Ketogenic dietary therapy for Lennox Gastaut syndrome

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First described in 1966 (1), Lennox-Gastaut syndrome (LGS) is a rare and severe epileptic encephalopathy which typically presents before eight years of age and accounts for up to 10% of all childhood epilepsies (2). It is characterized by multiple seizure types such as atypical absences, generalised tonic clonic, tonic and atonic seizures with progressive intellectual disability, behavioural problems and abnormal electroencephalographic (EEG) features. The EEG typically shows evidence of epileptic encephalopathy with slow background and slow spike wave discharges and paroxysmal fast activity in sleep (3). Anti-seizure medication (ASM) is the usual first-line treatment (4), but seizures are almost always refractory and associated with significant cognitive, learning and behavioural impairments, impacting health-related quality of life of the affected children and their carers (5). Lifelong persistence of LGS is usual (6) with drug refractoriness and high seizure burden associated with poor psychosocial outcomes and long-term dependence (7).

In view of these challenges, it is important that all therapy options for the LGS child are explored. Non-pharmacologic treatments include vagal nerve stimulation and ketogenic dietary therapy (KDT) (4, 8, 9). KDT is a high fat, restricted carbohydrate regime that has been used to treat epilepsy since the 1920s and includes the stricter Classical ketogenic diet (CKD) and Medium Chain Triglyceride diet, and less restrictive Modified Atkins diet (MAD) and Low Glycaemic Index Treatment (LGIT). Randomised trials have reported efficacy of all types of KDT (10, 11, 12, 13, 14), which has a 'relative risk' of 3.16 of achieving seizure freedom, and 5.80 of over 50% seizure reduction, compared to the usual care of children with medication-resistant epilepsy (15).

Retrospective reviews show KDT to be efficacious for treatment of LGS. One study of 71 children with LGS from USA reported 51% had over 50% seizure reduction after 6 months on CKD with 23% experiencing over 90% reduction and similar results after 12 months; 45% were able to reduce their ASM dose while on diet (16). Another study of 47 Chinese children with LGS reported over 50% seizure reduction in 49% after 3 months on CKD with four becoming seizure free after 6 months; response to diet was associated with positive EEG changes (17). A review of 25 LGS children treated with MAD in India reported a similar responder rate: 48% with over 50% seizure reduction after 3 months and 44% after 6 months (18). In a prospective study of 20 Argentinian LGS children on CKD, seizures were reduced by over 50% in eight (40%) after 18 months with three seizure free (19). A study of 36 Korean patients on the less restrictive LGIT included 12 with LGS, of whom 9 had over 50% seizure reduction after 3 months (20).

A literature review of 18 different studies with outcome data on 189 LGS children reported 88 (47%) with over 50% seizure reduction after 3-36 months on KD (16). One Korean study has assessed long term outcomes of 68 LGS patients over a mean follow up period of 19 years: of the 19 who tried diet therapy, 5 maintained seizure freedom on CKD and one on MAD (21). The same group reported KDT to be efficacious and feasible in a recent review of 20 LGS patients with mitochondrial dysfunction (22).

Based on literature evidence, revised international consensus recommendations describe KDT as moderately beneficial in LGS (23), with UK guidelines on management of epilepsy suggesting diet should be considered under the guidance of a tertiary epilepsy specialist in certain childhood-onset epilepsy syndromes including LGS (nice.org.uk:ng217). We recommend that LGS children who have failed appropriate ASM therapy are funded for an initial assessment of KDT suitability, with diet ideally followed for a minimum of 3 months to allow adequate assessment of benefit and appropriate fine-tuning of the dietary prescription to a child's individual needs. If seizure control is improved, it is likely that ASMs would be reduced or discontinued after that time. KDT is usually continued for at least two years if successful.

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