Clinical Guidance

Ketogenic diet for epilepsy

Summary

The purpose of this guideline is to aid staff in (1) commencing children on the ketogenic diet either as an inpatient or outpatient and (2) to help manage children already on the ketogenic diet admitted electively or as an emergency for other medical reasons.

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Clinical Neurosciences

The ketogenic diet for epilepsy

The purpose of this guideline is to aid staff in (1) commencing children on the ketogenic diet (KD) either as an inpatient or outpatient and (2) to help manage children already on the KD admitted electively or as an emergency for other medical reasons.

1 Background

The ketogenic diet (KD) is a high fat and carbohydrate restricted diet that contains adequate amount of protein to support growth. It is a therapeutic diet used to treat drug resistant epilepsy and specific metabolic conditions. The diet requires specialist supervision (see section 1.1 for KD team) and many parents and carers become very knowledgeable. There are several modifications of the KD used at the Evelina.

(1) The classical KD
   - The classical KD is calculated in a ratio of grams of fat to grams of protein plus carbohydrate combined. A ratio of 4:1 means that for every 4g of fat there is 1g of combined protein and carbohydrate.

(2) The medium chain triglyceride (MCT) diet
   - A KD where up to 60% of energy comes from MCT.

(3) The modified diet
   - This diet typically provides a 1:1-1.5:1 ketogenic ratio but no set ratio is mandated. The initial daily carbohydrate consumption varies between 10g and 30g and is adjusted according to individual response and needs. Moderate portions of protein, fluids or calories can be consumed to meet requirements.

1.1 The Epilepsy ketogenic diet team

Consultant	Dr Ruth Williams
Dietitian	Anne-Marie McKillup 0207 188 9610 (voicemail) or Bleep 2420
Specialist Nurse	Martin Smith 0207 188 4588
Pharmacist	Savannah ward pharmacist

1.2 Indications and contraindications of the KD

The KD should be considered in patients with a confirmed diagnosis of epilepsy (by a networked paediatrician with expertise or paediatric neurologist); who have failed two antiepileptic drugs, and continue to have troublesome seizures at least weekly, daily absences, or recurrent status epilepticus. It should be considered in such patients regardless of their age. Additionally, it is the treatment of choice for two specific metabolic disorders; glucose 1 transporter deficiency and pyruvate dehydrogenase deficiency. However, before starting the KD, one should consider whether the patient has specific inborn errors of metabolism that could lead to a severe metabolic crisis if placed on the KD (see Table 1).

Table 1: Contraindications to the use of the KD

Absolute contraindications - Primary Carnitine deficiency - Carnitine palmitoyltransferase I or II deficiency - Carnitine translocase deficiency - ß oxidation defects - Medium-chain acyl dehydrogenase deficiency - Long-chain acyl dehydrogenase deficiency - Short-chain acyl dehydrogenase deficiency - Long-chain 3 hydroxyacyl-CoA deficiency - Medium-chain 3 hydroxyacyl-CoA deficiency - Pyruvate carboxylase deficiency - Porphyria **Relative contraindications** - Inability to maintain adequate nutrition - Parent or caregiver noncompliance - Propofol concurrent use

2 Preparing to start the Ketogenic diet

2.1 Pre-diet evaluation and consultation

- The KD team will provide a KD information sheet to parents/carers and recommend the following KD information resources: www.matthewsfriends.org and www.epilepsy.org.uk.
- The KD team will identify key goals of dietary treatment such as seizure reduction, medication and cognitive expectations with parents/carers.
- The KD team will inform parents/carers that attendance at KD clinics and cooperation with regular blood testing at ELCH is a mandatory requirement.
- The KD team will discuss the expected length of time on the KD.
- The KD team will review the results of baseline investigations (section 2.2) and evaluate for contraindications to the KD.
- The KD team will evaluate for complicating comorbidities and discuss possible side effects such as constipation, possible hyperlipidaemia, renal stones, increased risk of fractures and poor growth.
- Most children start the KD diet at home on an outpatient basis but occasionally the KD is started as inpatient particularly in young infants (see section 3).

2.1.1 KD Dietitian assessment

- The KD dietitian will discuss the child's food preferences and usual mealtime regime with parents/carers.
- The KD dietitian will give parent/carers forms for a 3 day food diary and food information sheet to be completed at the assessment clinic. Parents/carers are given a return date 1 month post this assessment clinic. If this is not returned by the agreed date, the child will be discharged from the KD service.
- The KD team and parents/carers will decide which kind of KD diet is to be prescribed.
- The KD dietitian will calculate the child's energy and nutrient requirements and prepare some initial KD recipes and meal plans for the child.
- The KD dietitian will recommend appropriate supplementation including a daily multivitamin and calcium with adequate vitamin D.

2.2 Baseline investigations

Before starting the KD, children should have the following baseline investigations and growth measurements (Table 2) performed usually at ELCH (very occasionally at local hospital by arrangement).

Table 2. **Baseline and follow up investigations**

Blood tests:	FBC* U&E, bicarbonate, glucose* Amylase LFT, bone profile, magnesium* Acylcarnitines* Lipid profile* Glucose, Folate, Ferritin* Trace elements: Zinc, Copper, Selenium, Manganese* Vitamin D* Free fatty acids (betahydroxybutyrate) Serum amino acids (if diagnosis unclear) AED drug levels – valproate and others if relevant
Urine tests:	Urine calcium/creatinine ratio* Urine organic acids
Nutritional evaluation:	Height* Weight* Calculate BMI and plot on growth chart Head circumference in infants*
Other:	Renal ultrasound** (see section 6.4.1 for risk factors) ECG CSF: plasma glucose ratio** Neurodevelopmental assessment** Quality of life questionnaire** Enquire about risk factors of osteoporosis (see section 6.4.2)

*should have been performed in previous 3 months and three to six monthly whilst on KD
**Highly recommended to perform at baseline

2.3 Drug prescriptions

Ensure that prescribed medications are switched to a low carbohydrate alternative where possible. This should be discussed with the ward pharmacist. Certain brands are more “keto-compatable” than others, and prescribing a specific brand may be very important for some children who lose ketosis easily. If in doubt, substances ending in “ose” or “ol” are usually converted to glucose in the body. As a general guide, avoid medicines that contain sorbitol, glucose, lactose and fructose and allow medicines that contain saccharin. Additionally, tablets are preferred over liquid or chewable medications.

The Neurology ward pharmacist keeps an updated list of ketogenic diet compatible medications and formulations. Manufacturers do change formulations from time to time and any questions should be directed to the ward pharmacist during regular office hours. The pharmacist can contact the manufacturer directly and ask for clarification if necessary, and may also suggest alternative options if appropriate. Pharmacy can be contacted by email :letstalkmedicines@gstt.nhs.uk or telephone 0207 188 3003 (Monday to Friday 10am to 5pm). Additionally, www.matthewsfriends.org has information on KD compatible medications.

2.3.1 Concurrent antiepileptic drugs

At present, data are sparse supporting significant pharmacodynamics interactions between antiepileptic drugs and the KD. However, the KD is known to cause a chronic but often mild or asymptomatic metabolic acidosis. Therefore,

adding KD to an existing regime of carbonic anhydrase inhibitors (acetazolamide, topiramate, zonisamide) may worsen pre-existing metabolic acidosis with the greatest decrease in serum bicarbonate levels early after KD initiation. There may also be increased risk of kidney stones associated with carbonic anhydrase inhibitors. Therefore, it is recommended that bicarbonate levels and observing patients for stones should be monitored carefully in patients receiving these drugs alongside KD.

Discontinuing or weaning down AEDS is usually advised only after at least three months of successful dietary treatment. Phenobarbital and benzodiazepine reductions may be associated with a higher risk of seizures worsening on the KD and therefore should be tapered gradually.

3 Starting the KD diet for inpatients

Most children start the KD as outpatients, but occasionally children will complex medical problems, children <1 year or in-patients with intractable seizures are started on the KD on the ward. The same guidelines (see section 2) should be followed in preparation to start the KD.

Inpatient monitoring should involve the multidisciplinary team. The KD dietitian will supervise the diet and teach parents/carers how to prepare meals. Ward nursing staff or the Epilepsy nurse specialist will teach parent/carers how to perform urinalysis and if necessary fingerprick testing for glucose and/or ketones.

Nursing and medical staff should monitor for:

- Weekly weight.
- Fluid balance chart.
- Urinalysis for ketones on all urine samples.
- Some children may require bedside blood ketones or serum beta-hydroxybutyrate in infants.
- Seizure chart.
- BMstix if symptomatic of hypoglycaemia or hyperketosis (nausea, vomiting, excessive lethargy, pallor, sweatiness, flushing etc). See section 4.4.

3.1 Discharge procedures

(a) Dietitian

- The KD dietitian will prepare diet plans and recipes with parents/carers.
- The KD dietitian will write to the GP requesting continued prescription of vitamin supplements and any special feeds.
- The KD dietitian will arrange feeding pump, giving sets and syringes, and home delivery of feed via community services if the child is fed by nasogastric tube or via gastrostomy tube.

(b) Nursing staff

- Nursing staff will train parents/carers in using the feed pump where relevant and ensure parents are competent to measure and record blood/urine ketone testing.

(c) Medical staff

- Check blood and urine results and document that results have been seen.

- Prescribe discharge medication and urine testing sticks and any supplements as advised by KD dietitian.
- Ensure that parents/carers have emergency/illness plan.
- Ensure that medical record documentation contains
    - Discharge weight
    - Seizure frequency and severity
    - Urine ketone result
    - List of current medication and doses
    - Type and ratio of KD diet
- Follow up arrangements are in place (usually 1-2 months KD clinic)

(d) Parent/Carers need the following equipment/information

- Ketostix for urine testing/ blood ketone testing kit and strips
- BMstix where appropriate
- Digital scales (advice about appropriate models given by dietitian)
- Recipes and diet plans
- Record cards for seizures and urinary ketones
- Symptoms for high or low ketones given and how to treat (if blood ketones >6.0mmol/L give 50ml maxijul)
- Emergency/illness plan
- Follow up arrangements
- Contact details: KD dietitian, Epilepsy nurse specialist, Doctors, Ward, Matthew's Friends

4 Emergency illness plan for children established on KD

4.1 Admission and monitoring

- As soon as possible after admission contact the paediatric neurology registrar, KD team and KD dietitian.
- Medical records – Enoting and MedChart should be marked with a notice that the child is on the ketogenic diet.
- Test urine for ketones every time child passes urine.
- Check serum beta-hydroxybutyrate (free fatty acids on EPR) in infants.
- Weigh the child weekly.

4.2 Fluid regime if not tolerating KD

- Rehydrate with clear fluids such as water or sugar-free squash if tolerated orally.
- Avoid sugar and carbohydrate containing drugs and IV solutions (i.e. IV dextrose solutions). (see section 2.3)
- As soon as possible, regrade back onto usual KD.

4.3 Recommended investigations

- Perform urgent blood test if child is unwell: FBC, renal function, bicarbonate, liver function, lactate, beta-hydroxybutyrate (free fatty acids on EPR).
- BMStix 4 hourly for a sick child if the child is NBM, or if symptomatic of hypoglycaemia. See section 4.4 for management of hypoglycaemia when BMStix ≤2.5 mmol.

4.4 Management of hypoglycaemia

Symptomatic hypoglycaemia or
BMStix ≤2.5mmol

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Take venous sample for lab glucose and give emergency drink (see Box 1) or
IV bolus if nil by mouth (see Box 2) without waiting for results

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Review after 15 minutes for symptoms and repeat BMstix
The cycle may need to be repeated

Box 1: Emergency drink recipe*

Younger than 5 years: 5g (1 level of teaspoon) maxijul powder in 50mls water or low-carbohydrate squash
Older than 5 years: 10g (2 level teaspoons) maxijul powder in 100mls water or low-carbohydrate squash

*emergency drink can be given by mouth, through the nasogastric tube or via gastrostomy

Box 2: IV bolus regime if nil by mouth

Give 10% dextrose 1ml/kg slow bolus

5 Children on the KD undergoing General anaesthesia

- Inform the anaesthetist that the child is on the KD.
- Contact KD team (Paediatric neurology registrar, KD dietitian on bleep 2420 or Dr. Williams 07766254206).
- Check all urine for ketones on dipstix.
- Insert IV cannula.
- If emergency GA or prolonged GA procedure, take bloods for FBC, renal function, bicarbonate, liver function, blood gas, glucose, lactate and B-hydroxybutyrate (free fatty acids on EPR).
- Keep NBM for normal recommended time (6 hours food/milk; 2 hours for clear fluids).
- Give 0.9% sodium chloride at appropriate rate.
- Check BMStix frequently while NBM (at least 4 hourly). Treat if having symptomatic hypoglycaemia and or BM levels ≤2.5mmol (see section 4.4).
- Continue with carbohydrate-free solution through anaesthetic (use either 0.9% sodium chloride or Hartman's solution)
- If anaesthetic is likely to be > 3 hours in duration, monitor blood gas (pH and bicarbonate) and consider IV bicarbonate if increase in acidosis.

- Continue IV 0.9% sodium chloride until oral fluids tolerated. Monitor BMs 4 hourly and electrolytes whiles on IV fluids.
- Re-introduce ketogenic diet as soon as possible to avoid hypernatraemia and maintain ketosis.
- See section 3.1 for discharge procedures.

6 Outpatient review and home monitoring

The main purpose of outpatient clinics is to:

- assess effectiveness of KD by review of goals.
- review and monitor for side effects of the KD. Specific consideration should be given to renal and bone complications (see section 6.4).
- to assess decision whether to stop or continue KD. In general, dietary therapy should be provided for at least 3 months before considering the therapy non-efficacious and discontinuing.

6.1 Monitoring targets at 3 months:

- Weight and height, plot and calculate BMI. Head circumference in infants.
- KD blood and urine tests (see Table 2).
- Review of KD side effects including bone health risk factors.
- Review of KD goals and decision to stop or continue KD.
- Consider requesting baseline DEXA scan if plan is to continue diet long term and at high risk for low bone density.

6.2 Subsequent monitoring targets 6 monthly:

- Weight and height, plot and calculate BMI. Head circumference in infants
- KD blood and urine tests (see Table 2)
- Review of KD side effects including bone health risk factors.
- Review of medication including anti-epileptic drugs.
- Review of KD goals and decision to stop or continue KD.

6.3 Home monitoring

- Fortnightly weights until stabilised on diet then monthly.
- Twice daily urine ketones until stabilised on diet then 1-2 times weekly, more often if seizure control worsens and during inter-current illness.
- Seizure diary.
- Follow up KD clinic appointment within 1-3 months of commencement, and then 3-6 monthly with bloods.
- Telephone and email contact with KD dietitian and/or epilepsy nurse specialist.

6.4. Specific consideration in KD monitoring

6.4.1 Renal considerations

The renal team should be consulted in complicated cases or where issues of uncertainty arises. Consider renal ultrasound at baseline and every 12 to 18 months and alkalinising urine for patients:

- Taking topiramate/zonisamide/acetazolamide
- With a history of renal stones or calculi on ultrasound

- With a family history of renal stones on ultrasound
- With a high urine calcium/creatinine ratio
- Who have a poor fluid intake

Consider alkalinising urine for patients with osteopenic bone disease.

Urine alkalisation can be done using either potassium citrate or sodium bicarbonate as in Table 3. Oral citrates appear to prevent kidney stones and may also reduce acidosis and theoretically bone mineral loss. However, folic acid absorption could be theoretically negatively affected as well causing a higher risk of megaloblastic anaemia.

Table 3. Options for urine alkalisation.

Option	Dose	Preparation	Specific notes
Potassium citrate	0.5-1mmol/kg/day in three divided doses	Effercitrate tablets	Taste bitter Contains carbohydrate Contains about 1.5-2.5mmol K per kg/day
Sodium bicarbonate	1-2mmol/kg/day in divided doses	1mmol/ml capsules 500mg capsules (contains 6mmol bicarbonate)	Contains sodium 1-2mmol/kg/day

6.4.2 Bone health considerations

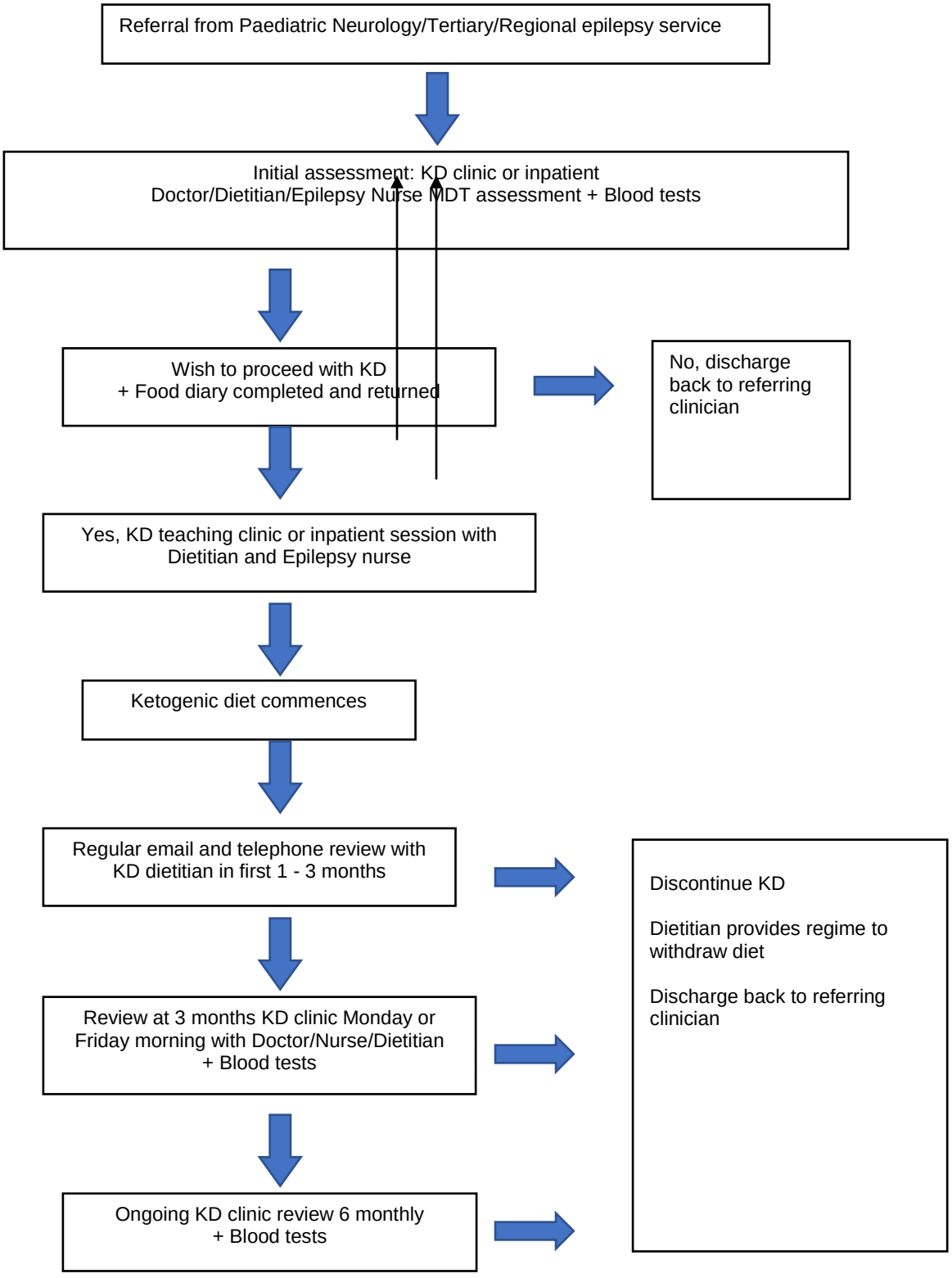
- Children on the KD are at increased risk of poor bone health and the following additional risk factors should be enquired about: (a) weight bearing, (b) AED exposure, (c) steroid exposure, (d) history of fractures, and (e) sun exposure.
- Consider additional supplementation of vitamin D and possibly calcium (see Table 4).
- Treat vitamin D insufficiency i.e <50nmol/L 25 hydroxy vitamin D level (see Table 4).
- Consider DEXA scan for those continuing KD after 3 months who are 4 years or older. This procedure requires children to lie still for a short time.
- Consider referral to metabolic bone disease clinic at ELCH.

Table 4: Vitamin D preparations and dosage

Preparations:	Cholecalciferol (vitamin D3) Liquid 3000units in 1 ml Capsules 20,000 units	
Supplementation dose:	All ages 0.2ml per day (=600 units/day)	
Treatment dose:	0-6 months 5 months – 12 years > 12 years	3000 units per day 6000 units per day 10,000 units per day
	Reduce dose within a few weeks and monitor bone profile and for hypercalcaemia.	

See BNFC and Guy's and St Thomas' Paediatric Formulary

7 Care pathway



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8 Ketogenic diet review clinic proforma

Clinic date:		
Re:		
Age:		
Diagnosis:		
School:		
Medication:		
Growth:	Weight: Height: BMI: Head circumference:	
Date KD commenced:		
Type of KD:		
Objectives of diet at commencement:		
Ketones (Blood/Urine):		Last BOHB:
Clinic urinalysis:		
Seizure (Type and frequency):		
Last EEG:		
Mood and general wellbeing:		
Bone Health:	Risk factors:	
Recent Investigations:	Blood: Urine: Other (DEXA/Renal USS):	
Conclusion:	Diet: Helpful Unhelpful Don't know	
Recommendations:	Continue / Stop diet	
Follow up:		

References

1. Optimal clinical management of children receiving dietary therapies for epilepsy: Updated recommendations of the International Ketogenic Diet Study Group. Kossoff et al. *Epilepsia Open* 2018

2. Ketogenic diet guidelines for infants with refractory epilepsy. Elles can der Louw et al. *European Journal of Paediatric Neurology* 2016

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