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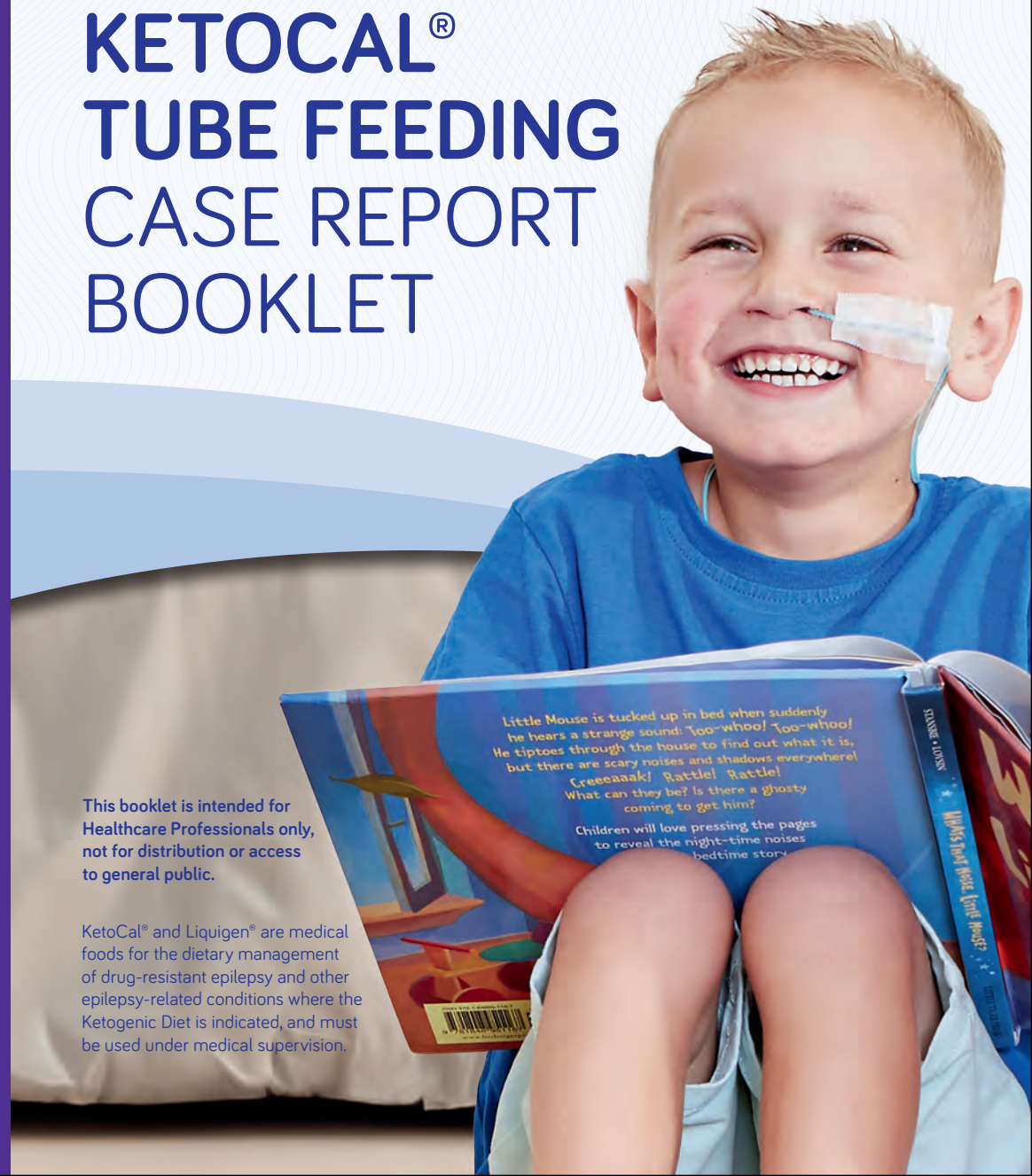
KETOCAL® TUBE FEEDING CASE REPORT BOOKLET



This booklet is intended for Healthcare Professionals only, not for distribution or access to general public.

KetoCal® and Liquigen® are medical foods for the dietary management of drug-resistant epilepsy and other epilepsy-related conditions where the Ketogenic Diet is indicated, and must be used under medical supervision.

Note from the author

The medical ketogenic diet (KD) is an effective management for drug-resistant epilepsy and should be offered after two failed anti-seizure medications[1]. The KD can be administered via feeding tube and has been shown to be more efficacious in this group[2,3].

The classical KD can be calculated and administered with accuracy, offering greater consistency in macronutrients and diet ratio provided. Diet adherence is easily achieved in tube-fed patients: Moving from a standard tube-feed to a ketogenic formula is quite acceptable to patients and families, as the feed can be designed to mirror their current feed in terms of energy and volume. Changing feeds has a minimal impact on their care-burden and KD management but may have a huge impact on quality of life.

Hannah Taylor, Specialist Ketogenic Dietitian, Sheffield Children's Hospital, UK

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Optimal clinical management of children receiving dietary therapies for epilepsy: Updated recommendations of the International Ketogenic Diet Study Group

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Ketogenic diets for drug-resistant epilepsy.

Martin-McGill KJ, Bresnahan R, Levy RG, Cooper PN. Ketogenic diets for drug-resistant epilepsy. Cochrane Database Syst Rev. 2020 Jun 24;6(6):CD001903. doi: 10.1002/14651858.CD001903.pub5. PMID: 32588435; PMCID: PMC7387249.

International recommendations for the Management of Adults Treated with Ketogenic Diet Therapies:

Cervenka MC, Wood S, Bagary M, Balabanov A, Bercovici E, Brown MG, Devinsky O, Di Lorenzo C, Doherty CP, Felton E, Healy LA, Klein P, Kverneland M, Lambrechts D, Langer J, Nathan J, Munn J, Nguyen P, Phillips M, Roehl K, Tanner A, Williams C, Zupec-Kania B. International Recommendations for the Management of Adults Treated With Ketogenic Diet Therapies. Neurol Clin Pract. 2021 Oct;11(5):385-397. doi: 10.1212/CPJ.0000000000001007. PMID: 34840865; PMCID: PMC8610544.

For the practical aspects of calculating KD, the following books are useful:

Neal E. The classical ketogenic diet. In: Dietary Treatment of Epilepsy Practical Implementation of Ketogenic Therapies, UK: John Wiley & Sons Ltd, 2012, p.70

Kossoff EH, Turner Z, Mackenzie C et al. Calculating the ketogenic diet. In: Ketogenic Diet Therapies for Epilepsy and Other Conditions, 7th edn. New York: Demos Health, 2020.

Contents

Introduction

Epilepsy is a common neurological disorder characterized by a predisposition to develop epileptic seizures. More than 2 million cases of epilepsy are diagnosed every year[1] with the greatest incidence in the first 2 years of life[2], a population that remains most at risk for neurodevelopmental compromise in the longer term[3]. Early seizure control is necessary to support better developmental outcomes[4]. Seizure freedom safeguards psychomotor development, and it has recently been demonstrated that even in critically ill children a higher seizure burden predicts further neurological decline, independent of the primary disease or etiology[5].

Achieving seizure control (including seizure freedom (SF), ≥90% seizure frequencies reduction (SFR) and ≥50% SFR), maintaining quality of life (QoL), and avoiding adverse events (AEs) are three fundamental goals of epilepsy treatment[6].

Although most people with epilepsy have a good response to and become seizure free by treatment with one or more anti-seizure medications (ASMs), up to 30-40% of children and adults have drug-resistant epilepsy and do not respond well to ASMs[7], failing adequate trials of two tolerated and appropriately chosen ASMs[8,9]. Updated recommendations from the International Ketogenic Diet Study Group state that the ketogenic diet should be considered after failure of 2-3 ASMs*[10]. The medical ketogenic diet (KD) is a well-established, tolerated and effective option for children of all ages with drug-restistant epilepsy.[10-14] There is also growing evidence for the use of the medical KD in adult drug-resistant epilepsy[15-17] with the first adult guidelines published in 2021[18].

It is not uncommon for those with neurological problems to experience other co-morbid conditions, such as swallowing difficulties and an inability to tolerate oral feeds. Consequently, enteral tube feeding is indicated for partial or full nutrition support. A KD can be easily delivered via a tube directly into the stomach or jejunum (post-pyloric feeding). Enteral tube feeding via a nasogastric or gastrostomy feeding tubes are most common.

Presented herein is a series of 7 case studies that initiated tube feeding with KetoCal for the management of drug resistant epilepsy.

The content is written by expert dietitians and neurologists, who kindly provided a clinical case and practical insights on their best clinical practice.

Disclaimer: The patient images used are not related to the case studies in this booklet, but the images used are of patients diagnosed with drug-resistant epilepsy. All case reports are de-identified and do not list actual patient names.

For references, see end of booklet.

At the beginning of the ketogenic diet management she was fed a combination of glucose polymers to complete the carbohydrate and KetoCal® 4:1 powder requirement. Taking into account the low weight and height/size, a slight increase in the protein intake was calculated. Zoe received 105 kcal/kg/weight. Resulting in a total of 890 kcal/day until she reached an appropriate weight for her size/ height and age.

Ratio 1.1 — KetoCal 4:1 powder 75% of the requirement + glucose polymer diluted in water and distributed in 6 intakes of 140 cc every 4 hours. Foods, tolerated without difficulty, administered without difficulty, administered by gavage. She maintains normal blood glucose (0.80-0.90 gr/ml) and a slight increase in ketonemia (0.4-0.8 mmol/l) is observed in the afternoon. This recipe was maintained for 48 hours.

Ratio 1.5:1 — KetoCal 4:1 powder 85% of the requirement + glucose polymer + fiber module is added due to constipation. She maintains normal blood glucose (0.75-0.80 gr/ml) and a slight increase in ketonemia (0.9-1.3 mmol/l) is observed in the afternoon. This recipe was maintained for 48 hours.

Ratio 2:1 — KetoCal 4:1 powder 95% of the requirement + glucose polymer + fiber supplement; blood glucose remains normal (0.70-0.75 gr/ml) increase in ketonemia (1.7-2.3 mmol/l) in the afternoon. The fiber supplement caused abdominal distension and gas, at least at the beginning, so the same proportion remained. This recipe was maintained for 6 days.

Ratio 2.5:1 — KetoCal 4:1 powder 95% of the requirement + glucose polymer + fiber supplement + Liquigen (MCT emulsion); blood glucose remains normal (0.70-0.75 gr/ml); increase in ketonemia (2.6-3.2 mmol/l) in the afternoon. This recipe was maintained for 4 days.

Ratio 3:1 — KetoCal 4:1 powder 100% of the requirement + glucose polymer + fiber supplement + Liquigen the blood glucose remains normal (0.65-0.70 gr/ml), the expected ketonemia (2.8-3.8 mmol/l) was achieved in the afternoon. This is the current recipe.

Clinical Outcome

Zoe was discharged from hospital 5 days after starting ketogenic diet management, with a crisis-free ratio of 2:1. We continued to increase the ratio from home by communicating by phone via WhatsApp, with a ketonemia and blood glucose monitor controlled by her mother, who twice a day took a sample telling us the result until we achieved proposed ketonemia.

Weight is checked after 7 days: 8.73 kg; after 15 days: 8.95 kg.

After 30 days of starting treatment, the weight was 9.2 kg.

After 60 days the weight was 10.1 kg having reached (P3) in weight and height /p age.

Learning Points

After 6 months of KD therapy, Zoe is free from focal seizures, some sporadic myoclonies persist. She improved her general condition, attention, she has less tremors and improved her nutritional status. She is in the process of having a gastrostomy button fitted.

She evacuates normally every 24 or 48 hours without difficulty.

She continues with a ketogenic ratio of 3:1; her weight is 11.4 kg and height 86 cm (P); total calories per day are 1026 kcal (90 kcal/kg/d).

"I am delighted to see the tube feeding information guide and case report booklet being made available by Nutricia. As mum to Matthew and having supported thousands of families over the years through their own ketogenic journeys, it has always been a frustration of mine that tube fed patients aren't given earlier access to Ketogenic Dietary Therapy, especially as there are Ketogenic formulas readily available.

In my opinion, the trialling of a Ketogenic Diet could not be simpler, so why there are so many tube-fed patients suffering unnecessarily is quite beyond me. Change their feed for

3 months and see what happens, what have you got to lose? These patients are supervised by dietitians in any event, so we already know they are well looked after. To me, it seems ridiculous that patients are being made to wait so long to gain access to a different feed, it is like keeping an infant on a cow's milk formula when they are allergic to it instead of putting them on a feed that could make their lives infinitely better.

I hope that these new materials go some way towards giving more medical professionals the confidence to change feeds and trial their patients on the medical ketogenic diet.

Emma Williams MBE – Founder of Matthew's Friends and mother to Matthew.

Summary Table

Case Report	Author	Patient	Diagnosis and history
1	Hannah Taylor, Specialist Ketogenic Dietitian, Sheffield Children's Hospital	'Aleena' 3 years old	• Infantile onset epilepsy. • Symptoms consistent with Lennox-Gastaut Syndrome (LGS). • Severe developmental impairments and likely cortical visual impairment. • Seizures started at 3 months of age and occurred 2-8 times daily. Anti-seizure medications were trialled without success. • Faltering weight on assessment, from 50th to 2nd percentile. Her swallow was deemed unsafe and nasogastric feeding initiated.
2	Jennifer Carroll, Consultant Ketogenic Dietitian, The Keto Dietitian	'Assan' 18 years old	• Myoclonic astatic epilepsy (Doose syndrome) • Six anti-seizure medications had been trialled and failed to control his seizures. Seizure occurrence on referral was 70-80 absence seizures and 3-5 tonic seizures daily. He had been fed via a gastrostomy since childhood and had a history of some poor feed tolerance, causing reluctance to commence KD previously.
3	Dr. María del Carmen Rivero de la Rosa, Spain	'Nina' 8 years old	• Cerebral palsy • Drug-resistant secondary epilepsy • Has required up to 4 epileptic medications without good control. • Nutritional status declined from 15 months of age and maintained moderate malnutrition until fed via gastrostomy from 2 years of age.
4	Zoe Simpson, Trainee Advanced Clinical Practitioner (tACP)– Dietetic Clinical Lead for Neurosciences, Great Ormond Street Children's Hospital London	'George' 2 years old	• Infancy onset epilepsy • Microcephaly and congenital pontocerebellar hypoplasia • Tonic seizures occurred 2-3 times every two weeks. Faltering growth was observed with weight <0.4th percentile. Unsafe swallow found and nasogastric tube in situ.
5	Margaret MacRae, Highly Specialist Adult Ketogenic Dietitian, UCLH	'Sebastian' 27 years old	• Lennox-Gastaut Syndrome (LGS) • Seizures had occurred from the age of 4 years, with 5-15 seizures per month and long recovery times. A gastrostomy tube had been in situ from 18 months prior to KD introduction.
6	Lauren Kronisch, Clinical Dietitian Coordinator, Houston-based top children's hospital	'Kevin' 9 years old	• Symptoms consistent with intractable epilepsy • Seizures started at 1 year of age after near drowning accident, multiple admissions for status epilepticus. At home baseline was 2 seizures/day lasting between 10 seconds to maximum 5 minutes. • Weight and growth normal, stature plateaued at seven years of age. • Swallow impairment required enteral access since near drowning accident.
7	Lic Lara González, Leader in Ketogenic diet in Neuquén, Argentina	'Zoe' 3 years and 9 months	• Phenotype consistent with Rett syndrome. • Developmental delay and acquired microcephaly were seen from 9 months of age. Zoe went on to develop frequent nocturnal focal seizures and less frequent myoclonic seizures which were drug-resistant. Nasogastric tube placement was required due to unsafe swallow with the onset of epilepsy. Zoe was underweight for her size.

*Ratio = fat:carbohydrate plus protein

CASE REPORT 7: ZOE

Lic Lara González

Leader in ketogenic diet in Neuquén, Argentina

Patient Profile

Zoe is a 3 year and 9 month old girl with phenotype consistent with Rett syndrome. She has a lower-middle class family. Her mum studies nursing and her dad is a truck driver.

Background

At the age of 6 months, she began to show visible evidence of global developmental delay together with acquired microcephaly. She presents generalized hypotonia with axial predominance, she achieved cephalic support at 13 months. However, she has not yet achieved autonomous sitting. She had an absence of language until 18 months, when she had started with babbling, a pattern that she later lost. She does not imitate sounds. She has trunk tremor, stereotyped hand movements continually and permanent bruxism during waking hours.

At 2 years and 6 months of age, she began with frequent nocturnal focal seizures and less frequent myoclonic seizures, drug-resistant, medicated with levetiracetam, valproic acid, clobazam and oxcarbazepine.

The electroencephalogram shows diffuse slow waves, multifocal spikes and right lateral spike paroxysms of high-frequency discharge.

A progressive deterioration was evident in the patient since the onset of epilepsy with loss of acquired motor patterns and loss of swallowing requiring nasogastric tube placement. Prior to the onset of epilepsy, she had a normal video swallowing. Left hemi-body focal statuses conditioned an acquired left hemiparesis.

Brain MRI with normal spectroscopy and normal complete spine.

PEAT with normal thresholds.

Normal metabolic study.

She shows normal microarray and normal exome (the exome will be checked).

Clinical Assessment

At 3 years and 3 months in context of drug-resistant status, she begins inpatient ketogenic diet (KD) therapy. Prior to starting ketogenic KD therapy, a video swallowing/swallow was indicated which showed that her swallowing was quite ineffective, therefore, she continued feeding via nasogastric tube. Although prior to her hospitalization she was fed by mouth, with a mixed diet, her mother stated that she accepted all foods in the form of porridge and the feeding time was prolonged. She took a bottle 3 times a day with milk.

She was underweight for her size/height and age.

Dietetic Intervention

At the time of starting therapy:

Her weight was 8.5 kg (PC 3) and her length was 83 cm with a BMI of 12.1 kg/m^2

Her weight after hospital discharge 8.37 kg (PC<3)

Ketogenic diet (KD)	Outcome with KetoCal 4:1
• A diet initiation plan was provided for 2:1 ratio*, with additional steps increasing the ratio up to 4:1. Additional increases were made every 2-3 days based on monitoring outcomes. • Optimal ratio was found to be 3:1 based on ketones, blood glucose and seizure activity. **The regime was formulated using the products below:** • 650 ml KetoCal 4:1 LQ. • 8 g Polycal™ powder.	• After 3 months on KD, Aleena was seizure free for 5–8-day periods and seizures were less severe. Tonic seizures stopped, head control improved, she was brighter and more alert. • No abnormalities seen on ketogenic monitoring bloods. Anti-seizure medications were reduced. • After 6 months on KD, ketones remained stable and seizure control remained as at 3 months. There were no new side effects and attendance to nursery school improved.
• A 2.2:1 ratio* (limited by lower energy requirements) was used and the final regime was achieved through gradual introduction of KD and reduction of existing enteral feed formula every 5 days. **Consisted of the following products:** • 750 ml KetoCal 4:1 LQ • 36 g Protein supplement • 40 ml Calogen® (changed to Liquigen)	• After 3 months on KD, there was a 70% reduction in seizure activity. Less daytime sleeping was observed. Assan was brighter and more alert and attending school more regularly. • After 6 months on KD the positive effects continued and anti-seizure medication was reduced.
Diet regimen: • A 3:1 ratio* was used for initiation of KD using KetoCal.	• After 2 years of KD, there was improvement in cognitive, behavioral and motor state. Ketone levels were stable and normal blood glucose levels were maintained at all times. This lead to a decrease in antiseizure treatment.
• Initially, KD was introduced gradually alongside 1 kcal/ml fiber-containing formula at 2:1 fat:carbohydrate ratio*, then increased over 4 weeks with monitoring. **4:1 ratio, with 10% increase after 8 weeks to improve growth, using the following:** • KetoCal 4:1 LQ (+ Pediatric 1 kcal/ml fiber-containing formula on initiation)	• After 12 weeks on KD, seizures had reduced, with up to 16 days between and more becoming more subtle. Weight gain increased by 1SD to 0.3 percentile.
• KD was introduced alongside Sebastian's existing feed, starting with 1.8:1, then 2.2:1, 2.5:1 and a target of 2.8:1 ratio*. **2.8:1 ratio using a combination of the products below:** • 1000 ml KetoCal 4:1 LQ • 135 ml Protein supplement • 120 ml Fat supplement • 15 g Fiber supplement	• After 3-month trial of KD, a 20% reduction in seizure activity was seen and a 30% reduction in recovery time. • Energy levels improved and there was increased engagement in activities. Ketone readings remained consistent and weight was stable.
• A diet initiation plan was provided for a 1:1 ketogenic diet ratio diet. Additional increases were made daily based on monitoring outcomes. The optimal ratio was found out to be 2.5:1 based on ketones, blood glucose level, and seizure activity. **The regime was formulated using the following products:** • KetoCal 4:1 Liquid Vanilla plus a medical nutritional milk protein powder • Water to meet estimated fluid needs via Holliday-Segar method • After three years on the diet, a 3:1 ketogenic diet ratio with the same products was trialed; however, due to vomiting, was switched back to a 2.5:1 ratio after a few weeks.	For the first two years on the ketogenic diet, seizures decreased to two seizures per week. After five years on the same ketogenic diet ratio and formula (with gradual calorie increases to meet growth needs), seizures were now once every other day to once per day. Growth continues to be appropriate by weight, though length has plateaued after five years on the ketogenic diet. All labs are normal for a child on the ketogenic diet, and optimal ketosis continues with an average beta-hydroxybutyrate measurement of 2-4 mmol/L.
KD was commenced as an inpatient via nasogastric feeding: • Initial ratios* were introduced using KetoCal 4:1 – 1.1:1, 1.5:1, 2:1, 2.5:1 and 3:1, these were progressed over a number of days with monitoring. • Optimal KD ratio maintained was 3:1.	• After 6 months on KD, Zoe was free from focal seizures and still had some sporadic myoclonies. Her general condition and attention improved, and her tremor had reduced. Her nutritional status had improved as evidenced by weight gain. She is due to have a gastrostomy fitted.


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Liquigen
Emulsified MCT Oil
A high energy medium chain triglyceride (MCT) emulsion
8.5 fl oz (250 mL)

Estimated Nutritional Requirements by Age

Energy: 70 kcal/kg/day (method: Current regimen)

Protein: 0.95 g/kg/day (method: DRI/age)
Fluids: 1640mL/day (method: Holliday-Segar)

Current Intake

Current feed plans: 2.5:1 Ketogenic Diet Ratio: 1155mL KetoCal® 4:1 LQ Vanilla (4 packs + 207mL from a 5th pack) + 28.5g of a medical nutritional milk protein modular + add water to 1200ML total volume

Schedule: 61mL/hr x 20 hours/day via g-tube
Additional Water: 110mL 4x/day with medications via GT

Total Daily Kcal Intake: 1818 kcal/day (69 kcal/kg/day)

Total Daily Protein Intake: 60.11g/day (2.28 g/kg/day)

Total Daily Fluid Intake: 1560mL/day

Ketogenic Ratio: 2.5:1

Most Recent Dietetic Interventions (3 Months Ago)

Increased estimated fluid needs related to growth as evidenced by current enteral fluid intake meets 96% estimated fluid needs. Increased free water to 110mL 4x/day to better meet estimated fluid needs.

Reviewing KetoCal to Determine Most Appropriate Feeding Considerations

- KetoCal 4:1 LQ Vanilla, plus milk protein modular, added water, and ½ scoop/day of a low-carb multivitamin together are currently meeting all estimated needs.
- Parental preference
- Ease of preparation
- Local medical supplies company delivery of formula and feeding supplies

The initial keto diet ratio can be increased if a change in seizure control warrants further ketogenic diet ratio optimization.

Clinical Outcome:

After seven years on the ketogenic diet, Kevin has stable optimal ketosis. For the first two years on the ketogenic diet, seizures decreased to two seizures per week. After five years on the same ketogenic diet ratio and formula (with gradual calorie increases to meet growth needs), seizures occurred once every other day to once per day. He has occasional constipation treated with 1 Tbsp flaxseed oil every other day, which enables 1 bowel movement every one to two days. Kevin's weight is stable along his own growth curve (3% on CDC 2-20 Years for Boys Weight-for-Age), though his stature increases are slower than expected (tracking at <1% on CDC 2-20 Years for Boys Height-for-Age), which is a 68% BMI-for-Age on CDC 2-20 Years for Boys. He is followed by endocrinology for his slow stature growth.

Today, his seizure episodes are stable at one seizure episode every one to two days, and developmental gains continue since starting the ketogenic diet, including increased ability to participate in therapies like physical therapy.

CASE REPORT 1: ALEENA

Hannah Taylor
Specialist Ketogenic Dietitian, Sheffield Children's Hospital

Patient Profile

Aleena is 3 years old with a background of infantile onset epilepsy, evidence of structural abnormality, drug-resistant epilepsy with tonic seizures and spasms consistent with Lennox-Gastaut Syndrome (LGS). She also has severe developmental impairment and likely cortical visual impairment.

Aleena started to have seizures at 3 months of age starting with spasms and quickly developing tonic seizures. She trialed several seizure medications which at times provided short periods of relief but were ultimately unsuccessful.

Background

Aleena was seen in the Ketogenic Diet (KD) clinic after referral from her consultant neurologist. At the time of referral Aleena was managed on a combination of sodium valproate, zonisamide and nitrazepam and was having tonic seizures characterized by a sudden stiffening and posturing of all 4 limbs with her eyes rolling up and down for up to 20 seconds, followed by a cluster of spasms. She was having 2-8 of these clusters per day with each cluster lasting 4-8 minutes. Aleena previously had spasms which were associated with squeezing of her eyes, shoulders crunching and arms coming up which tended to occur in clusters but these were under control. Her recent 24-hour video telemetry pattern showed features of epileptic encephalopathy, tonic seizures with epileptic spasms and slow spike wave discharges, all consistent with a diagnosis of LGS.

At this time, Aleena was demonstrating faltering growth. Her weight had dropped from 50th centile to 2nd centile when she was measured in clinic. She was eating mashed texture meals and using a food thickener in foods and fluids. Her parents reported some coughing when eating and her breathing could be noisy. They also reported that she regularly regurgitates small amounts of food, but does not vomit. Assessing her current dietary intake was difficult as her daily intake was very variable, and if seizures were bad, then intake would be no greater than a few mouthfuls of food and fluid. Her parents reported no issues with constipation or diarrhea.

At this appointment, her parents were keen to go ahead with KD management however, it was agreed that Aleena would have a video fluoroscopy to assess the safety of her swallow and a referral to Ear, Nose and Throat (ENT)/ respiratory specialist for her breathing before commencing the KD.

Aleena's video fluoroscopy showed she had an unsafe swallow. She was commenced on nasogastric (NG) feeds and was referred for a gastrostomy insertion. ENT assessed and advised that Aleena likely had neurological laryngomalacia for which no active treatment was required. Gastroenterology had also started anti-reflux treatment (lansoprazole). Aleena's pre-diet bloods had shown no abnormal results.

Aleena, now ready to start the KD, was provided with a plan to wean from her current feed onto a KD and the family were trained to measure blood ketones and glucose.

Clinical Assessment

Weight and weight history

Weight history showed Aleena tracking 50th centile until ~ 2 years of age, then had a slow decline to 2nd centile at 3 years, 4 months, when she first assessed for KD. Height has tracked 50th centile since ~18 months of age.

At 3 years, 7 months, Aleena was ready to start KD and had been tube fed for approx 4 weeks. Her weight was on the 9th centile at 12.1 kg with her height remaining on 50th centile.

Dietetic Intervention

Energy requirements are calculated using data from SACN 2011 report on dietary reference values for energy[1]:

EAR/kg for a 3-year-old girl is 78 kcal/kg

78 kcal x 12.1 kg = **943.8 kcal/day**

Extra energy may be needed to promote catch up weight gain.

Protein recommendations are based on the FAO/WHO/UNU 1985 report for Energy and Protein requirements[2]:

Children aged 1-3 years recommended nutrient intake for protein is **14.5 g/day**

Fluid requirements can be calculated using an adaptation of the Holliday-Segar formula[3]:

100 ml fluid/kg for the first 10 kg body weight = 10 x 100 = 1000 ml

50 ml fluid/kg for the next 10 kg body weight = 2.1 x 50 = 105 ml

1000 + 105 ml = **1105 ml fluid/day**

Other information considered:

Aleena's current feed plan had resulted in a weight increase up to 9th centile.

Current feed: 1000 ml/day Nutrini (Nutricia)

1000 ml Nutrini provides; 1000 kcal and 27 g protein

This as given as 5 x 200 ml bolus feeds via NG tube with 10-20 ml water flush pre and post each feed.

As Aleena was having some catchup weight gain (increased from 2nd to 9th centile for weight) from 1000 kcal per day it was sensible to continue with this daily energy intake.

Choosing type of KD

As Aleena was solely tube-fed, the classical ketogenic diet was most appropriate. The feed recipes can be calculated to specific ratios and easily adjusted when fine-tuning the diet.

Calculating the diet

The classical diet can be calculated using dietary units. Dietary units are the sum of the kcal from the macronutrients in the desired ratio.

2:1 ratio
1000 / 22 = 45.45
45.45 x 2 = 90.9 g fat
45.45 – 14.5 g protein = 30.95 carbohydrate

3:1 ratio
1000 / 31 = 32.25
32.25 x 3 = 96.8 g fat
32.25 – 14.5 g protein = 17.75 g carbohydrate

4:1 ratio
1000 / 40 = 25
25 x 4 = 100 g fat
25 – 14.5 g protein = 10.5 g carbohydrate

(Dietary...) treatment of epilepsy, practical implementation of KD therapy, Elizabeth Neal 2012[4]; 'KD therapies for epilepsy and other conditions, seventh edition, Eric Kossoff 2021[5]).

CASE STUDY 6: KEVIN

Nine-Year-Old Male

By Lauren Kronisch, MS, RDN, LDN
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Patient Profile

Kevin is a 9-year-old male. Seizure onset was at one year of age after being resuscitated after an accidental drowning from falling into a pool. On target with all growth parameters and developmental milestones before the accident. Afterwards, suffered from HIE (hypoxic-ischemic encephalopathy), medically drug-resistant focal onset epilepsy, status epilepticus, and spastic quadriplegia.

Background

The ketogenic diet referral was placed by his epilepsy doctor two years after his near drowning incident occurred. At this time, Kevin had tonic clonic seizures multiple times per day, typically two, lasting a range from ten seconds to five minutes. He had had multiple hospital admissions due to recurring status epilepticus. Kevin had intractable epilepsy, as seizures were not able to be well-controlled with two to three medications. At the point of his referral, his medications consisted of levetiracetam (1.4 mg/kg/day), clobazam (0.9 mg/kg/day), lorazepam, and diazepam as a rescue medication. Three weeks before the ketogenic diet was started, prescription L-carnitine was prescribed to correct a low free carnitine value evidence from ketogenic diet pre-screening labs.

An enteral diet initiation plan was provided for a 1:1 ketogenic diet ratio using KetoCal 4:1 LQ Vanilla and his previous enteral formula. Kevin was already 100% enterally fed due to dysphagia resulting from the near drowning incident. A ½ scoop per day of a tube feeding-friendly powdered multivitamin covered by his insurance via a medical supplies company was part of this diet regimen. Additional keto diet ratio increases were made daily based on monitoring outcomes. The optimal ratio was found out to be 2.5:1 based on ketones, blood glucose level, and seizure activity. The first few years after starting the ketogenic diet, there was a 75% improvement in seizures. After three years on the diet, a 3:1 ketogenic diet ratio with the same products was trialed; however, due to vomiting, was switched back to a 2.5:1 ratio after a few weeks. At seven years on the ketogenic diet, there is a sustained 50-65% improvement as compared to before the diet.

As previously stated, Kevin was receiving nutrition enterally before he started the ketogenic diet due to dysphagia via gastrostomy tube. He received nothing by mouth, which continues today. His growth is developmentally appropriate, and his length was as well, until five years on the ketogenic diet. At that point, his length plateaued, and he was referred to endocrinology. The medical team did not recommend any medical interventions but are monitoring his growth. His length plots along below the 3rd percentile, and his weight along the 3rd percentile. His BMI-for-age is along the 68th percentile.

Clinical Assessment

Weight: 27kg (3%, Z=-1.9 on CDC 2-20 Years for Boys)

Length: 119 cm (<3rd percentile, Z=-3.47 on CDC 2-20 Years for Boys)

BMI: 18.21 kg/m2 (68%, Z=0.47 on CDC 2-20 years for Boys)

Creating a diet initiation plan

A slow and steady diet initiation plan has been shown to result in fewer adverse events and is tolerated better overall while maintaining the efficacy of the KD[6]. Calorie and fluid restriction are no longer recommended[7].

As Aleena is over 12 months of age, medically stable and already established on tube-feeding, the plan was to start the diet as an outpatient.

The KD initiation plan needs to achieve the following:

- The feed must meet nutritional requirements
- The feed recipes must allow for a steady increase in ratio of the diet
- The feed recipes must be easy and practical for the family to make up and fit in around the child's daily routine

Creating the feed recipes

As Aleena was solely tube-fed, each feed recipe needed to meet her full nutritional requirements.

KetoCal® 4:1 LQ is a high fat, low carbohydrate, nutritionally complete liquid feed with vitamins, minerals, trace elements and fiber, which is suitable as a sole source of nutrition. It is a 4:1 ratio. Feed recipes were based on this product with the addition of Polycal powder to alter the ratio of the feed.

When making a ketogenic feed recipe, KetoCal 4:1 LQ is the sole source of fat.

2:1 ratio feed requires 90.9 g fat.

KetoCal 4:1 LQ contains 14.8 g fat per 100 ml therefore you will need 614 ml to give the amount of fat required.

614 ml KetoCal 4:1 LQ contains 19 g protein and 3.7 g carbohydrates. The following calculates the amount of carbs required to make a 2:1 ratio using the dietary units.

2:1 ratio

1000 / 22 = 45.45
45.45 x 2 = 90.9 g fat
45.45 – 19 g protein = 26.45 g carbohydrate

26.45 – 3.7 = 22.75 g carbohydrate – this is the amount of carbohydrate required to be added to the 614 ml KetoCal 4:1 LQ to make the ratio 2:1. 23.7 g Polycal powder can provide this.

Final recipe is 614 ml KetoCal 4:1 LQ and 23.7 g Polycal powder.

	Fat	Protein	Carbs
KetoCal 4:1 LQ (614 ml)	90.9 g	19 g	3.7 g
Polycal™ powder (23.7 g)			22.75 g
Totals	90.9 g	19 g	26.45 g

These volumes and weights are not very practical for the family to weigh out; therefore it is sensible to create a plan using amounts that are easy to measure out. A sensitive weighing scale is recommended for making up special feeds. However, if this equipment is not available, round numbers for liquids are easier to measure accurately using home equipment. In this case, KetoCal 4:1 LQ is 1 g/ml in weight so the volume can be weighed accurately.

Final feeding plan for starting the KD

Here are the recipes used for Aleena's plan:

Ratio	KetoCal® 4:1 LQ(ml)	Polycal™ powder (g)	Feed provides
2:1	610	23	1003 kcal 90.3 g fat 18.9 g protein 25.8 g carbs
2:5:1	630	14	999 kcal 93.2 g fat 19.5 g protein 17.3 g carbs
3:1	650	8	1006 kcal 96.2 g fat 20.1 g protein 11.5 g carbs
3:5:1	660	4	1005 kcal 98 g fat 20.4 g protein 7.9 g carbs
4:1	670	0	1005 kcal 99.2 g fat 20.7 g protein 4.1 g carbs

Each of the recipes above were made up to a volume of 1000 ml with water. This was then split into 5 x 200 ml feeds.

The remainder of Aleena's fluid requirements (105 ml left of 1105 ml) were made up with water flushes pre and post each feed. As ketogenic feeds are high in fat, it can sometimes be helpful to flush the tube with warm water.

As Aleena did not have a lower energy requirement than is usual for her age, it was likely that KetoCal 4:1 LQ meets her micronutrient requirements. If a child has a low energy requirement, then it is important to check micronutrients are met. If they are not, then further supplementation may be required using low carb vitamin and mineral supplements such as Phlexy-Vits®. If sodium and potassium requirements are not met, then a prescription of sodium chloride or potassium chloride may be required – neither of these micronutrients are contained in Phlexy-Vits. An electrolyte mix may be useful in this situation. However, they often contain carbohydrate, and this will need to be counted in the diet prescription.

The plan also included advice on how to make up and safely store the feed. The feed plan was to mirror the current NG feeding plan for Aleena; 5 x 200 ml bolus feeds via NG tube with 10-20 ml water flush pre and post each feed. Feed was to be made up at the beginning of the day and stored in the fridge until use. Unused feed should be discarded after 24 hours.

The plan also included advice on starting the diet and moving through the recipes. It was advised that the family change the recipe to the next ratio every 2-3 days whilst monitoring ketones, glucose and seizures. There is no level of ketones that guarantees seizure control, instead the broad aim is to have ketones between 2-6 mmol/L, depending on seizure control. For example, if seizure freedom achieved on a 2:1 ratio and ketones were 2-3 mmol/L, there would be no need for further recipe changes as the desired outcome of seizure reduction has been achieved.

Diet training

Aleena's family were invited to an outpatient clinic appointment where diet training took place. During the training, the family were provided with the following information:

- An initiation plan containing all recipes
- Blood ketone and glucose monitoring training
- A management plan for high ketones and low blood glucose
- Contact information for the team

They were also provided with blood monitoring equipment and set up for delivery of their feed prescription.

Target regimen:

Feed Product	Amount	Fat (g)	CHO (g)	Fibre (g)	Protein (g)	Kcal
KetoCal® 4:1 LQ	1000 ml (5 cartons)	148	6.1	11.2	30.9	1500 kcal
Protein supplement	135 ml (3 sachets)	0	3		33	132 kcal
LCT fat module	120 ml	60	0.3	-	-	540 kcal
Fiber supplement	15 g (3 scoop)	-	0.9	12.9	<0.225	30 kcal
	TOTAL	**208**	**10.3**	**24.1**	**64**	**2202 kcal**

PEG feeding regimen:

6 boluses per day:

3 x (KetoCal 4:1 LQ + Protein supplement + 1 scoop fiber supplement)

2 x (KetoCal 4:1 LQ + 40 ml fat module - neutral)

1 x fat module - neutral (40 ml)

Water flushes: Made up with 2 sachets of rehydration salts mixed in.

Fluid ~2055 ml/day

Outcome

After Sebastian's 3 month trial, Sebastian reported noticeable differences in his energy level with support staff stating his engagement with day-to-day activities had improved. Sebastian's seizure frequency reduced by ~20%. Support staff and Sebastian's family reported his recovery time improved to 30 minutes, representing a 30% reduction in his recovery time. Sebastian's weight remained stable on his ketogenic feed. Sebastian's ketone readings remain consistent with levels between 2.3-3.0 mmol/L.

Learning Points

Using KetoCal 4:1 LQ helped facilitate meeting the dietetic goals. KetoCal 4:1 LQ provided an easy and low-burden alternative for support staff to facilitate transition when titrating to the KD. Sebastian has seen an improvement in his seizure frequency and recovery time since remaining on the KD.

After discussion with the family, they were keen to transition Aleena from her current feed to the new feed, and they agreed to a few days of transition before fully starting the first ketogenic recipe at 2:1 ratio. This was achieved by mixing 500 ml of the current feed and 500 ml of her new feed recipe and following the same feeding plan of 5 x 200 ml bolus feeds via NG tube. This recipe provided; 0.7:1 ratio, 1002 kcal, 67 g fat, 23 g protein and 74 g carbs.

This is an appropriate approach if there are concerns about tolerating a new feed or to allow parents to feel more comfortable with the transition.

Dietetic support for the family

Support from the ketogenic team, particularly the dietitian, is really important for supporting the family and helping them negotiate their first few weeks on the KD.

Regular contact via telephone or video review, 2-3 times per week in the first 2 weeks is essential for supporting the family. With regular contact, it is possible to assess the blood ketone and glucose results and seizure frequency changes – this can inform the decision to move onto the next ratio quicker than is on the plan, or in contrast to stay on the same recipe for longer.

It also gives the opportunity to check if the family are making up the feed correctly and have adequate supplies of their prescribable products.

In Aleena's case, the family had planned telephone reviews every 2-3 days in the first 2 weeks. Training took place on a Friday, parents were able to administer the mixed feed over the weekend and were ready to start the 2:1 ratio on the Monday. At the planned review on Wednesday, Aleena had ketones around 1 mmol/L, glucose 4-5 mmol/L and no change to seizures, so it was agreed to move onto the next ratio, 2.5:1. At the planned review on Friday, ketones were between 2-3 mmol/L, glucose remained 4-5 mmol/L and her parents had started to note some positive changes in seizures. It was agreed to stay on the same recipe and review on Monday.

At the review on Monday, Aleena's ketones were consistently above 3 in the evening and no lower than 2.5 mmol/L in the morning. Glucose was between 3.5-4.5 mmol/L and seizures had continued to improve. It was agreed to step up to the next ratio (3:1) to see if further improvement in seizures occurred.

At the next review, ketones were 3.5-4.5 mmol/L, glucose was 4-4.5 mmol/L and seizures had reduced further. It was agreed to stay on this recipe and review again in a few weeks.

Clinical Outcome

After 3 months of being on diet, Aleena was seen in KD clinic. Aleena had remained on the 3:1 ratio recipe. Ketones were 3.5-5.5 mmol/L and glucose was no longer being checked unless Aleena was unwell or showing signs of hypoglycemia. Aleena was now seizure-free for stretches of 5-8 days. On the days she was having seizures, they had reduced to 1-2 clusters of spasms which her parents reported were less severe. Tonic seizures had completely stopped. Aleena's parents also reported that Aleena's head control had improved and that she seemed brighter and more alert. Aleena had become constipated, therefore a prescription for a laxative was provided. Ketogenic monitoring bloods were taken and the results showed no abnormalities. At this point, a plan for weaning off zonisamide was given.

At the 6-month review in KD clinic, Aleena had continued to do well. Ketones continued to be 3.5-5.5 mmol/L, and seizure control remained the same. Parents reported no new side-effects but were able to tell us that Aleena's attendance to nursery school had improved vastly – she was able to arrive on time and be more involved in the activities due to the reduced burden of seizures.

Learning Points

For Aleena, KD management was minimally invasive and improved her epilepsy control, leading to improved quality of life.

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CASE REPORT 5: SEBASTIAN

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Patient profile

Sebastian is a 27-year-old male who was referred for the Ketogenic Diet (KD) by his Neurologist, on his and his family's request. Sebastian was diagnosed with Lennox-Gastaut Syndrome associated with epilepsy, learning difficulties, ataxia and hypothyroidism. Sebastian has had longstanding seizures from the age of 4 years old. Sebastian was prescribed clobazam, leviteracetam, perampanel, sodium valproate, phenytoin and midazolam. Sebastian started the KD when he was 23 years old.

Background

Sebastian was having 5-15 seizures/month in the form of generalised seizures and myoclonic jerks. Sebastian's seizures were mainly nocturnal or on waking, usually lasting between 2-3 minutes. Sebastian would experience long recovery times usually 1.5-2 hours.

Sebastian lives in supported accommodation in the community. Sebastian has a PEG tube which was inserted 18 months prior to his KDT appointment. Sebastian's PEG feed was providing his sole source of nutrition and hydration.

Clinical Assessment

On referral, Sebastian's weight on referral was 59.9 kg and height 1.74 m, with a BMI of 19.7 kg/m^2. Sebastian had been weight-stable since his PEG had been inserted.

Sebastian is nil by mouth, with a 15Fr Freka PEG in situ. Sebastian was on a bolus feed regimen of standard feeds including Fortisip® Compact Fibre, Calogen extra and Fortisip Compact (available from Nutricia in the UK). Sebastian would have 6 bolus feeds a day which provided 2200 kcal, CHO 204.7 g (37%), Fat 115.5 g (47%), Prot 76.2 g (14%), Fluid ~2050 ml from feed regime + additional fluid for meds.

Dietetic Intervention

Engagement of staff was key to initiating and monitoring KD in the community. This included the support staff at the home, community dietetics, Neurology team and Sebastian's G.P. The Neurologist and Neurology CNS were contacted to ensure all Sebastian's medications contained the minimal amounts of carbohydrates, for example phenytoin liquid was switched to phenytoin capsules. Sebastian's support workers were trained on blood glucose and blood ketone measurements. Protocols were agreed with support staff including management of hypoglycaemia and hyperketosis.

Sebastian was weaned on to the KD across 7 days to mitigate gastrointestinal symptoms.

- On day 1 and 2, 50% of bolus feeds (3 out of 6 feeds) were ketogenic. The remaining bolus feeds were standard feed. The ratio equated to 1.8:1.
- On day 3, 4, 5 66% of bolus feeds (4 out of 6 feeds) were ketogenic. The remaining bolus feeds were standard feed. The ratio equated to 2.2:1.
- On day 6, 83% of bolus feeds (5 out of 6 feeds) were ketogenic. The remaining bolus feeds were standard feed. The ratio equated to 2.5:1.
- On day 7, achieved his target regimen with a ratio of 2.8:1.

Sebastian tolerated initiation of the ketogenic diet well with no reports of nausea or diarrhea. Blood ketone levels were checked twice daily while weaning on to the KD.


NUTRICIA
KetoCal® 4:1 LQ
Multi Fiber
Unflavored
Non aromatisé
8 fl oz (237 mL)
NUTRICIA
KetoCal® 4:1 LQ
Multi Fiber
8 fl oz (237 mL)
NUTRICIA
KetoCal® 4:1 LQ
Multi Fiber
Chocolate

Initial feed plans

400 ml KetoCal 4:1 LQ

125 ml Pediatric 1 kcal/ml fiber-containing formula

Made up to 1000 ml with water

Ratio: 2:1

Provides per 100 ml: 72 kcal, 1.6 g protein.

Feeding regimen: 4 x 200 ml

Initiated feeding by alternating feeds between Pediatric 1 kcal/ml fiber-containing formula and ketogenic formula (Ratio 2:1). Within one week George was fully on the ketogenic diet at a ratio of 2:1. Ketones range between 0.9 – 1.5 mmol/l. Over the next 4 weeks the ratio was increased to 4:1. Ketones increased to 4.5 – 5.5 mmol/l. His feed was diluted KetoCal 4:1 LQ, 72 kcal and 1.5g protein per 100ml.

Clinical Outcome

Over the first 8 weeks George tolerated the feeds well. However, weigh gain slowed and his weight percentile was moving closer to -4SD below 0.4th percentile. Therefore, the recipe was increased by ~10% in two increments with the feed providing 79 kcal and 1.6 g protein per 100 ml which helped improve growth.

Outcome

At 12 weeks on diet he had a clinical follow-up. George had stable ketosis for 8 weeks. He had suffered with constipation; his bowels were opening every 48-72 hours and involved straining, and despite dietetic management he required a laxative to regulate bowels to open daily. His weight was tracking along -3SD below the 0.4th centile.

He continued to have seizures; however, he had not had any prolonged clusters of seizures since initiating the ketogenic diet and could have up to 16 days seizure-free. In the last 4 weeks, he had 4 seizures which were more subtle. Therefore, it was agreed to continue ketogenic diet due to the improvements in seizure control.

Estimated Nutritional Requirements Weight Age

Energy: 567 – 756 kcal (72 – 96 kcal/kg)

Protein: 9.8 - 12.7 g (1.24 g/kg, safe intake - RNI)

Estimated fluid requirement: ~800 - 1000 ml

Estimated current intake:

250 ml whole cows milk: 160 kcal

3 meals per day: 300 - 400 kcal

Total energy: 460 - 560 kcal

Takes a vitamin supplement (Vitamin A, C and D)

Speech and language therapy recommendations:

- Unsafe swallow currently to both fluids and food due to risk of aspiration.
- Can continue tastes.
- Repeat assessment in 6 months.

Therefore need to provide 100% nutrition and fluids via NGT. Poor growth on current intake therefore consider adding additional 10% energy to current estimated intake with the aim for improved weight gain.

Target energy requirements: 600 kcal, 14.5 g protein.

Dietetic interventions:

1. Change macronutrient composition of diet to a classical ketogenic diet to initiate ketosis.
2. Improve growth aiming for increases towards 0.4th centile.

Upon discussion with the family they would like to initiate 4 feeds per day, ideally if tolerated via gravity bolus feeding. Parents asked about the available products, discussed the need to ensure the recipe is simple and easy and meets his nutritional needs. Parents expressed a preference for liquid feeds with their main reasoning that they are expecting a new baby in the next 8 weeks and time at home is under pressure. Mum also expressed that she is concerned that having multiple powder formulas might be difficult to manage.

Reviewing KetoCal® formula feeds to determine most appropriate feed considering:

- Initial ratio and potential for ratio changes
- Patient age
- Nutritional completeness of the feed including at a ratio 4:1
- Is a multivitamin supplementation required?
- Ease of preparation e.g. number of ingredients, mixing of ingredients
- Parental preferences
- Local home enteral feeding contract company

The initial ratio target was 2:1, with a potential transition to a 4:1 ratio, if clinically indicated. Initial target regime was to reduce side effects, improve tolerance and initiation of ketogenic diet. Through considering both the current plan and potential future needs this can help reduce risk of feed changes increasing workload and waste. KetoCal 3:1, KetoCal 4:1 Powder and KetoCal 4:1 LQ meets vitamin, mineral requirements but does not meet reference nutrient intake (RNI) for protein. Although KetoCal 2.5:1 LQ meets and exceed protein RNI, it is also higher in vitamins, mineral and trace elements and not indicated for those under 3 years of age. It is important to consider the proper choice of formulas and tailor to each patient's needs. There was also a need to consider the challenges of measuring and mixing on ingredients whether using scoops, syringes and/or scales.

CASE REPORT 2: ASSAN

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Background and referral information

Assan was diagnosed with myoclonic astatic epilepsy (Doose syndrome) as a toddler and had trialled and failed six anti-seizure medications. Assan had severe learning disabilities and relied on his family and carers for around the clock care. During childhood, his swallow had deteriorated, resulting in weight loss, and he was fed via a nasogastric tube, followed 18 months later by a gastrostomy tube. Since Assan attended a school for special educational needs, he would be under the pediatric epilepsy service until he turned 19 years old.

Assan is an 18-year-old man who commenced a ketogenic diet (KD) just before his seventeenth birthday. When referred for assessment for KD, he was having 70-80 seizures daily presenting as clusters of absence seizures characterized by head drops and myoclonic upper limb jerks. In addition, he was having 3-5 tonic seizures each day.

His consultant neurologist referred him to the keto team for assessment. KD therapy had been discussed a few times in the past, but Assan's parents had been reluctant to trial it. There was no local adult keto service that Assan could transition to, so it was felt that this would be his last opportunity to trial KD. His parents agreed to meet with the keto team to discuss their concerns.

Assan had struggled with poor feed tolerance as a child, which had been a very difficult, stressful and worrying time for the family. Although he was very settled on a standard whole protein feed and tolerating it well, these early experiences made them reluctant to make significant changes. It was also very hard for him to have his blood taken, and his parents were worried about the need for regular blood tests on KD. They were concerned that so much fat would cause him to gain weight which would mean his wheelchair would need resizing and replacing. We had a long discussion about the potential for KD to help manage Assan's seizures and that the response rate in those with Doose syndrome was as high as 60-70%[1-2]. This together with the reassurance that the KD prescription would match Assan's current energy intake and be phased in slowly, helped reassure Assan's parents, and they agreed to a 3 month trial of classical KD. Baseline KD bloods and urinalysis were undertaken[3,4]. Assan's calcium/creatinine ratio was significantly raised which prompted a renal ultrasound. His ultrasound was normal, so the KD commenced, and potassium citrate was started to alkalize the urine and reduce the risk of a renal calculi.

Clinical assessment

Weight: 72.6 kg (stable)

Feed regimen: t ml Nutrison® (available in the UK from Nutricia) per day providing 1400 kcal and 56 g protein. 280 ml x 5 pump-assisted boluses per day and additional fluid flushes with feeds and medications.

Expectations of KD: Reduction in seizure frequency, ideally 50% or more. Parents keen to wean 1 anti-seizure medication. Assan sleeps a lot during the day and poorly at night, waking and seizing often, so keen to monitor for any change in sleeping patterns, too.

Dietetic intervention

Assan had lower energy requirements than is typical for a man his age, so this would limit the ratio of classical KD we could achieve. It is not uncommon for energy and protein needs to be our ratio-limiting step with adults on a classical KD regime. Here we could achieve a maximum of a 2.2:1 classical KD. Assan's weight was stable, so we used the minimum protein/kg/day of 0.75g/kg/day. Table 1 outlines the calculation of the classical prescription using the dietary unit method and table 2, the feed recipe using KetoCal® 4:1 LQ as a base.

Table 1. Classical KD calculations

2.2:1 Classical KD

2.2:1 diet unit = 23.8 kcal

1400/23.8 = 59 diet units/day

Fat = 2.2 x 59= 129.8 g fat

Pro = 54.5 g

CHO = 59-54.5 = 4.5 g

Total energy = 1404 kcal

Table 2. Classical KD feed recipe

Product	Fat (g)	Pro (g)	CHO (g)
750 ml KetoCal 4:1 LQ	111	23.2	4.6
36 g Protein Module	-	31.4	-
40 ml Fat Module	20	-	-
Total (g)	131	54.6	4.6
Energy (kcal)	1179	218.4	18.4
1416 kcal at 2.2:1 ratio			

Ingredients were combined and water added up to 1400 ml to mimic his existing regimen and feed volumes. The recipe met at least the lower reference nutrient intake for all vitamins and minerals, except potassium which was slightly lower; however the potassium citrate addressed this shortfall. Classical KD was phased in slowly as per table 3. Typically, we would increase the percentage contribution of the ketogenic feed every 1-3 days; however, we increased more slowly owing to Assan's parents' concerns of poor tolerance.

Table 3. Phased introduction of 2.2:1 classical KD

Phase 1	Duration	Existing feed	Ketogenic feed
1	5 days	75% of energy	25% of energy
2	5 days	50% of energy	50% of energy
3	5 days	25% of energy	75% of energy
4	Day 16 onwards		100% of energy

Assan tolerated the introduction of KetoCal 4:1 LQ (+ additions) very well with no adverse effects. He became ketotic on day 13 and thereafter produced good ketones despite the low ratio classical KD. Morning serum ketones averaged 1.5-2 mmol/l and evening 2-3 mmol/l. The ratio could not be increased further (owing to low energy requirements). However, his starter regimen was fine-tuned by replacing the existing long-chain fat source with Liquigen. This provided 12% of total energy (8.3 kcal/g fat = 166 kcal) as MCT fat, which can help boost ketosis. Assan's respite center were very keen to support his KD. The center had not had a patient on KD for many years, so a training session was arranged with parents and the respite team to ensure all were comfortable with the feed regimen, ketone testing and management of hyperketosis should it occur.

CASE REPORT 4: GEORGE

Zoe Simpson

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Patient Profile

George is a 2 year old male. His birth weight was 2.319 kg (below 0.4th centile). Infancy onset epilepsy occurred at 3-month-old. He was diagnosed with microcephaly and congenital pontocerebellar hypoplasia.

Background

His current medication consists of carbamazepine (120 mg, oral, twice daily) and Levetiracetam (300 mg, oral, twice daily).

An internal referral from the epilepsy team was made due to drug-resistant epilepsy.

George has tonic seizures, described by his parents as arms and legs outstretched and stiff, head turns to the left. They currently occur 2-3 times every other week and last less than a minute, previously they occurred up to 6 times per week. They can also come in clusters lasting up to two hours requiring hospital intervention.

George has poor oral intake and associated faltering growth. He has only gained 1.4 kg over a year, his weight dropping from the 0.4th centile to between -3 and -4 SD below the 0.4th centile. His length plots along the 2nd centile. In the initial appointment, maintaining his nutritional status was difficult due to his decreased intake of milk. George was not taking sufficient formula from a bottle, and parents were using a syringe to give milk and fluids. He was managing three small pureed meals per day and ~ 500 ml fluid daily. Meals take 45 to 90 minutes to finish. There were no overt signs of aspiration, for example coughing or choking, but he does drool. It was felt prior to ketogenic diet a speech and language assessment was appropriate to ensure safety of swallow. It was also apparent that medication adherence was impacted by George spitting out medications. Dietetic input and the need for a nasogastric tube (NGT) and the likely long term need for gastrostomy was discussed.

The multidisciplinary team (MDT) agreed on the need for nutritional support via a tube to support nutritional and hydration status and medication adherence. Referrals were made to a local dietitian, to speech and language therapy, and a local pediatrician for urgent placement of a NGT and a possible gastrostomy.

Clinical assessment

Weight: 7.88 kg (-3 and -4 SD below the 0.4th centile)

Weight age: 5/6 months

Height age: 14 months

Estimated Nutritional Requirements Actual Age

Energy: 646 - 1000 kcal (82 kcal – EAR)

Likely low estimated energy requirements due to low activity, therefore consider low physical activity energy expenditure for growth and maintenance estimated at 77%: 497 – 770 kcal

Protein: 7.6 - 14.5 g (0.97 g/kg, safe intake - RNI)

Could also consider weight age due to significant difference from actual age.

Clinical Outcome

Outcomes were assessed at 3 months on KD, daily seizures had reduced by approximately 70%. Parents and carers reported Assan to be sleeping less during the day and he was brighter and more alert when awake. His personality and cheekiness were coming through! Assan's parents felt the greatest impact was Assan's ability to attend school more regularly and be more engaged while doing so. Overall, they felt his quality of life was improved, and by default theirs too, now that Assan's epilepsy was better controlled. The positive outcomes continued and at 6 months on KD, clobazam was slowly weaned.

Learning Points

Arguably, Assan should have been referred earlier for KD but there were many factors influencing his parents' understandable reluctance to trial KD. Initially managed by a community home enteral feeding team, his care was transferred to the keto team, but the community team remained aware of his progress. It was an excellent opportunity to share the potential benefits of KD for adult patients and prompted discussions regarding other patients who may benefit. It would be ideal, in the long run, for patients such as Assan to be transferred back to the enteral feeding team once stable on KD, with support as required from the keto team. Shared care may be one approach for improving access to KD for adult patients.

If Assan's parents had met with the keto dietitian or an experienced dietetic assistant earlier, perhaps their fears and worries would have been allayed.

Often a 2 - 2.5:1 ratio is the highest that can be achieved owing to protein needs and low energy requirements: it is still worth trialing the KD at this low ratio. Once KD is established, then consider fine tuning by replacing some long chain triglycerides (LCT) with MCT fat if needed to optimize ketosis. Start at 10% and increase in 5% increments as required.

Ensure the limitations of protein, energy and hence maximum ratio of classical KD are discussed with the family to ensure they have realistic expectations of KD .

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Learning Points

In the case of our patient it has been evident that the use of the diet has allowed an important cognitive-behavioral improvement but, in addition, it has allowed maintenance without crisis, also achieving the withdrawal of pharmacotherapy.

But perhaps the most interesting thing to emphasize is the fact that the patient has a tube in place, which allows to establish a diet more easily and precisely thanks to the formula used (KetoCal®). The formula adapts perfectly to the nutritional needs of the patient, maintaining the proper range of ketosis, adequate levels of macro- and micronutrients and allowing simple use by the family. It meant better adherence to the diet and the achievement of such good results.

We therefore propose that the use of exclusive gastrostomy feeding with a specific formula facilitates the fulfilment and achievement of the objectives, allowing control of epilepsy, improving the quality of life, reducing the number of consultations to emergency services, hospital admissions, medical visits and complementary examinations both at the psychomotor level and the rest of the associated symptoms — without adding complexity for the family and the caregivers.

Therefore, we propose the initiation of diet in drug-resistant epilepsy early in those patients with a probe or gastrostomy, since it entails little family repercussion and numerous benefits in the control of these patients.

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In a state of fasting, our greatest energy source is found in fatty acids, which will be transformed into ketone bodies, and these will serve as our beta precursors for obtaining ATP through beta-oxidation in the mitochondria.

There are multiple theories about its mechanism of action at the brain level, although, to this day, none are conclusive. Among them we find: increased production of glutamate and GABA, activation of K channels with hyperpolarization effect of synaptic membrane, increased levels of cerebral ATP as a membrane stabilizer, among others. But in addition to the antiepileptic effect of ketone bodies, its direct neuroprotective effect stands out due to its antioxidant capacity.

The design of this type of diet is based on the ketogenic capacity of each macronutrient. A classic KD is one in which 90% of the energy consumed comes from fats, with a minimum amount of carbohydrates and adequate protein. This should be individualized in each case and assess the possible existence of harmful effects. An attempt is made to maintain a level of ketonemia between 2-5 µmol/L. In addition, taking into account the swallowing and digestive disorders that affect these type of patients, we can make this diet with natural foods, with special formulas or through preparations for the parenteral route. These accomodations allow the adherence and maintenance of this diet to be improved.

Despite this, many patients feel it is “difficult” to manage the diet, cook and adapt foods etc. This difficulty can be overcome more easily in tube-fed patients.

CASE REPORT 3: NINA

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KETOGENIC DIET, THE RECIPE AGAINST DESAFÍOR CHILDHOOD DRUG-RESISTANT EPILEPSY.

The control of childhood drug-resistant epilepsy is one of the most complex medical challenges in pediatric neurology. It is a very disabling disease with a great impact on the quality of life, both of the patient and of their entire family.

In addition, we must not forget, the health expenditure generated by this pathology due to multiple treatments, hospital admissions, specialty consultations and multidisciplinary sessions.

We present the case of a patient from our unit who after years of multiple treatments, manages to control her epilepsy thanks to starting a KD. The good control of their crises, allows improvement of the behavioural and motor state of these patients and consequently, an improvement of other associated pathologies such as gastroesophageal reflux and nutritional status.

Patient profile

Girl of 10 years and 6 months, in follow-up in our unit from 4 months for connatal multicystic encephalopathy that occurs with:

- Cerebral palsy with spactic-dystonic tetraparesis and left predominance
- Secondary drug-resistant epilepsy
- Disorder of the development of intelligence
- Moderate malnutrition. Carrier of percutaneous endoscopic gastrostomy (PEG)

Background:

During pregnancy, Nina’s mother had gestational maternal arterial hypertension. She was induced at 38 weeks due to severe pre-eclampsia; however, after a failed induction Nina was born by a caesarean section. At birth Nina’s Apgar test showed 9/10/10 to 1/5/10 minutes of life respectively.

No incidents occurred in the perinatal period. No neonatal jaundice occurred and the extended neonatal metabolic screening was normal. Nina was exclusively breastfed.

FAMILY HISTORY:

- A 35-year-old father. Psoriasis, treated with immunomodulators. No toxic habits, no other health incidents.
- Mother of 35 years. No previous pregnancies. Gestational arterial hypertension. Vitiligo and autoimmune hypothyroidism. No toxic habits.
- No other family history of interest.

Clinical Assessment:

The patient at 4 months of age is evaluated for the first time in our center, after referral by her primary care pediatrician for difficulty in acquiring developmental milestones. In the first consultation of Neuropediatrics, there is little cephalic control, as well as axial hypotonia and microcephaly. She does not present a social smile or persecution with his gaze. She also associates convergent strabismus of the left eye. She does not show dysmorphic features or other alterations noteworthy to exploration.

Given these findings, an expanded study is requested including: Complete blood analysis (blood count, general profile, liver profile, renal profile, ferric profile, celiac profile, thyroid, as well as vitamins, trace elements and autoimmunity, including TORCH serology), brain magnetic resonance and tandem mass study to rule out possible metabolopathy.

In the following months, Nina presents an unfavorable evolution from the psychomotor point of view. She initiates clonal movements of the left lower limb and spasticity of both lower limbs. A requested imaging study of objective multicystic encephalomalacia, together with anodyne blood analysis and negative metabolic study, leads to a diagnosis of cerebral palsy of the spastic tetraparesis type of left predominance. Possible anoxic encephalopathy or previous infarction in the territory of bilateral middle cerebral artery in perinatal period.

In this context, multidisciplinary follow-up of the patient by: Neurology, Maturation, Early Care, Ophthalmology, Child Rehabilitation and Pediatric Gastroenterology begins from this moment. From the neurological point of view, the patient presents unfavorable evolution during the first years of life. At 10 months of age, she presents with myoclonus of the left lower limb increasingly frequent, subsequently associating palpebral myoclonus and hyper extension of the upper limbs. In the study of electroencephalogram (EEG), paroxysms of a complex tip-wave type at high amplitude in right temporo-parieto-occipital regions are objectified. It therefore begins with anticomyceal treatment (firstly, with alproic V-acid at standard doses).

For the next 2 years, she maintains a secondary epilepsy that is difficult to control. It requires treatment with multiple associated antiepileptics in different combinations and in increasing doses (valproic acid, levetiracetam, lamotrigine, piracetam, clobazam, clorazepam) without finding a satisfactory response to the control of seizures. In total, she has required up to a total of 4 simultaneous antiepileptics without good control.

In multiple reviews, the patient maintains generalized epileptic seizures with continuous electrical activity. In addition, due to the use of multiple treatments and high doses, her parents observe a worsening of Nina's general condition and found her more disconnected with the environment. This situation is a great professional challenge, causing repeated visits to the Emergency Department by the family and great anguish.

From the nutritional point of view, she is exclusively breastfed until 7 months of age. Complementary feeding is initiated without incident. She maintained an acceptable nutritional status until 15 months of age, after which, due to the evolution of basic disease, she presents with greater spasticity and crisis of difficult control, presenting difficulties to cover caloric-protein requirements; nutritional support with hypercaloric formulas begins at this time.

During the following months, she maintains a state of moderate malnutrition, with progressive deterioration at the neurological and nutritional level, starting with severe oropharyngeal dysphagia, so that at 2 years of age a percutaneous endoscopic gastrostomy is performed. From this moment, she begins being fed via her PEG with habitual feeding and supplements presenting favorable nutritional evolution.

At 8 years of age she maintains drug-resistant secondary epilepsy that motivates numerous hospital admissions and outpatient reviews for treatment adjustment and reversal of epileptic status.

Dietetic Intervention

Given the unfavorable situation, at this time the possible realization of KD as a management is raised from Child Neurology consultations, so a multidisciplinary consultation is carried out with Neurology and Pediatric Nutrition, and the family is and we propose the KD as an option to the family.

The family accepts and carries out initial study, as well as training of the parents, starting KD with 3:1 ratio with good tolerance and acceptance. Ketonemia levels are maintained in an adequate range without relevant side effects and normal blood glucose at all times.

The evolution of the patient after 2 years of initiation of KD is very favorable. A decrease in antiseizure medications is achieved, requiring only monotherapy with levetiracetam; after a new consultation she begins a withdrawal regimen and can be completely suspended.

Clinical Outcome

At present, she is with total absence of crisis. She also has a noticeable improvement in both her cognitive-behavioral and motor state (appreciated by parents and specialists), even allowing her to wander with the help of a walker, among other advances.

Refractory or drug-resistant epilepsy is epilepsy that, despite a correct diagnosis, presents an unsatisfactory control of seizures despite the appropriate use of antiepileptic drugs, alone or in all possible combinations and at maximum tolerable doses. This type of epilepsy occurs in up to 30% of patients. The KD, despite being a well-known management, has now opened up as a new path in the management of drug-resistant epilepsy, achieving promising results. This diet is based on the state theory of anabolism by metabolic fasting thanks to ketosis. For this, a diet rich in fats and with the lowest possible contribution of carbohydrates must be carried out, maintaining the necessary protein intake.