Ketogenic dietary therapy for Lennox Gastaut syndrome

Written by:

Elizabeth Neal MSc PhD RD
Specialist Ketogenic Dietitian, Matthew's Friends Clinics
Honorary Research Associate, UCL - Institute of Child Health

First described in 1966 (1), Lennox-Gastaut syndrome (LGS) is an 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 (most commonly tonic or atonic drop attacks) and abnormal electroencephalographic (EEG) features; with progressive intellectual disability and behavioural problems that may both present later (3). Anti-epileptic drug (AED) therapy is the usual first-line treatment (4) however LGS seizures are difficult to control with medication and failure of a first drug will significantly reduce the likelihood of subsequent seizure freedom (5). Intractable seizures and adverse effects on cognitive and social functioning (6) will have a major impact on the health-related quality of life of those affected (7) with considerable NHS and social cost implications for supporting medical and educational needs. Lifelong persistence of LGS is usual (8) with poor outcomes continuing into adulthood and long-term dependence on caregivers for daily living abilities (9),

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 dietary therapy (4, 10). The ketogenic diet (KD) is a high fat, restricted carbohydrate dietary regime that has been used as a treatment for epilepsy since the 1920s, newer modified variants include the modified Atkins diet (MAD). Efficacy of these diets has been demonstrated in many prospective studies and randomised trials (11, 12, 13).

Retrospective reviews show KD to be efficacious for treatment of LGS. One study of 71 LGS patients from USA reported 51% had over 50% seizure reduction after 6 months on KD with 23% experiencing over 90% reduction and similar results after 12 months (14). Another study of 47 LGS patients from China reported over 50% seizure reduction in 49% after 3 months on KD with four becoming seizure free after 6 months; response to diet was associated with positive EEG changes (15). 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 (16). In a prospective study of 20 Argentinian LGS children on KD, seizures were reduced by over 50% in eight (40%) after 18 months with three seizure free (17). 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 (14). 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 classical KD and one on MAD (18). The same group reported diet therapy to be efficacious and feasible in a recent review of 20 LGS patients with mitochondrial dysfunction (19).

International consensus recommendations suggest that the KD should be strongly considered in a child with epilepsy which has failed to respond to two or three AEDs (20). Guidelines (NICE) on management of the epilepsies in the UK also suggest that children and young people with epilepsy whose seizures have not responded to appropriate AEDs are referred to a tertiary paediatric epilepsy specialist for consideration of the KD (CG137, nice.org.uk). In view of these recommendations, we would propose that all children with LGS who have failed

appropriate AED therapy are funded for an initial assessment of suitability for dietary therapy. Children who start KD will require a minimum of three months on treatment to allow adequate assessment of benefit and appropriate fine-tuning of the diet prescription to individual needs; it is recommended that successful treatment is continued for at least two years during which the potential for weaning AEDs will be regularly reviewed.

References:

1. Gastaut H, Roger J, Soulayrol R, et al (1966) Childhood epileptic encephalopathy with diffuse slow spike-waves (otherwise known as "Petit Mal Variant") or Lennox syndrome. Epilepsia 7(2):139–79.
2. Camfield PR (2011) Definition and natural history of Lennox–Gastaut syndrome. Epilepsia 52: 3–9.
3. Cross JH, Auvin S, Falip M, Striano P, Arzimanoglou A (2017) Expert Opinion on the Management of Lennox-Gastaut Syndrome: Treatment Algorithms and Practical Considerations. Front Neurol.8:505.
4. Strzelczyk A, Schubert-Bast S (2021) Expanding the Treatment Landscape for Lennox-Gastaut Syndrome: Current and Future Strategies. CNS Drugs 35(1): 61-83.
5. Kwan P, Brodie MJ (2000) Early identification of refractory epilepsy. N Engl J Med. 342 (5):314-9.
6. Asadi-Pooya AA (2018) Lennox-Gastaut syndrome: a comprehensive review. Neurol Sci. 39(3):403-414.
7. Gibson PA (2014) Lennox-Gastaut syndrome: impact on the caregivers and families of patients. J Multidiscip Health. 7:441-8.
8. Samanta D (2021) Management of Lennox-Gastaut syndrome beyond childhood: A comprehensive review. Epilepsy Behav. 114(A):107612.
9. Reyhani A, Özkara Ç (2021) The unchanging face of Lennox-Gastaut syndrome in adulthood. Epilepsy Res. 13(172):106575.
10. Kossoff EH, Shields WD (2014) Nonpharmacologic care for patients with Lennox-Gastaut syndrome: ketogenic diets and vagus nerve stimulation. Epilepsia 55(4):29-33.
11. Neal EG, Chaffe HM, Schwartz R, et al (2008) The ketogenic diet in the treatment of epilepsy: a randomised controlled trial. Lancet Neurol. 7:500-6.
12. Sharma S, Sankhyan N, Gulati S, Agarwala A (2013) Use of the modified Atkins diet for treatment of refractory childhood epilepsy: a randomized controlled trial. Epilepsia 54(3):481-6.
13. Lambrechts DA, de Kinderen RJ, Vles JS, et al (2017) A randomized controlled trial of the ketogenic diet in refractory childhood epilepsy. Acta Neurol Scand. 135(2):231-9.
14. Lemmon ME, Terao NN, Ng YT, Reisig W, Rubenstein JE, Kossoff EH (2012) Efficacy of the ketogenic diet in Lennox-Gastaut syndrome: a retrospective review of one institution's experience and summary of the literature. Dev Med Child Neurol. 54(5):464-8.
15. Zhang Y, Wang Y, Zhou Y, Zhang L, Yu L, Zhou S (2016). Therapeutic effects of the ketogenic diet in children with Lennox-Gastaut syndrome. Epilepsy Res. 128:176–80.
16. Sharma S, Jain P, Gulati S, Sankhyan N, Agarwala A (2015) Use of the Modified Atkins Diet in Lennox Gastaut syndrome. J Child Neurol. 30 (5): 576-9.
17. Caraballo RH, Fortini S, Fresler S, et al (2014) Ketogenic diet in patients with Lennox-Gastaut. Seizure 23(9):751-5.
18. Kim HJ, Kim HD, Lee JS, Heo K, Kim DS, Kang HC (2015) Long-term prognosis of patients with Lennox-Gastaut syndrome in recent decades. Epilepsy Res. 110:10-9.
19. Na JH, Kim HD, Lee YM (2020) Effective and safe **diet** therapies for **Lennox**-**Gastaut** syndrome with mitochondrial dysfunction. Ther Adv Neurol Disord. 13:1756286419897813.
20. Kossoff EH, Zupec-Kania BA, Amark PE, et al (2009) Optimal clinical management of children receiving the ketogenic diet: recommendations of the international ketogenic diet study group. Epilepsia 50:304-17.

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@ Young Epilepsy ● St Piers Lane ● Lingfield ● Surrey ● RH7 6PW
☎ 01342 836571