Diet therapy for Epilepsy: From bench to bedside, over the years

CLAE Plenary session
September 22, 2018

Canadian League Against Epilepsy
Objectives

• Outline the clinical practise of ‘liberalized’ forms of diet therapy for epilepsy in Canada
• Discuss the role of ketogenic diet in adult patients with epilepsy
• Understand the management of side effects related to ketogenic diet and issues related to transition to adult care
• To share the new findings on the mechanism of action of ketogenic diet.
Changes in the clinical practise of diet therapy in Canada over the years
Rajesh RamachandranNair, Hamilton

Diet therapy for epilepsy in adult patients (two parts)

Question: Should I offer KD in a new adult epilepsy Program-Medical director’s dilemma
Tadeu Fantaneanu, Ottawa

Answer: Experience at the adult ketogenic diet clinic/TWH
Eduard Bercovici, Toronto

Management of side effects and issues with transition
Alex Printis (Vancouver), Helen Lowe & Maria Zak (Toronto)

Mechanism of action of ketogenic diet- Is it still a mystery?
Jong Rho, Calgary
Changes in the clinical practise of diet therapy in Canada over the years

Rajesh RamachandranNair, MBBS, FRCPC
Medical Director, Comprehensive Pediatric Epilepsy Program
McMaster Children’s Hospital
Faculty/Presenter Disclosure

• Relationships with financial sponsors:
  • Grants/Research Support: Ontario Brain Institute
  • Speakers Bureau/Honoraria: Nothing to disclose
  • Consulting Fees: Nothing to disclose
  • Patents: Nothing to disclose
Disclosure of Financial Support

- This program has not received financial support
- This program has not received in-kind support

Potential for conflict(s) of interest:
- None to disclose
Mitigating Potential Bias

• None
Medically refractory epilepsy: Options

• Another drug????
• Surgery
  • Resection
  • Stimulation

• Diet therapy
Classic ketogenic diet

• Ratio  = Fat (weight) : (Protein + Carbohydrate weight)
• 4:1 ratio = 4 g fat : 1 g (protein + carbohydrate)
• 1 g fat = 9 kcal, 1 g protein/carbohydrate= 4 kcal
• Classic KD is
  • High in fat (usually LCT)
  • Low in carbohydrate
  • Moderate protein
  • 3: 1 or 4: 1 ratio
  • Total daily calorie fixed
  • Daily amount of fat, protein and carbohydrate fixed
  • Each meal weighed/measured

J Child Neurol. 2009;24:979-988.
Regular diet (of total calories)

• Fat 20-35%
• Carbohydrate 50-70%
• Protein 15-20%
• Ratio 0.2:1 (fat 31%)
• Ketogenic Diet
  • 4:1 90% Calories from fat
  • 3:1 87% Calories from fat
  • 2:1 82% Calories from fat
  • 1:1 69% Calories from fat

Continuum (Minneap Minn) 2013;19(3):756–766
When to consider diet therapy

- Seizures not responding to 2-3 AEDs
- Some specific epilepsies- ?early
  - Myoclonic Atonic Epilepsy
  - Dravet syndrome
  - Epilepsies with myoclonic seizures
  - Infantile spasm
- Specific metabolic conditions
  - Glucose Transporter GLUT-1 deficiency
- Caution
  - Surgical candidate

Kossoff EH Epilepsia Open 2018
Classic KD: Initiation

• 2 methods
  • Inpatient
  • Outpatient

• Inpatient admission
  • Usually rapid advancement
  • Over 3-5 days
  • To 3:1 or 4:1 ratio

• Outpatient initiation
  • Same method

Kossoff EH Epilepsia Open 2018
Classic Ketogenic Diet (3 : 1) Example for a day (it is fixed)

<table>
<thead>
<tr>
<th>Energy</th>
<th>1500 kcal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat</td>
<td>87% total kcal</td>
</tr>
<tr>
<td>Protein</td>
<td>7% total kcal</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>6% total kcal</td>
</tr>
</tbody>
</table>

Fat 145 g/day
Protein 26.25 g/day
Carbohydrate 22.5 g/day
Retrospective data

- Retrospective studies; Meta-analysis of 19 studies
  - >1000 patients
  - 30% had >90% reduction in seizures
  - 50% had >50% reduction in seizures

History: from Torture to Nurturing

- Fasting
- Calorie restriction
- Fluid restriction
Fasting versus Gradual Initiation of the Ketogenic Diet: A Prospective, Randomized Clinical Trial of Efficacy

*A. G. Christina Bergqvist, †Joan I. Schall, ‡Paul R. Gallagher, ‡Avital Cnaan, and †Virginia A. Stallings

Divisions of *Neurology, †Gastroenterology and ‡Pediatrics, and †Neurology.

Ketogenic Diet: Outpatient Initiation, Without Fluid, or Caloric Restrictions

Inna I. Vaiselit, MD, Jeffrey R. Buchhalter, MD, PhD, and Mary L. Zupanc, MD

Although the ketogenic diet has been used for more than 80 years, the optimal methods of initiating the diet and its maintenance have not been clearly defined. This retrospective study was performed to review our experience with initiation of the ketogenic diet in the outpatient and inpatient settings and maintenance of the diet without fluid or caloric restrictions. We analyzed 51 patients who had medically intractable epilepsy of whom 44% manifested some degree of mental retardation, 60% had multiple seizure types, and failed on average 4.6 antiepileptic drugs. Forty-one patients underwent initiation of the ketogenic diet on an outpatient basis and 20 as inpatients. Three patients in each group were found at the initiation of the diet. No significant differences were observed with regard to seizure control in that 57% and 75% had greater than 50% improvement in the outpatient and inpatient groups, respectively. Both groups manifested improvement in alertness and social interaction. The efficacy of a ketogenic diet in the symptomatic epilepsy was confirmed, and benefit for medically refractory childhood absence epilepsy was documented. We conclude that a prospective, randomized trial is necessary to compare outpatient vs. inpatient initiation of the ketogenic diet and the utility of fluid and caloric restriction.

© 2001 by Elsevier Inc. All rights reserved.

SUPPLEMENT - KETOGENIC DIET AND TREATMENTS

Ketogenic ratio, calories, and fluids: Do they matter?

Elaine C. Wirrell
Divisions of Epilepsy and Child and Adolescent Neurology, Department of Neurology, Mayo Clinic, Rochester, Minnesota, U.S.A.

SUMMARY
The ketogenic diet (KD) traditionally was initiated using specified ketogenic ratios, limited calories, and fluids. Recent work has shown that lower ketogenic ratio diets are frequently as efficacious as higher ones and result in fewer adverse effects. In animals, calorie restriction is anticonvulsant. In children, however, the need for calorie restriction is less clear, but avoidance of excessive calories may improve efficacy of the diet. There is no evidence that fluid restriction is a necessary component of the KD. Given the higher risk of nephrolithiasis, adequate fluid intake should be encouraged.

KEY WORDS: Calorie restriction, Ketogenic diet, Ratio, Fluids.
A welcome change

- Last 10-15 years
- No fluid restriction
- No calorie restriction
- No fasting
Modifications to Diet

- MCT oil diet
- Modified Atkins Diet (MAD)
- Low Glycemic Index Therapy (LGIT)

Carbohydrate 10-20 g/day
No restriction on Calories
No restriction on fat
No restriction on protein
But high fat and protein is encouraged
No weighing
Flexible

1:1 ratio

Level of ketosis: Low

Similar to MAD
But uses carbohydrates with Glycemic index <55%
Carbohydrate per day 40-60g

Epilepsy Behav. 2013;29(3):437-42
Evolving practice in Canada
Gradual initiation of classic diet

- McMaster Children’s Hospital
- Children’s Hospital, London

- Outpatient basis
- Starting ratio 0.67-1:1
- Increase every 1-2 weeks
Our experience

• 40 patients (M:F 20:20)
• Median age of 4 yr 4 mo (5 mo - 16 yr 5 mo)
• Overall, seizure frequency at 6 months
  • Baseline 516/month
  • At six months 118/month (SD 178) with p= 0.049 (two tailed).
• 21 patients (52.5 5%) had good seizure control at 6 months.
  • This included 13 (32. 5%) who had excellent seizure control
    • 7 of whom were seizure free; 17.5%.
Ratio

- Effective ratio: 2 :1 (median) in patients who had excellent seizure
  - including 7 seizure free patients, ratio 1.5 :1.
- Ratio was 2.16 :1 (median) in those who had 51-90% reduction in seizures.
- 13 (62%) of the 21 patients with good seizure control were on a low ratio at 6 months.
2 year

• Good seizure control 14/18
  • Excellent control 13
    • Seizure free 7
What did we learn

• Ratio - high or low: It works
• Gradual titration- advantage
• Common element in all forms of diet
  • Low carbohydrate
Combined principle

• Low ratio initiation, gradual titration
• Principle of Modified Atkins Diet

• **Try**: Gradual reduction in carbohydrate

• Our patient
Caution

• Some epilepsies: rapid response
• Depends on parents
Message

• Diet therapy is helpful in children with medically refractory epilepsy
  • Patient selection
• Several modifications exists
  • All work
• Seizure control alone should not be the goal