Medication Selection for Patients on Ketogenic Diets
June 2017

Patient Case
SK is a 16 month old boy admitted to hospice with a primary diagnosis of Sandhoff disease. He has a history of epilepsy and malnutrition and weighs 11.2kg (24.8 lbs). SK has been on and off service since he was 9 months old and has no other health conditions or known drug allergies. He lives at home with his parents and 2 older sisters.

Current meds:
- Albuterol 2.5mg/3ml; Inhale 1 ampule via nebulizer 4 times daily as needed for shortness of breath
- Acetaminophen 160mg/5ml; Give 3.75ml (120mg) via G tube (VGT) every 4 to 6 hours as needed for pain or fever
- Clonazepam 0.125mg disintegrating tablet; Give 1 tablet VGT 3 times daily as needed for seizure control
- Diazepam 5mg sup insert 1 suppository rectally for seizures lasting greater than 5 minutes; may repeat one time in 4 to 12 hours and contact hospice
- Ibuprofen 400mg/5ml; Give 1ml (80mg) VGT every 6 hours as needed for pain or fever
- Levetiracetam 100mg/ml oral soln; Give 5ml (500mg) VGT twice daily for seizure control
- Pedia-sure; Give 4oz VGT every 3 hours for nutritional deficiency
- Simethicone 40mg/0.6ml; Give 0.3ml (20mg) VGT 4 times daily as needed for gas
- Valproic acid 250mg/5ml; Give 3ml (150mg) VGT 3 times a day for seizure control
- Glycerin pediatric suppository insert 1 into rectum daily as needed for constipation

Seizures are a common complication of Sandhoff disease and SK was initiated on a ketogenic diet to help manage them. In accordance with the diet, many liquid medications were switched to tablet dosage forms to limit the amount of carbohydrates. SK is prescribed glycerin suppositories as needed for constipation, however glycerin is not recommended for patients on a ketogenic diet.

WHAT IS SANDHOFF DISEASE?
Sandhoff disease is an inherited lipid storage disorder that is characterized by a progressive deterioration of the central nervous system. Specifically, Sandhoff disease “is an autosomal recessive genetic disorder caused by an abnormal gene for the beta subunit of the hexosaminidase B enzyme. This gene abnormality results in a deficiency of hexosaminidase A and B that results in accumulation of fats (lipids) called GM2 gangliosides in the neurons and other tissues.”¹ Sandhoff disease is clinically indistinguishable from Tay-Sachs disease.²
There are three types of Sandhoff disease:

- **The most common and severe form of Sandhoff disease appears in infancy.** Infants with this disorder typically appear normal until the age of 3 to 6 months when their development slows and muscles used for movement weaken. Affected infants typically lose motor skills such as turning over, sitting or crawling. As the disease progresses, seizures, vision and hearing loss, intellectual disability, and paralysis may occur. An eye abnormality called a “cherry-red spot” is characteristic of this disorder. Some affected children also have an enlarged liver and spleen, frequent respiratory infections, or bone abnormalities.

- **Juvenile and adult onset** Sandhoff disease are very rare and also limit life expectancy.

The prevalence of Sandhoff disease varies among populations and seems to be more common in the Creole population of northern Argentina, the Metis Indians of Saskatchewan Canada, and Lebanese. There is no cure for Sandhoff disease and the prognosis is poor. Current treatment focuses on supportive measures. Anticonvulsants are used for seizures and treatments for associated respiratory tract infections are also utilized. Affected children typically only live until 3-4 years of age, and most die due to respiratory tract infections.

**WHAT IS THE KETOGENIC DIET?**

The Ketogenic Diet is a high fat, adequate protein, low carbohydrate meal plan developed in 1924 by Dr. Russell Wilder at the Mayo Clinic. In a normal diet, carbohydrates are converted to glucose, which fuels brain function and serves as an energy source. In a ketogenic diet, carbohydrate consumption is intentionally limited. Instead of carbohydrates being converted to glucose, the liver converts fat into fatty acids and ketone bodies. Ketone bodies then replace glucose as an energy source; known as ketosis.

A ketogenic diet is highly individualized and is typically initiated in a hospital setting under medical supervision. The ketogenic diet is not well-balanced and many vitamins must be artificially supplemented. It is not fully known how the ketogenic diet controls seizures, although emerging research at Emory University School of Medicine proposes that the “diet alters genes involved in energy metabolism in the brain, which in turn helps stabilize the function of neurons exposed to the challenges of epileptic seizures.”

Foods commonly used in a ketogenic diet include eggs, full fat cheese, meats and nuts. In order to increase fat content of the diet, heavy cream, butter, and oil are used frequently in meal preparation. Foods to avoid include all grain products (bread, rice, pasta...), soft drinks, juices, sugar and sweets (cake, ice cream, chocolate...). The strictly measured and regulated portions can make the diet hard to follow. For sample ketogenic diet menus, refer to the Boston Children’s Hospital website.
WHAT ARE THE SIDE EFFECTS OF THE KETOGENIC DIET?  
- Sluggish feeling after initiation of the diet  
- Kidney stones  
- Dehydration  
- GI disturbances, such as nausea/vomiting, diarrhea and constipation  
- Slowed growth or weight loss

HOW SUCCESSFUL IS THE KETOGENIC DIET FOR SEIZURE CONTROL?  
The ketogenic diet is typically used to treat pediatric patients with refractory or drug-resistant epilepsy, defined as failure of two appropriate anticonvulsant medications at the recommended dose. Up to 30-40% of people with epilepsy continue to have seizures despite anticonvulsant medications. The ketogenic diet was the standard of care for seizure control in the 1920s until anticonvulsant drugs became the norm in the following decade. 

Prospective studies in children demonstrate that about 50% of children will continue on the diet for at least a year, with 40-50% of those starting the diet having a >50% reduction in seizures after 12 months. In a study published in March 2017, patients stopped the ketogenic diet due to problems with compliance, side effects and efficacy. It showed that while GI side effects were more pronounced than “care as usual” at 4 months post-initiation of the diet, at 16 months there were less complaints of behavior/irritability, motor problems/coordination, and cosmetic and dermatological problems in patients utilizing the ketogenic diet.

For seizures controlled for 2 years, physicians may consider a trial off the diet—this is similar to conventional treatment using medication to assess if control can be maintained without intervention. Children coming off the ketogenic diet will typically remain on their anticonvulsant medication, though some are able to take lower doses and/or fewer medications. Eighty percent of children who become seizure-free on ketogenic dietary therapies remain so after stopping the diet. Most research has focused on pediatric patients. The diet may be effective for adults, however controlled studies are needed. Some theorize the restrictive nature of the diet turns many adult patients away. In one study, only 18 out of 130 eligible adults consented to start the diet.

WHAT ARE SOME CONSIDERATIONS FOR THE HOSPICE POPULATION?  
Maintaining ketosis means that patients must avoid carbohydrates in their diets as well as in medications. Liquid medications are especially problematic as many contain sweeteners for palatability, and thus contribute to the carbohydrate load. Adhering to a ketogenic diet presents a challenge for patients near end-of-life with a loss of appetite. Many hospice patients are encouraged to eat by selecting foods they most enjoy, often “comfort foods” containing high carbohydrates. These patients may also experience difficulty swallowing, making liquid medications essential.
Being familiar with medications that contain low or no carbohydrates is important. Below is a list of carbohydrate and non-carbohydrate ingredients common in medications.

**CARBOHYDRATE INGREDIENTS:**
- Glycerin
- Maltodextrin
- Organic acids: ascorbic acid, citric acid, lactic acid
- Propylene glycol
- Sugars: dextrose, fructose, glucose, lactose, sucrose, sugar, palm sugar, agave nectar, cane syrup, cane juice, corn syrup, honey
- Sugar alcohols: erythritol, isomalt, glycerol, mannitol, maltitol, sorbitol, xylitol
- Starches: cornstarch, hydrogenated starch hydrolysates (HSH), pregelatinized starch, sodium starch glycolate

**NON-CARBOHYDRATE INGREDIENTS:**
- Asulfamine potassium (AceK)
- Aspartame
- Carboxymethylcellulose
- Hydroxymethylcellulose
- Magnesium Stearate
- Microcrystalline cellulose
- Polyethylene glycol
- Saccharine
- Superose
- Stevia (rebiana)\(^4\)

**Pharmacist Assessment**
SK is currently using glycerin suppositories and as the name implies, glycerin is the active ingredient and a carbohydrate. Other laxatives appropriate for a 16-month old include docusate sodium, senna, bisacodyl, lactulose, and Miralax\(^{®}\). Upon review of the active and inactive ingredients of these laxatives, bisacodyl suppositories, Miralax and senna tablets are carbohydrate-free or low in carbohydrates.

**Recommendation**
Miralax was recommended as the best option. Initial dose suggested is 0.4g/kg/day.\(^{11}\) SK has been stabilized on Miralax 8.5 grams (measured to one-half line in the cap) mixed in water and given once daily as needed.
References:


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