Guideline

Ketogenic diet (KD) – managing complications

This guideline includes the management of:

1 Scope

Children's services.

2 Purpose

To help clinicians in the management of children on a ketogenic diet. Please also see the ketogenic diet pathway.

3 Definitions

BNF	British National Formulary
CDC	child development centre
FBC	full blood count
IV	intravenous
KD	ketogenic diet
NGT	nasogastric tube
NBM	nil by mouth
SpR	specialist registrar
PEG	percutaneous endoscopic gastrostomy
PICU	paediatric intensive care unit
pH	(acidity/ alkalinity)
UTI	urinary tract infection

4 Management

4.1 Excess ketosis

Ketones are measured either by testing urine (acetoacetate) or blood (ß-hydroxybutyrate). The aim is to achieve values in the following ranges:

Urine (measures acetoacetate) • tested using Ketostix® (Bayer)	**4-16mmol/L**
Blood (measures beta-hydroxybutyrate) • On ward: use ward ketone testing meter • At home Optium Xceed® (Abbott) or Glucomen LX Plus® (a. menarini) meter	**2-5 mmol/L** If >5.9mmol **monitor carefully** as patient is at increased risk of becoming hyperketotic

Important: Some children may show signs of excess ketosis with levels lower than those above.

Occasionally ketone levels can become too high. This may occur after starting the diet, if the diet has recently been modified, or during illness. The signs of excess ketosis may include:

- rapid, panting breath ('Kussmaul' breathing)
- increased heart rate
- facial flush
- irritability
- vomiting
- unexpected lethargy

Important: Excess ketosis may also mimic non-convulsive status as the children are often less responsive.

Diagnosis - the above symptoms may be related to excess ketosis if:

- **urinary** ketones (acetoacetate) are **>16mmol or 4+** and test strip changes to a deep purple straight away **or**
- **blood** ketones (beta-hydroxybutyrate) **>5.9mmol/L**

4.1.1 Treatment for excess ketosis

The aim is to provide some carbohydrates to stop excess ketosis.

- If the child is alert and able to take oral fluids safely, go to **step 1**.
- If the child is **not** safe to take oral fluids, go to **step 4**.

1. Give 50ml of pure fruit juice or 50ml Lucozade (original) or 50ml **regular** CocaCola® (*in infants and young children 1/2x tube glucogel can be offered)

   Wait for 15-20 minutes.

2. If the symptoms have not improved after 15-20 minutes, this should be repeated.
3. Inform the dietitian of the episode. It may be necessary to alter the diet ratio if ketone levels are persistently excessive and the child is symptomatic – liaise with the dietitian in working hours.
4. **In exceptional cases** - if child is unwell and does not tolerate oral fluids because of excessive vomiting, is unconscious, etc:
    - IV fluids as 2.5% (preferable) or 5% dextrose/ saline, given as maintenance fluids, are required.
    - **The child will require hospital admission and an urgent clinical medical evaluation**.
    - Investigations should include, as appropriate:
        - urea
        - creatinine
        - electrolytes
        - glucose
        - capillary blood gas
        - infection screen

4.2 Metabolic acidosis

A patient who is taking topiramate, zonisamide or acetazolamide will be at a higher risk of developing metabolic acidosis, as the pH (acidity/ alkalinity) of the blood may be decreased. Treatment with bicarbonate is rarely required, liaise with the neurology team if needed.

4.2.1 Symptoms

- increased seizures
- clamminess and pale skin
- nausea, vomiting
- abdominal pain
- chest pain and palpitations
- confusion
- in severe forms, 'Kussmaul' breathing (increased rate and depth of breathing)

4.2.2 Diagnosis – aim to establish underlying cause

- excess ketosis
- effect of antiepileptic medication:
    - topiramate
    - zonisamide
    - acetazolamide
- infection and dehydration
- other metabolic causes

4.2.3 Management (metabolic acidosis)

1. Check blood gas (capillary), urea, creatine, electrolytes, bicarbonate, glucose, and ketones (urinary ketones or blood ketones) - for measurement and abnormal values.
2. Treat excessive ketones using the guidelines in treatment for excess ketosis above
3. Consider diet manipulation (to be initiated by dietitian): Either increasing daily caloric intake or reducing the ratio of the diet.
4. **Treat dehydration** adequately with fluids [carbohydrate free squash orally, water via NGT or gastrostomy or normal saline (0.9% NaCl) as IV fluids if enteral hydration is not tolerated]. Carbohydrate free squashes contain <0.1g of carbohydrate/ 100ml of ready to drink squash, or <0.6g of carbohydrate/ 100ml of undiluted fruit squash.
5. **Investigate for infection** or sepsis as in clinically indicated and manage accordingly.
6. **Consider other causes** of metabolic acidosis – test lactate – and consider discussion with metabolic team.
7. Consider reduction/ withdrawal of the topiramate, zonisamide or acetozalomide. Discuss with the KD team (09:00-17:00 only).

4.3 Hypoglycaemia

Emergency management of symptomatic hypoglycaemia or low glucose levels [**blood glucose (BM) <2.6 mmol/L**] associated with abnormal clinical manifestations.

4.3.1 Signs and symptoms of symptomatic hypoglycaemia

Due to counter regulatory sympathetic response	**Due to cerebral glycopenia**
anxiety perspiration pallor palpitations (tachycardia) tremulousness weakness nausea vomiting hypothermia	headaches confusion irritability/ fussiness behavioural change dysarthria ataxia, incoordination hypotonia (infants) dizziness amnesia somnolence, lethargy apnoea (infants) seizures coma stroke, hemiplegia, aphasia

Check blood sample/ lab sugar and treat, if appropriate, as below.

4.3.2 Management (hypoglycaemia)

1. Treat hypoglycaemia with rapidly absorbed carbohydrate, such as:
    - 50ml of **regular** CocaCola®
    - 50ml of Lucozade®, Energy Original
    - 50ml of pure fruit juice
    - 1 tsp of sugar, ordinary jam, honey or syrup
    - 5g (1 level teaspoon) dextrose powder in 100ml water

    If the response to the above treatment is inadequate, more can be administered after 10-15 minutes.

2. Treat hypoglycaemia with Glucogel® (formerly known as 'Hypostop'):
    - give Glucogel® (BBI Healthcare) (5g glucose per 1/2 tube)
    - or Dextrogel® (M & A Pharmachem) (5g glucose per 1/2 tube)

    This can be squeezed into the child's mouth if the child is uncooperative or not able to take the items suggested above (eg infants or young children)

3. For patients with reduced a consciousness level and/or seizures:
    - give 5 ml/ kg 10% Dextrose intravenously. *European Paediatric Life Support, 3rd edition April 2011, Resuscitation Council (UK)*

4.4 Gastrointestinal illness

When children established on KD present with intercurrent or gastrointestinal illness (diarrhoea and/or vomiting) it is important to inform the ketogenic dietitian and/or neurology team as soon as possible.

KD dietitian 09:00-17:00 weekdays only	bleep 154-663 or 154-475 extension 2790
Paediatric neurology consultant	bleep SpR 156-2178 extension 2662
Epilepsy nurse specialist	bleep 152-555 extension 6618

If the child is significantly unwell, clinical medical assessment and urgent bloods to include:

- FBC
- urea
- creatinine
- electrolytes
- bicarbonate
- blood gas
- lactate
- liver function tests
- blood or urinary ketones
- infection screen (urine test for microbiology; chest x-ray; blood culture, as appropriate in any unwell child).

Check blood glucose levels 2 to 4-hourly if children are unwell, especially if 'nil by mouth' (**note**: if the child is ketotic, blood glucose may be low but still acceptable, ie >2.6 -3 mmol/L).

If the child is asymptomatic, see clinical manifestations of hypoglycaemia under emergency management of symptomatic hypoglycaemia above, and of excess ketosis under treatment for excess ketosis above.

4.4.1 Emergency management of symptomatic hypoglycaemia or BMs <2.6mmol/L and/or dehydration

KD may need to be temporarily stopped due to illness.

1. Check blood glucose levels and give emergency treatment if required (see management guidelines for symptomatic hypoglycaemia for further information).
2. Test urine for ketones every time child passes urine, watching for excessive ketosis.
3. Rehydrate with low carbohydrate clear fluids if tolerated orally eg sugar-free squash. Dioralyte® can also be used if necessary.
4. If IV fluids are required use normal saline (0.9% NaCl) or if BMs <3mmol/L - 2.5% or 5% dextrose/ saline solution to maintain BMs between 3 and 4 mmol/l.

If considering making changes to anti-epileptic medications, **please discuss with the KD team**.

- Where possible avoid sugar and carbohydrate containing drugs. If you are unsure of the carbohydrate content of medications, you should contact the ward pharmacist or medicines information.
- Weigh the child weekly on the same scales.
- Consider contacting the KD team if further advice is needed.

4.4.2 Re-introducing the ketogenic diet after illness

If KD has had to be stopped because of an illness, aim to re-grade back onto the diet as soon as possible (liaise with the ketogenic dietitian for advice).

Some children may have a ketogenic meal replacement recipe which may be used as an alternative to a meal when a child is unwell.

A ketogenic formula feed, Ketocal® is available for use with tube feeds. The amount of Ketocal® given needs to be adjusted to meet a child's energy needs and provide the correct KD ratio (please liaise with the ketogenic dietitian for advice).

If the child has a gastrointestinal illness, consider reducing the fat portion of the diet initially and gradually increasing this back up, as tolerated, over three to four days.

If the child is on a NGT or PEG feed, the feed should be re-introduced as follows:

Transition from clear fluids to ketocal			
Phase	**Time**	**Dioralyte**	**Ketocal**
1	1-2days	50% of usual feed volume	50% of usual feed volume
2	Full feeds		

4.5 'Nil by mouth' status (NBM)

4.5.1 Management guidelines for children on the ketogenic diet

[Adapted from: The Charlie Foundation (2007) *Professional's Guide to the Ketogenic Diet*]

The high fat diet regimen of the ketogenic diet (70-90% of calories) forces the body into a dietary induced ketosis. The acidosis that occurs when the diet is first initiated corrects itself within days and is not sustained.

The literature on KD and general anaesthetic is scarce, with very little consensus on management. The most comprehensive study undertaken so far suggests that carbohydrate-free solutions are safe and blood glucose remains stable throughout surgical procedures up to 1.5 hours.

The most common effect noted in procedures >3 hours was a significant decrease in pH, requiring IV bicarbonate. Current advice suggest therefore monitoring blood pH in procedures >3 hours and administering IV bicarbonate where necessary.

4.5.2 Sedation for procedures including general anaesthetic

1. Inform KD team of patient's admission:

KD dietitian	bleep 154-663 or 154-475 extension 2790
Paediatric neurology consultant	bleep SpR 156-2178 extension 2662
Epilepsy nurse specialist	bleep 152-555 extension 6618

2. Test urine for ketones every time child passes urine.
3. Take bloods:
    - FBC
    - urea
    - creatinine
    - electrolytes
    - bicarbonate
    - liver function tests
    - urinalysis
    - blood gas
    - glucose
    - lactate.
4. General anaesthetic: Keep NBM for normal recommended time period.
5. If IV fluids are required give normal saline (0.9% NaCl) or Ringers lactate at appropriate rate.
6. If anaesthetic is >3 hours monitor blood glucose and blood gas (pH and bicarbonate) 1-2 hourly. Consider IV bicarbonate if increase in acidosis.
7. If blood glucose <3mmol/L use dextrose containing solutions (ie 5%) to maintain blood glucose between 3-4mmol/l. Blood glucose to be tested at least 3-4hrly. Blood glucose <3mmol/L is more likely to occur if fasting extends beyond 12 hours.
8. Continue IV normal saline until oral fluids tolerated.
9. Re-introduce normal (ketogenic) diet as soon as possible. Please contact KD dietitians to discuss a suitable diet, or if nasogastric tube or gastrostomy are required, the type of formula to be given. A ketogenic meal can be ordered from the diet kitchen on 3024. Please state whether you need an emergency classical ketogenic meal or an emergency MCT ketogenic meal.

Important: Where possible, **avoid** sugar and carbohydrate containing drugs and IV solutions. Contact ward pharmacist for advice about preparation with lowest carbohydrate content.

4.6 Children on KD admitted to PICU

1. Inform the KD team of patient's admission. Contact details:

KD dietitian	bleep 154-663 or 154-475 extension 2790
Paediatric neurology consultant	bleep SpR 156-2178 extension 2662
Epilepsy nurse specialist	bleep 152-555 extension 6618

2. Intravenous fluids: use normal saline (0.9% NaCl) or Ringers lactate, unless blood glucose levels are low (<3 mmol/l).
   If low then give dextrose/ saline solutions (5%), aim to maintain blood glucose between 3-4 mmol/l.
3. Monitor for hypoglycaemia and metabolic acidosis: blood glucose levels and blood gas 1-2 hourly as appropriate.
4. Investigations should also include measurement of ketones (urine or blood; see management of excess ketosis above), excessive ketosis and acidosis may require treatment with IV bicarbonate.
5. A base excess of -10 indicates significant metabolic acidosis and should be half corrected over 4 hours with intravenous bicarbonate.
6. **If acidosis is explained by excess ketosis**, dextrose containing maintenance fluids (5% dextrose) would be appropriate.
7. If acidosis is not completely explained by excess ketosis ie high blood lactate this could be discussed with the metabolic team (choice of maintenance fluids (normal saline/ saline).
8. Medication: must be in lowest carbohydrate form. Contact pharmacy or medicines information to check carbohydrate content of preparations. If you are unsure of the carbohydrate content of medications, you should contact the ward pharmacist, or contact medicines information. If in doubt, substances ending in 'ose' or 'ol' are usually converted to glucose in the body (cellulose is an exception and is suitable).
9. Enteral feeding: Please contact ketogenic dietitians to discuss the type of formula to be given by NGT or gastrostomy.

4.7 Constipation

Constipation is a relatively frequent complication of the ketogenic diet. Although not life-threatening it can be troublesome. Reducing water input will worsen constipation, so ensure they are taking enough water.

Unfortunately, many first-line agents, such as:

- lactulose
- bran
- fruit juices
- fibre containing foods (eg Weetabix)

contain a significant amount of carbohydrate. As a result the majority of children are managed on sachets of Movicol, the number and frequency should be titrated against bowel opening as per BNF.

In general, children should be encouraged to open their bowels at least once every couple of days. As a first-line children might take one sachet of Movicol daily but under consultant neurologist advice other children have taken more than this.

4.8 Kidney stones

Whilst on the ketogenic diet there is an increased incidence of renal calculi.

Children should be started on potassium citrate if they are in an at-risk group. These would include:

- children who previously had renal calculi
- those with calcinosis evident on renal ultrasound scan
- family history of stones
- taking drugs which we know increase the incidence – carbonic anhydrase inhibitors ie acetazolamide, topiramate and sulthiame.

If a child is noted to have renal symptoms an ultrasound should be performed.

With nephrocalcinosis a risk-benefit assessment should be made by the consultant neurologist. In the first instance, potassium citrate supplementation could commence. Alternatively the diet could be withdrawn but if it has been dramatic in controlling the seizures then appropriate negotiation with the parents might be more sensible and referral onto a nephrologist. The dosage would be that prescribed for alkalinisation of the urine, with the best preparation in terms of cost/ palatability/ carbohydrate.

Prescription of potassium citrate if concerned about nephrocalcinosis: After some debate and advice from the pharmacy here, we would suggest that we give effervescent tablets rather than syrup as the latter contains too much sugar for KD. We were amazed at the price discrepancy, but would recommend the following (BNFc 2012) as it is by a long way the cheapest and should be just as efficacious as other versions.

Effercitrate as 1.5 gram potassium citrate tablets – **for a 30 kg child** – to take three grams twice daily to continue until reviewed at our next ketogenic appointment. It is available over the counter in a community pharmacy (licensed for alkalinisation of the urine in UTI).

4.9 Nutrient deficiency

In the ketogenic diet, as free food choice is denied, a suitable broad spectrum vitamin and mineral supplement is pertinent.

If patients are on a nutritional complete food substitute, this may provide their micronutrient requirement. However, if they are not taking 100% of their food as a nutritional complete food substitute, it is likely they will need vitamin supplementation. We choose a carbohydrate-free form so that ketosis is not hindered.

At present the only formulation that meets this need would be Phlexy-Vits, which we recommend all children should take on a daily basis – unless they are taking the diet as a liquid formula only. However, this formulation can be somewhat unpalatable, and if the child cannot tolerate it then one could reconsider a carbohydrate containing vitamin preparation and watch ketosis.

4.10 Pain control

The information found on the commonly used medications in day surgery is below. The brands mentioned are all ones that pharmacy currently (2012) have as stock.

It is important to remember that different brands may have a different carbohydrate content than mentioned below.

Preparation	**Carbohydrate content**
Paracetamol 500mg tablets (Bristol)	Contains maximum of 50mg/ tablet
Paracetamol 120mg/5mL liquid (Orbis)	Total 1.605g/5mL
Paracetamol 250mg/5mL liquid (Rosemont)	Total 3.025g/5mL
Paracetamol 250mg/5mL liquid (Pinewood)	Total 3.027g/5mL
Paracetamol IV (Perfalgan)	3.850g of Mannitol in 100mL
Ibuprofen 200mg tablets (Wockhardt)	Contains maximum of 210mg/ tablet
Ibuprofen 100mg/5mL (Fenpaed)	Total 1.925g/5mL
Codeine 15mg tablets (Wockhardt)	Contains maximum of 35mg/ tablet
Codeine suppositories	Nil carbohydrates
Codeine 15mg/5mL linctus (Care brand)	250mg/5mL
Morphine 10mg/ml injection (Hameln)	Nil carbohydrates
Oramorph 10mg/5mL	0.48g of alcohol, 1.5gm sucrose and 50-100mg glucose per 5mL
Fentanyl 50mcg/mL injection (Antigen)	Nil carbohydrates

For tablets the amount of carbohydrates is normally considered to be insignificant and manufacturers are unhappy to supply information. So we have weighed the tablets and deducted the weight of the active ingredient and then used this as a maximum unless the daily dose in an adult is likely to exceed 1gm daily.

Please remember that the above information is brand specific.

5 Ordering a meal during an emergency admission

If a patient has an unplanned admission, please contact the kd dietitian to discuss a suitable diet. A meal can be ordered from the diet kitchen on 3024. Please state whether you need an emergency classical ketogenic meal or an emergency MCT ketogenic meal.

6 Monitoring compliance with and the effectiveness of the guideline

Every child should receive care as per the guideline.

Any breaches in care will be picked up and monitored by the Trust's incident reporting system and discussed at the monthly child development centre (CDC) clinical governance meetings.

Audit criteria includes:

- Review of ketogenic diet integrated care pathway (ICP)

The audit criteria will be monitored using regular audits within the child development centre.

7 References

Neal L & McGrath G. 2007. Ketogenic Diets. In: Clinical Paediatric Dietetics. P 305.

Sperling, MA (2000) in Behrman RE, Kliegman RM, Lenson HB (eds) *Nelson Textbook of Pediatrics,* 16th edition (pp. 439-450); Dekelbab BH and Sperling MA. (2006) 'Hypoglycaemia in newborns and infants', *Advanced Paediatrics,* 53

British National Formulary for Children Information for treatment of hypoglycaemia from 2010-2011

European Paediatric Life Support, 3rd edition April 2011, Resuscitation Council (UK)

8 Associated documents

- Ketogenic diet integrated care pathway

Equality and diversity statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

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Document management

Approval:	Dr Alistair Parker- 20 April 2015 (minor amendments made July 2015)		
Owning department:	Child development centre		
Author(s):	Helena Champion and Dr Alistair Parker		
File name:	f557ef3584c244b291603006687f5b85		
Supersedes:	Version 5, April 2015		
Version number:	6	Review date:	April 2018
Local reference:		Media ID:	24969