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Problem Solving GI Issues in the Ketogenic Diet

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About the Ambassador



Lindsey Thompson is a registered dietitian in the Comprehensive Epilepsy Center at Children’s Mercy Hospital in Kansas City, Missouri, and is currently in pursuit of her PhD in Nutrition from the University of Kansas Medical Center. With 7 years of experience in the area, Lindsey currently follows over 100 patients on the ketogenic diet and is actively involved in research at her center. Lindsey is passionate about the ketogenic diet because of the remarkable difference it makes in the lives of patients, families and caregivers affected by epilepsy and other neurological disorders. While the concepts of the ketogenic diet date back to the early 20th century, Lindsey believes we are just now paving the way for modern medicine to seek and employ diet and nutrition as a first-line treatment for both chronic and debilitating disease states.

Objectives



Participants will be able to:

- List potential gastrointestinal (GI) complications of the ketogenic diet (KD)
- Evaluate possible interventions for GI complications of the KD

Side Effects of the KD



- Hyperlipidemia
- Cardiac disease
- Growth failure
- Kidney/ Uric acid stones
- Osteopenia
- Vitamin/ Mineral Deficiencies
- **GI disorders**

GI Problems



- Common problems:
 - Gastro-esophageal reflux disease (GERD)
 - Constipation
 - Vomiting
- Less common problems:
 - Pancreatitis
 - Fatty liver
 - Gallstones

GI Problems



- GI problems may occur in up to 75% of all KD patients



Bergqvist, et al. 2012. *Epilepsy Res*
Jenkins, et al. 2016 *Nutrients*
Kang et al. 2004 *Epilepsia*

GI Problems- Epilepsy



- Gut-brain axis links brain with the peripheral functioning of the GI tract
 - The brain directs digestion and movement of the GI tract
 - GI tract under sympathetic (tensing) and parasympathetic neuronal control
 - Neurotransmitters responsible for motility
- Seizures/spasticity: ↑ intra-abdominal pressure
- Genetic/other causes of epilepsy may result in hypotonia or other physical impairments
 - Low tone of GI tract (esophageal sphincter, peristalsis)
 - Limited mobility
- Many AEDs have GI side effects

Jenkins, et al. 2016
Chong, SK. 2001

GI Problems- Ketogenic Diet



- Fat can slow gastric emptying
- Fat can decrease intestinal transit time
- Fat can lower the esophageal sphincter tone/pressure
- Fluid restrictions

Bergqvist, et al. 2012

Nebel, et al. 1973

Baseline: GI History



- The International Ketogenic Diet Consensus Statement recommended a GI history taken prior to initiation of KD (Kossoff, et al 2008)
 - If GI problems are present, interventions should be started before the diet is initiated
- Referral to GI
 - Establish a GI-keto “champion”
- Jung, et al showed that by managing the GI problems, tolerance of KD can be improved

Jung et al 2008; Bergqvist et al 2012; Kossoff et al 2008

Common GI Problems

Gastrointestinal Reflux Disease (GERD)



- Typical medical recommendations (managed by PCP or GI specialist)
 - Manage constipation as needed
 - Medications (H2 blockers, proton pump inhibitors)
 - Fundoplication
 - Consider side effects of medications

GERD- Nutrition Assessment



- Seizure History
 - Do seizures cause vomiting?
 - Postictal issues
- Diet History
 - Timing/amount of meals/snacks/formula boluses
 - Timing/amount of water flushes
 - Positioning during feedings
- Labs
 - BMP (CO₂)

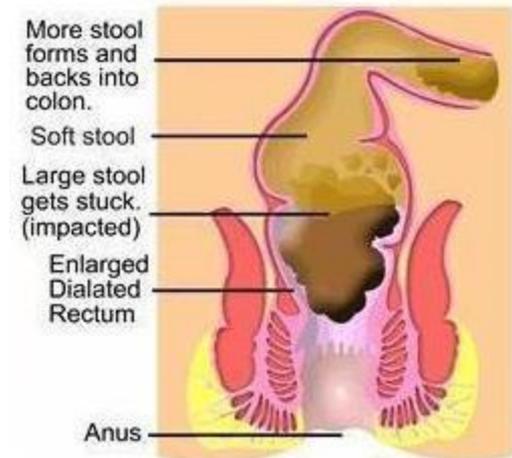
GERD- Nutritional Interventions



- Adjust feeding regimen:
 - Less volume, more often (both PO or tube fed)
 - Slow the rate of feeding
- Concentrate kcal of formula (less volume required)
- Change formula
 - Hydrolyzed, amino acid-based or whey
 - Blenderized diet
- Decrease ketogenic diet ratio (acidosis)
 - Also consider bicarb supplementation
- Water bolus 30 minutes prior to feedings
- Continuous feedings
- GJ feedings

Constipation

- Has been reported as the most common side effect of the ketogenic diet, up to 85% of patients (Hassan, *et al* 1999)
- Medical interventions (work with your physician to determine the appropriate amount for the child's age and weight)
 - Polyethylene glycol (Miralax™)
 - Glycerin suppositories
 - Enemas
 - Milk of Magnesia™, Natural Calm™ or other magnesium supplements



Constipation



Nutritional interventions

- Increase fluid intake
 - Ensure maintenance needs are being met
 - Increase to 110-120% of maintenance as needed
- MCT oil: start at 5-10% of kcal, increase up to 40% of kcal slowly as tolerated
- For PO fed, increase fiber content of meals (minimal impact noted clinically)
- Use more oils vs saturated fats

Case Study- CM



- 2 y/o male
- PMH: epilepsy, cortical dysplasia, diffuse polymicrogyria, microcephaly, GDD, hypotonia
- Epilepsy Medications: Clobazam, Keppra[®], Topiramate
 - Previously failed Trileptal[®]
- Followed in GI for reflux/vomiting
 - On Zantac[®] (previously on Prevacid[®])
- G-tube placed at 15 months d/t FTT

Case Study- CM



- Ketogenic Diet initiation
- Feeding regimen: 200 ml milk-based formula with 15 ml water flush x 4 via GT
 - Tolerating fair; vomiting 1x/week
 - Anthropometrics WNL
- CO₂ 19 at baseline
- Started on 3:1 Ketogenic diet on milk based formula with above regimen
- Discharged home on 1/8 tsp baking soda BID

Case Study- CM



- 1 month f/u
- Parents reporting increase in vomiting after feedings
 - Tried slowing rate of feedings
 - Interested in blenderized diet
- Inadequate weight gain
- Labs indicate acidosis: CO₂ 12
- Intervention: increased baking soda to ¼ tsp BID, repeat labs in a week

Case Study- CM



- 3 month f/u
 - Continued issue with vomiting, however parents reporting improvement in frequency/amount
 - Weight gain age appropriate
 - CO₂ 16
 - Intervention: trialed blenderized feedings for 2/4 feeds (boluses decrease from 200 to 90 ml each)
- 6 month f/u
 - Parents giving 3 of 4 feeds blenderized
 - Gaining weight well
 - CO₂ 20

Case Study- CM



- 1 year f/u
 - 3 Blenderized feeds (milk-free) + 1 formula feed daily via GT
 - Vomiting worsened over last 2 months
 - Significant weight loss
 - CO₂ WNL
- GI recommendation: Nissen fundoplication
- Vomiting has subsided since procedure although CM continues to have some retching
 - Remains on Zantac[®] and baking soda

Less Common Side Effects

Acute Pancreatitis



- Rare but serious complication
- Can be caused by
 - Hypertriglyceridemia
 - Notably with use of AEDs (especially VPA)
- Labs indicating acute pancreatitis
 - Elevated amylase
 - Elevated lipase
- Intervention KD typically discontinued

Stewart , et al. 2001

Toskes, et al. 1990

Acute Pancreatitis



- Stewart, et al (2001) reported death in a patient on the ketogenic diet
- 9-year-old girl with GLUT 1
- MCT KD initiated at 7 mos
- No anticonvulsants
- Presented in coma with decreased respiratory effort and shock, requiring resuscitation
- Despite fluid resuscitation and inotropic support, she had prolonged hypotension and acidosis
- Cause of death: hemorrhagic pancreatitis

Acute Pancreatitis



- Lab values: **low** / **high**

	Actual	Normal
Ionized Calcium (mmol/L)	0.62	1.15-1.28
Phosphorus (mmol/L)	4.14	1.3-1.8
Albumin (mmol/L)	20.4	30-45
Amylase	2810	15-109
ALT	1569	5-45
AST	2738	20-60
Bilirubin	20	0-17

Hepatitis



- Rare, but reported side effect
- Kang, et al reported:
 - 2.3% of 129 patients with hepatitis after <12 months on KD
 - 5.4% of 73 patients with hepatitis after >12 months on KD
 - All patients AST and ALT levels were < 200 mg/dl and persisted with KD
- De Vivo and DiMauro suggest that hepatitis could be caused by impairment of fatty acid oxidation or carnitine deficiency
 - Especially in patients also receiving VPA

Kang, et al. 2004

De Vivo, DiMauro 1999

Gallstones



- Incidence has been reported in patients on KD
- Hassan et al, *Pediatric Neurology* 1999
- 13 yo female put on the classic 4:1 KD
- Medications: primidone and lamotrigine
- 4 months post-initiation, CC: food refusal, N/V, lethargy, intermittent abdominal pain
- Serum ALT elevated at 336 U/L (normal range = 10-40 U/L)
- Normal serum alkaline phosphatase level
- Abdominal ultrasound demonstrated multiple small gallbladder calculi
- KD was discontinued



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Clinical Observations

Management of Symptomatic Cholelithiasis While on Ketogenic Diet: A Case Report



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ABSTRACT

INTRODUCTION: The ketogenic diet is a treatment modality used for patients with refractory epilepsy. Development of cholelithiasis while on the ketogenic diet is a potential side effect that has been described in the literature. There however have not been any reports on the outcomes of continuing the diet after cholecystectomy. **PATIENT:** We present a 5-year-old boy with history of pharmacologically intractable epilepsy that was well controlled on the ketogenic diet. He underwent laparoscopic cholecystectomy for the development of symptomatic cholelithiasis 12 months after the initiation of ketogenic diet for seizure control. **RESULTS:** Patient tolerated the surgery well and was able to continue the ketogenic diet postoperatively. **DISCUSSION:** There have been no reports describing the continuation of ketogenic diet after cholecystectomy. This child demonstrates the safety of the procedure and the ability to continue the ketogenic diet without further biliary or surgical complications.

Keywords: ketogenic diet, cholelithiasis, pediatric, cholecystectomy

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Case Study: Gallstones



- 5-year-old boy
- PMH: ex-25 weeker, static encephalopathy with GDD, focal epilepsy with h/o status epilepticus
- Failed 4 AEDs
- 3:1 KD initiated via GT (RCF[®] Formula + LCT)
 - Became seizure-free
- Increased to 3.5:1 (recurrence of seizures after weaning of AEDs)
 - Remained seizure-free after the adjustment

Case Study: Gallstones



- 1 year after KD he began to experience postprandial colicky abdominal pain that persisted for several months
- Transitioned to continuous feeds
- GI evaluation identified a 0.9-cm large mobile gallstone
- Surgery: laparoscopic cholecystectomy
- What diet changes would you consider?

Case Study: Gallstones



- Diet changes made:
 - Slow weaning up on MCT oil (16% of kcal)
 - Carnitine supplementation 330 mg TID (50 mg/kg/day)
 - Pancreatic enzymes: 1 tablet every 4 hours (contains 10,440 units lipase, 39,150 units protease and 39,150 units amylase)
- Follow Up:
 - His episodes of abdominal pain disappeared
 - No change in his stooling pattern
 - Neither the frequency nor the severity of his seizures changed

Conclusions



- The KD can cause or exacerbate various GI problems
- Most of these can be managed or improved without having to stop the KD
- A few problems (i.e. pancreatitis) are more serious and may require discontinuation of the KD

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