

KD intervention manual

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1. SUMMARY OF DIET IMPLEMENTATION

- Infants will be initiated on the classical ketogenic diet (KD).
- This will usually be started at a 2:1 ratio and increased to a 3:1 ratio (or 4:1 ratio) as tolerated; younger infants under 12 months old may be initiated in hospital.
- Blood ketone levels of at least 2mmol/l will be aimed for. Ideal therapeutic levels are usually over 4mmol/l but this will depend on an individual's seizure control and tolerance to ketosis.
- Blood glucose should be monitored during initiation.
- Breast feeding can be incorporated into a KD in conjunction with a ketogenic formula where possible if this is the parent's preference. Standard weaning guidelines should be followed.

2. CALCULATON OF CLASSICAL KD

Energy prescription

Energy intake is carefully controlled on the classical KD. The energy prescription (calories) should be sufficient to allow for normal growth and development however excess dietary energy and weight gain will cause poor ketosis which can in turn compromise potential seizure control. An energy prescription should always be individually calculated, taking into account the following:

- a. Age
- b. Current weight and length and recent growth trends
- c. Individual pre-KD energy intake, assessed by a food/feed record diary for 3 or 4 days
- d. Medication use
- e. Energy expenditure based on mobility, level of physical activity, and seizure activity
- f. UK recommendations for energy requirements/intakes for infants of different ages (Scientific Advisory Committee on Nutrition, 2011).

An initial dietary energy prescription must be closely monitored and adjusted as needed, especially during the first few weeks and months of treatment. If the prescribed energy intake does not maintain growth it must be increased, and likewise if weight gain is excessive it will lead to poor ketosis and energy will need to be reduced. Dietary energy increases and decreases should always be done in controlled increments.

Protein intake

Guidelines for 0-2 year olds suggest a prescription of 1.1-2.6g/kg/day: the UK recommended nutrient intake (RNI) for protein according to age (taken from Great Ormond Street Nutritional Requirements booklet 2014). In practice, this may not be achievable and so the protein prescription may be set somewhere between the World Health Organisation (WHO) recommendations for 'safe' levels of protein intake and the RNI. WHO recommendations for 'safe' levels of protein intake in infants are 1.36g/kg body weight at 3 months of age, 1.24g/kg at 4 months of age, 1.14g/kg body weight at 6 and 12 months of age, 1.03g/kg at 18 months of age and 0.97g/kg at 2 years of age (taken from WHO technical report No. 935 (World Health Organisation, 2007)). The amount of protein allowed in a classical KD prescription will usually include that provided from all types of food but protein quality must also be considered due to the importance of meeting requirements of all indispensable amino acids. The allowed amount

of protein will be in many cases be only just above the recommended safe levels, so high biological value sources (e.g. meat, fish, eggs, dairy products) should be chosen wherever possible. If these foods are not routinely used in the diet, this must be taken into account and the prescription adjusted to allow more protein.

Diet ratio

The classical KD is calculated using the original ratio method (Talbot, 1930). A ketogenic ratio tells us the proportion (in grams) of fat in the diet as compared with carbohydrate and protein, e.g. a typical 4:1 ratio refers to a diet with a ratio of 4g of fat to 1g of protein plus carbohydrate combined. Most infants on classical KDs will start at 2:1 ratio, with a likely increase of up to 3:1 however some require higher to achieve the necessary seizure control. Some children with very low energy requirements may not meet their safe protein requirements on a 4:1 ratio. For these children it may be necessary to add extra protein to feeds or meals to meet safe protein levels and hence it may be difficult to achieve a 4:1 ratio. **Table 1** gives more detail on KD ratios.

Table 1. Explanation of the ratio system used to calculate the classical KD (taken from Magrath and Neal, 2012)

Diet ratio	Macronutrient proportions		Percentage of dietary energy from macronutrients	
	Fat (grams)	Protein and carbohydrate combined (grams)	Fat (%)	Protein and carbohydrate combined (%)
1:1	1	1	69	31
2:1	2	1	82	18
3:1	3	1	87	13
4:1	4	1	90	10

Diet prescription

Once the required energy, protein and ketogenic ratio have been determined, the rest of the prescription can be calculated to give the prescribed daily amounts of fat, protein and carbohydrate. The easiest method is by using dietary units; a unit is calculated from the calorie content of each of the macronutrients in the chosen diet ratio, based on fat providing 9 kcals per gram and protein and carbohydrate providing 4 kcals per gram each. This is based on a method described in more detail by authors from Johns Hopkins Hospital, USA (Kossoff et al., 2011), and shown below for the 4:1, 3:1 and 2:1 ratios:

Ratio 4:1: Each dietary unit = 4g fat and 1g protein and carbohydrate.

Energy content of each dietary unit = $(4 \times 9 \text{ kcals}) + (1 \times 4 \text{ kcals}) = 40 \text{ kcals}$.

Ratio 3:1: Each dietary unit = 3g fat and 1g protein and carbohydrate.

Energy content of each dietary unit = $(3 \times 9 \text{ kcals}) + (1 \times 4 \text{ kcals}) = 31 \text{ kcals}$.

Ratio 2:1: Each dietary unit = 2g fat and 1g protein and carbohydrate.

Energy content of each dietary unit = $(2 \times 9 \text{ kcals}) + (1 \times 4 \text{ kcals}) = 22 \text{ kcals}$.

The total daily dietary energy allowance is divided by the kcals per dietary unit (this will depend on which ratio is to be chosen. This number is then multiplied by the units of fat in the ratio to give the total daily allowance of fat. The unit of carbohydrate and protein combined in the ratio is one; this is multiplied by the number of allowed daily dietary units to give the total daily amount of both macronutrients together. The protein allowance has already been determined; this can be subtracted to give the carbohydrate allowance.

3.

DIET IMPLEMENTATION

Fluid

Normal fluid requirements should be maintained with no fluid restriction.

Food and feeds

Once total daily amounts of fat, protein and carbohydrate are calculated they can be divided up over the day in feeds or meals and snacks as required, all keeping to the same ketogenic ratio. If using meals and snacks, these can be calculated using recipes or exchange lists, depending on the practice implemented by the hospital centre.

The classical KD can be given as a complete or part liquid feed, either taken orally (e.g. for young infants) or given enterally, using a ketogenic formula such as KetoCal (Nutricia: available as 3:1 and 4:1 ratio powders and 4:1 ratio liquid feed). This may need adjusting with an added carbohydrate module to the appropriate ketogenic prescription. If an infant is using this as a complete feed, extra supplemented micronutrients are not usually necessary but this should be checked against requirements. However KetoCal 4:1 (powder or liquid) does not meet recommended guidelines for nutritional content of infant formulae so is not suitable as a sole source of nutrition without careful consideration of individual nutrients. In particular the sodium content of KetoCal 4:1 is higher than that of normal infant formulae; potassium content is also higher and the calcium:phosphate ratio is too low (Dos Santos, 2012).

If an infant is being breastfed, this can be continued at a lower volume, with a prescribed amount of KetoCal given before each feed based on the theoretical fluid and dietary energy intake for age. This will limit intake of breast milk and thus maintain a ketogenic ratio. If breastmilk is expressed, this can be mixed with KetoCal, ensuring each bottle contains the combination feed in the correct ratio (Dos Santos, 2012).

Feed thickeners can be used if required but the carbohydrate content should be considered.

Infants should be weaned as per Department of Health (DOH) and British Dietetic Association guidelines (DOH, 200; British Dietetic Association, 2010). Nutritional requirements should be assessed and supplementary micronutrients may be needed at this stage. Foods which are good sources of vitamin C should be encouraged in the weaning diet; vegetable or fruit purees can be combined with added oil or cream (and a prescribable protein supplement if necessary) to maintain the correct ketogenic ratio. The progression onto meat and fish will allow for more variety. Finger foods tend to be higher in carbohydrate, however appropriate KD choices could include boiled carrot sticks, cubes of cheese, avocado, or soft pieces of fruit such as banana, soft pear or slightly cooked apple. Weaning breakfasts on the KD could include slices of omelette or hard-boiled egg, pieces of slightly mashed or soft fruit, with a ketogenic 'yoghurt' made with Ketocal and crème fraîche (Dos Santos, 2012).

Free foods are very limited on the classical KD, and most are unsuitable for infants.

Supplementation

Requirements for vitamin, mineral and trace elements should be assessed on an individual basis, depending on the provision from the prescribed KD and age-specific nutritional

requirements. Supplementation may be needed if an infant has low calorie requirements or is not fully ketogenic formula-fed. On-going intake of all micronutrients should be closely monitored, and it is the responsibility of the individual dietitian to recommend the most appropriate supplement available for each child to ensure nutritional adequacy.

In some cases additional carnitine may be needed if blood levels of free carnitine fall. Alkalisiation of the urine may also be required if there is increased risk or evidence of renal stones.

Initiation

Infants under 12 months will be admitted to their local hospital for initiation; medically stable children over 12 months old can start the diet at home with close supervision from their local team after a teaching program, including instructions on the daily home monitoring of blood or urine ketones and the management of possible early side effects such as excess ketosis and hypoglycaemia. The classical KD will usually be built up slowly to an initial 2:1 ratio; this initiation process will depend on the individual and the local centre protocol. Ketogenic ratio can be increased to 3:1 (or 4:1) if needed, depending on ketone levels, seizure control and dietary tolerance.

Fine tuning

Fine tuning and on-going modification of a KD are an essential part of the dietetic care and may involve alterations to the energy prescription or an increase or decrease of ketogenic ratio. These changes should be done in a stepwise process, making only one change at a time, to allow assessment of benefit. Other modifications may be the increase of protein intake with body weight and age changes, alterations in meal, snack or feed distribution to fit with lifestyle, and adjustments to micronutrient supplementation dose if other diet components are changed, or in line with age increase or blood test results.

Medium chain triglyceride (MCT) supplement can be added in small amounts to an infant's diet if needed to improve ketosis and seizure control AFTER the initial 8 week period on diet treatment. However, if the dietitian feels that MCT supplementation is necessary within the 8 week trial period, this takes priority. If the diet remains a 'classical' KD (this is to be discussed on a case-by-case basis by dietitians and the Dietetic Assistant) then the participant should not have to be withdrawn from the trial, although it will still result in a protocol deviation.

Illness and medications

When an infant is ill the KD takes second place to the necessary treatment and medical assistance should always be sought if there is any concern about health. It is common for ketone levels to fluctuate during illness and seizures can also worsen. Local centres should all have illness protocols in place that are clearly explained to the families/caregivers.

All medications such as antibiotics or painkillers should be as low in carbohydrate as possible. Intravenous (IV) dextrose infusions should be avoided if possible but if continued IV support is necessary a small amount of dextrose may be needed to maintain blood glucose levels which can be monitored.

REFERENCES

BRITISH DIETETIC ASSOCIATION SPECIALIST PAEDIATRIC GROUP (2010). BDA Paediatric Group Position Statement: *Weaning infants onto solid foods*. (www.bda.uk.com/publications/statements/PositionStatementWeaning.pdf)

DEPARTMENT OF HEALTH (2003) Infant Feeding Recommendation. Gateway reference 3269. (www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4097197)

DOS SANTOS N (2012) Dietary treatment of epilepsy in infants. In: Neal, EG (Editor). *Dietary Treatment of Epilepsy: Practical Implementation of Ketogenic Therapy*. John Wiley & Sons: Oxford, UK

Great Ormond Street for Children NHS Foundation Trust. *Nutritional Requirements for Children in Health and Disease*. 5th edition, 2014.

KOSSOFF, E.H., FREEMAN, J.M., TURNER, Z. & RUBENSTEIN, J.E. (2011) *Ketogenic Diets: Treatments for Epilepsy and other Disorders* (5th edition). Demos Medical Publishing: New York.

MAGRATH G & NEAL EG (2012) The classical ketogenic diet. In: Neal, EG (Editor). *Dietary Treatment of Epilepsy: Practical Implementation of Ketogenic Therapy*. John Wiley & Sons: Oxford, UK

SCIENTIFIC ADVISORY COMMITTEE ON NUTRITION (2011) Dietary Reference Values for Energy. SACN, London.

TALBOT, F.B. (1930) *Treatment of Epilepsy*. New York: Macmillian Co.

WORLD HEALTH ORGANISATION (2007) *Protein and amino acid requirements in human nutrition: Report of a joint WHO/FAO/UNU Expert Consultation* (WHO Technical Report series 935).