

CASE STUDY 1: ALEENA

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Patient Profile

Aleena is 3 years old with a background of infantile onset epilepsy, evidence of structural abnormality, refractory 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 trialled several seizure medications which at times provided short periods of relief but were unltimately unsucessful.

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 characterised 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 Carobel 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 diarrhoea.

At this appointment, her parents were keen to go ahead with KD treatment 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 diet is 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]).

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 supplemented with vitamins, minerals, trace elements and fibre 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 the 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. To work out 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 the 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 or Fruiti-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 or Fruiti-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.

After discussion with the family, they were keen to transition Aleena from her current feed to the new feed and they agreed a few days of this before 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 and 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 hypoglycaemia. 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 of Movicol was provided for prn use. Ketogenic monitoring bloods were taken and the results showed no abnormalities. At this point as 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 treatment was minimally invasive and improved her epilepsy control, leading to improved quality of life.

References

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