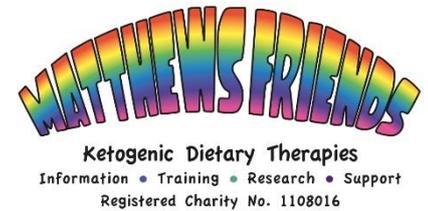


# Ketogenic dietary therapy for Tuberous Sclerosis Complex



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Tuberous sclerosis complex (TSC) is a neurocutaneous genetic multi-systemic disorder associated with age-related development of benign tumours affecting the skin and brain, and other organs including heart, kidneys, lungs and eyes (1,2). Epilepsy is very common in patients with TSC and the majority develop epilepsy in infancy with development of focal seizures and infantile spasms. Most infants with TSC will develop epilepsy during the first year of life, mainly presenting as focal seizures and epileptic spasms although a variety of other seizure types may also be seen (1,2). First line management of TSC seizures is anti-seizure medication (ASM), vigabatrin being particularly effective for spasms (2,3,4) although other seizures may be more pharmacoresistant. Drug refractory epilepsy is common in TSC, uncontrolled seizures are strongly associated with poor cognitive and developmental outcomes. TSC is also often associated with significant adverse neurocognitive and behavioural outcomes and early treatment of epilepsy results in better long term neurological outcomes (5,6), non-pharmacological interventions for refractory seizures should be explored as early as possible; these include surgery, vagal nerve stimulation and ketogenic dietary therapy (KDT) (1,2,3).

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 (7, 8, 9, 10, 11), 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 (12).

There are positive reports of the benefits of KDT on seizure control in TSC. A retrospective review of twelve TSC children reported that eleven had over 50% seizure reduction on CKD and five achieved seizure freedom for at least 5 months (13). Another group of twelve KDT-treated TSC children has been reviewed (CKD or MAD): ten had over 50% seizure reduction after 3 months with improvements in cognition and behaviour in seven (14) Case reports are published of two young boys with TSC and refractory partial seizures who experienced seizure freedom after 2 months on KDT with a third boy having significant reduction in drop attacks (15), and one adult with TSC who has successfully remained on dietary treatment for over 20 years (16).

A longer-term prospective and retrospective observational study of 31 diet-treated TSC patients (28 CKD and 3 MAD) reported 21 (68%) had over 50% seizure reduction and 13 (42%) were seizure-free after 3 months; dropping to 10 (32%) with over 50% seizure reduction and six (19%) seizure free after 24 months on diet (17). A retrospective multi-centre study looked at seizure reduction and cognitive improvement in 53 children with TSC on KDT (50 CKD and 3 MAD): after 3 months, 24 of the 46 who were still on diet therapy had over 50% seizure reduction, including 12 who were seizure free. After 12 months, 16 remained on a diet, of whom 13 had over 50% seizure reduction and three were seizure free. Additionally, of the 51 children with psychomotor retardation, 36 (71%) had improved cognition and behaviour on diet (18).

The LGIT diet has also been successful in seizure management: a retrospective review of 15 TSC patients aged 1 to 20 years reported almost half to have over 50% seizure reduction after 6 months (19). The mechanism by which the diet may bring benefit is unclear; in a series of five KDT-treated TSC patients there was no evidence of dietary induced regression in tumour size or growth (20). There is evidence from the animal studies that KDT may have m-TOR inhibitor effect and may be one of the mechanisms potentially.

International consensus recommendations suggest that KDT should be strongly considered early in the course of epilepsy management in children with certain specific conditions, including TSC (21). This is also supported by UK guidelines on management of epilepsy which recommend KDT should be considered under the guidance of a tertiary epilepsy specialist in certain childhood-onset epilepsy syndromes ([nice.org.uk:ng217](http://nice.org.uk/ng217)). We therefore propose that children with TSC who have failed appropriate ASM therapy are funded for an initial assessment of suitability for KDT. Children who start a diet will require a minimum of 3 months on treatment to allow adequate assessment of benefit and appropriate fine-tuning of the prescription to individual needs. If seizure control is improved, it is likely that ASMs would be reduced or discontinued after that time. In view of the risk of seizure recurrence in children with TSC who become seizure-free on KDT, it has been suggested that a diet may need to be continued for longer than the recommended two years in this group (22).

#### References:

1. Islam MP (2021). Tuberous Sclerosis Complex. *Semin Pediatr Neurol.* 37:100875.
2. Specchio N, Nabbout R, Aronica E, et al (2023). Updated clinical recommendations for the management of tuberous sclerosis complex associated epilepsy. *Eur J Paediatr Neurol.* 47:25-34.
3. Northrup H, Aronow ME, Bebin EM, et al (2021) Updated International Tuberous Sclerosis Complex Diagnostic Criteria and Surveillance and Management Recommendations. *Pediatr Neurol.* 123:50-66.
4. van der Poest Clement EA, Sahin M, Peters JM (2018). Vigabatrin for Epileptic Spasms and Tonic Seizures in Tuberous Sclerosis Complex. *J Child Neurol.* 33(8):519-24.
5. Capal JK, Bernardino-Cuesta B, Horn PS, et al. (2017) Influence of seizures on early development in tuberous sclerosis complex. *Epilepsy Behav.* 70:245-52
6. Bombardieri R, Pinci M, Moavero R, Cerminara C, Curatolo P (2010) Early control of seizures improves long-term outcome in children with tuberous sclerosis complex. *Eur J Paediatric Neurol.* 14:146-9
7. 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.
8. 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.
9. 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.
10. Lakshminarayanan K, Agarawal A, Panda PK, et al (2021) Efficacy of low glycemic index diet therapy (LGIT) in children aged 2-8 years with drug-resistant epilepsy: A randomized controlled trial. *Epilepsy Res.* 171:106574.
11. Manral M, Dwivedi R, Gulati S, et al (2023) Safety, Efficacy, and Tolerability of Modified Atkins Diet in Persons With Drug-Resistant Epilepsy: A Randomized Controlled Trial. *Neurology* 100(13):e1376-e1385.
12. Martin-McGill KJ, Bresnahan R, Levy RG, Cooper PN. (2020) Ketogenic diets for drug-resistant epilepsy. *Cochrane Database Syst Rev.* 6(6):CD001903.
13. Kossoff EH, Thiele EA, Pfeifer HH, et al (2005) Tuberous sclerosis complex and the ketogenic diet. *Epilepsia.* 46 (10):1684-6.
14. Park S, Lee EJ, Eom S, Kang HC, Lee JS, Kim HD (2017) Ketogenic Diet for the Management of Epilepsy Associated with Tuberous Sclerosis Complex in Children. *J Epilepsy Res.* 7(1):45-9.
15. Coppola G, Klepper J, Ammendola E, et al (2006) The effects of the ketogenic diet in refractory partial seizures with reference to tuberous sclerosis. *Eur J Paediatr Neurol.* 10(3):148-51.
16. Kossoff EH, Turner Z, Bergey GK (2007) Home-guided use of the ketogenic diet in a patient for more than 20 years. *Pediatr Neurol.* 36(6):424-5.
17. Youn SE, Park S, Kim SH, Lee JS, Kim HD, Kang HC (2020). Long-term outcomes of ketogenic diet in patients with tuberous sclerosis complex-derived epilepsy. *Epilepsy Res.* 164:106348.
18. Fang Y, Li D, Wang M et al (2022) Ketogenic diet therapy for drug-resistant epilepsy and cognitive impairment in children with tuberous sclerosis complex. *Front. Neurol.*, 13:863826.
19. Larson AM, Pfeifer HH, Thiele EA (2012) Low glycemic index treatment for epilepsy in tuberous sclerosis complex. *Epilepsy Res.* 99(1-2):180-2.
20. Chu-Shore CJ, Thiele EA (2010) Tumor growth in patients with tuberous sclerosis complex on the ketogenic diet. *Brain Dev.* 32(4):318-22.
21. Kossoff EH, Zupec-Kania BA, Auvin S, et al (2018) Optimal clinical management of children receiving dietary therapies for epilepsy: Updated recommendations of the International Ketogenic Diet Study Group. *Epilepsia Open.* 3(2):175-92.
22. Martinez CC, Pyzik PL, Kossoff EH (2007) Discontinuing the ketogenic diet in seizure-free children: recurrence and risk factors. *Epilepsia.* 48(1):187-90.