discontinuation
- Some have recurrence or worsening seizures with weaning
  - Long-term dietary management

### 26 **LITERATURE REVIEW**

### 27 **Literature**

- Long-term data of response in adults is limited
- Meta-analysis by Ye et al
  - Summarized studies to identify the efficacy and compliance with KD in adults

28  **Literature**

- Nei et al: Ketogenic diet in adolescents and adults with epilepsy

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29  **Nei et al**30  **Nei et al**

- Majority of pts had increase in total cholesterol and cholesterol/HDL ratio
  - HDL tended to stay the same
- Total carnitine tended to decrease while triglycerides (TG) increased
  - Supplementation of carnitine decreased TG

31  **Nei et al**

- Author's conclusions:
  - Consider Modified Atkins as first line, but KD is an alternative that is effective in this age group
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32  **BACK TO JG**33  **Patient Case Updates**

- Fycompa dosing was increased on admission 6mg to 12mg
- JG started on KD via g-tube on hospital day 6
- All set to start CBD oil (Epidiolex) as an outpatient
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34  **Patient Case Updates**35  **Patient Case Updates**36  **Patient Case Updates**37  **Pharmacist Role in KD**

- Combined with AEDs
- Medications containing carbohydrates
  - Formulations of AEDs and other medications may contain carbohydrates or sugar additives
- Pharmacologic management & prevention of adverse effects
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38  **Pharmacist Role in KD**

- Called drug manufacturers for carbohydrate content information
- Changed as many solution formulations to tablets
- Problem with ethosuximide liquid
  - Tried to order a capsule but it ended up being a gel cap which was not convenient for administration
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39  **Patient Case Example**40  **Take-away Points**

- The KD has been utilized for almost a decade
  - Can be an option for patients with pharmaco-refractory epilepsy
  - Has been shown to reduce frequency of seizures
- Mechanism is not completely understood
- Pharmacists can have an important role in the implementation and maintenance phases

41  **Resources**

- The Charlie Foundation:
  - <https://charlifoundation.org/>
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- Epilepsy Foundation:
  - <https://www.epilepsy.com>

42  **QUESTIONS**43  **References**

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