Ketogenic Diet Initiation & Management for Refractory Status Epilepticus

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February 24, 2016
I have no financial disclosures or conflicts of interest to report
Objectives

- Define Status Epilepticus and discuss current research that supports the use of the ketogenic diet as a viable treatment option
- Analyze ketogenic diet initiation and management protocol
- Review Case Studies
- Discuss challenges and pitfalls of diet initiation and management in the ICU
Defining Status Epilepticus (SE)

- SE is a medical emergency associated with significant morbidity and mortality.
- SE is defined as a continuous seizure lasting more than 30 min or two or more seizures without full recovery of consciousness in between.
- It has been estimated that up to 150,000 cases of SE occur annually in the US, with 55,000 associated deaths.
Seizure activity is refractory to anti-seizure drug therapy and requires general anesthesia.
SE that continues or recurs 24 hours or more after the onset of anesthetic therapy.
Prolonged treatment with IV anesthesia can result in hypotension, immunosuppression, gastric paresis, and pneumonia which may contribute to the high mortality rate of up to 30% in RSE.
Limited research on treatment information for RSE
Ketogenic diet should probably be tried in all severe cases

Between 2008 and 2013 there were ten publications describing KD therapy for SE

Best responders:
- Those with underlying autoimmune or inflammatory conditions leading to SE
- Encephalitis and Rasmussen syndrome
- Febrile illness related epilepsy syndrome
Diet therapy usually worked within 7-10 days of initiation.

Nine Patients with FIRES received a 4:1 diet ratio.
In 7 patients, KD was efficacious within 2-4 days following the onset of ketosis and 4-6 days within starting the diet
In one responder, early disruption of the diet was followed by a relapse and the patient died

Ten adult patients from 4 medical centers were started on KD for RSE

Median duration of RSE before initiation of KD was 21.5 days

Median number and AED’s used before initiation was 7

90% of patients achieved ketosis and RSE ceased in all patients achieving ketosis in average of 3 days

3 had minor complications and 2 died

Drawing Screening Labs
Orders prior to formula initiation
Designing Ketogenic Formula
Formula Initiation and Advancement Protocol
Diet maintenance protocol
Goals
Plasma Amino Acids
Urine Organic Acids
Plasma Acylcarnitine profile
CMP
CBC w/diff
Fasting lipid panel
Prealbumin
Free and Total Carnitine
Ica, phos, mag

Zinc, selenium
25-hydroxy vitamin D
Urinalysis
  - Results may be pending at the time of initiation
Orders Prior to Formula Initiation

- NPO x 24 hours prior to initiation
- Check accu-check q 4 hours during fast
- Convert all medications to pill/tablet form if possible
- IV fluids without dextrose at least 1x maintenance
  - Use sodium chloride or normal saline solution
Design Ketogenic Tube Feeding

Choose a Formula
- Ketocal 4:1 Liquid, Ross Carbohydrate Free Concentrate
- Various Modular Products: MCT oil, beneprotein powder, duocal, microlipid

Choose a diet ratio
- 4:1 diet ratio preferred unless protein need cannot be met at goal calorie level then a lower ratio is chosen (3:1, 2:1 etc)
Design Ketogenic Tube Feeding

- Choose a Calorie Level
  - Take into account growth history if available and current feeding regimen
  - If patient is comatose/sedated calorie needs likely much lower
- Define Feeding Regimen
  - Formula provided continuously via NG or NJ tube x 24 hours
Formula Initiation

- Initiate formula at half calories x 24 hours and advance to goal gradually over 3-5 days
Accu-check protocol:
- Every 3 hours and PRN if blood glucose ≤ 60
- Every 1 hour and PRN if blood glucose ≤ 50
- Every 15-30 minutes and PRN if blood glucose ≤ 45, then administer IV D5 100cc x1.
- Check urine ketones q void
- Check urine specific gravity q void
- Carnitine: Start empirically
  - 50mg/kg/day divided into 3 daily doses
Ketogenic Diet Initiation Protocol

- Daily beta-hydroxybutyrate (BHB) and CMP until ketosis well-established
- Recheck free/total carnitine levels in 2 weeks
- Check Prealbumin weekly
Establish ketosis and stop seizures!
Goal blood sugar: 50-80
Positive serum and urine ketones
Co2 >17
Try for at least 2 weeks before discontinuing diet therapy
Case Study: L.G 23 y.o Female

- History of epilepsy
- Admitted to outside hospital with altered mental status and went into SE
- Transferred to UCLA in pentobarbital induced coma with outside team unsuccessful at weaning sedation
- On multiple AED’s
- Following Modified Atkins Diet PTA
Case Study: L.G 23 y.o Female

- **Anthropometrics:**
  - Weight: 53 kg (116 lbs 13.5 oz)
  - Height: 64” (162.5 cm)
  - ~97% IBW

- **Estimated Needs**
  - 25 kcal/kg, 0.8-1.5 g protein/kg

- NG Tube in place. Tolerating Jevity 1.2 @ 50 ml/hr
Ketogenic diet started on day 4 of admission to UCLA

Goal Ketogenic Formula:

- 643 g Ketocal 4:1 liquid +
- 25 g beneprotein powder +
- 80 g liquigen (equivalent to ~40g MCT oil) +
- 458 ml water.

- Total Volume 1260 ml

Provided 3:1 ratio, 1400 calories, 135.6 g fat, 41.3 g protein, 3.9 g carb
Case Study: L.G 23 y.o Female

- Fasted for 24 hours
- Initiated full strength @25cc/hr (provides half calories) day 1
- High residuals prevented advancement of rate
- GJ tube placed ~7 days later and formula advanced to goal
Case Study: L.G 23 y.o Female

- Negative urine ketones and BHB <1 until day 9 of diet
- Day 9, BHB=2.52 and Urine ketones=moderate
- Glucose ranged from 73-127 mg/dL while receiving diet
- After about 2 weeks on KD, family decided to pursue palliative extubation due to poor prognosis and patient passed away.
Diagnosed with intractable epilepsy 1 year prior to admission

Transferred from outside hospital in pentobarbital induced coma in SE

Etiology of SE unknown
Case Study: S.C 6 y.o Male

- **Anthropometrics**
  - Weight: 19.2 kg (10-25\textsuperscript{th} %ile)
  - Height: NA

- **Estimated Needs**:
  - 60-70 kcal/kg, 1.3-1.5 g protein/kg

- NG tube in place. Receiving Pediasure with Fiber @50 ml/hr
In pentobarbital induced coma and on multiple AED’s including topamax

Ketogenic diet started on day 36 of admission to UCLA

Initiated diet full strength and full calories:
- 2:1 ratio day 1
- 3:1 ratio day 2
- 4:1 ratio (goal) day 3
Goal Ketogenic Diet Formula:
- 167 g ketocal 4:1 liquid +
- 1030 ml water =
- Total Volume ~1200 ml

Provided 4:1 ratio, 120.2 g fat, 25 g protein, 5 g carb
Case Study: S.C 6 y.o Male

- Anesthetics weaned 3-5 days post diet initiation
- Seizures became shorter in duration
- Moderate urine ketones after 2 days at goal diet
- BHB 3.70 mmol/L by day 5
- BHB ranged from 2.9-4.7 mmol/L while in PICU
- Blood sugars usually ranged from 80-100 and never dropped below 70
Case Study: S.C 6 y.o Male

- Developed nephrolithiasis shortly after initiating diet
  - Treated with Bicitra which lowered diet ratio and d/c topamax
Case Study: S.C 6 y.o Male

- Discharged from UCLA to rehab facility on ketogenic tube feeds after 3 month stay
- Calories were increased and he started ketogenic purees by mouth 1-2 months post discharge in addition to tube feedings
Case Study: S.C 6 y.o Male

- Progressed textures and continued diet at 4:1
- Became seizure free 4 months after diet initiation
- Weaned diet after 15 months
Managing Pitfalls and Challenges

- Poor Ketosis
- High Blood Sugars and Stress
- Hyperglycemia
- Carbohydrate Containing Medications
- Intolerance
Overfeeding

- Estimating calorie needs often difficult in sedated patients
  - Predictive equation suggestions
    - 50% of RDA
    - WHO Equation w/o activity factor
Obtain Resting Energy Expenditure test prior to diet initiation if possible

Patients on continuous oxygen excluded

Consider incorporating MCT oil early on
Stress Hyperglycemia

- Peripheral and hepatic insulin resistance, certain drugs, and increased stress hormone release have all been implicated as causes.
- Etiology and management requires further study.
- May be an unrecognized obstacle to ketogenic diet initiation.

Work with pharmacy to review carb content of meds and for suggestions on alternatives if available

- Pentobarbital IV solution contains propylene glycol which can prevent ketosis
- Propofol is administered in a 10% fat emulsion and contains glycerol (carb) and lecithin (protein)

Educating nursing staff
Vomiting/High Residuals
- Consider adding antiemetic
- Jejunal feeding tube placement (NJ tube) recommended to improve tolerance and prevent aspiration of formula into the lungs

Acidosis
- Bicitra is carb containing
Unanswered Questions

- What is the optimal timing to start KD?
- Best way to design and initiate KD? Fasting?
- Duration of treatment to observe any effect?
  - O’Conner et al suggested trailing KD for 2 weeks
- Duration of treatment after seizure control?
- Could predetermined KD formulas (based on average weights/gender) be designed to allow for quick diet implementation when RD not available?

Unanswered Questions

- Likelihood of improvement with KD?
- Which etiologies best respond?

The ketogenic diet is an exciting and efficacious treatment option for refractory status epilepticus for both adult and pediatric patients. Implementation requires an experienced ketogenic diet team.
References and Further Reading


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