

# **Ketogenic dietary therapy for Tuberous Sclerosis complex**

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Tuberous sclerosis complex (TSC) is a genetic neurocognitive disorder caused by inactivation of the tumour suppressor genes hamartin (TSC1) or tuberin (TSC2) (1). It is characterized by development of non-malignant tumours and affects many organs in the body including the central nervous system. Up to 90% of TSC patients will develop epilepsy, usually from early childhood with about 50% of TSC seizures presenting as infantile spasms (2,3). First line management of TSC seizures is anti-epileptic drugs (AEDs); vigabatrin being particularly effective for infantile spasms (1,2,3). Other seizure types may be pharmacoresistant and failure of a first medication will significantly reduce likelihood of subsequent seizure freedom (4).

The developmental delay, behavioural, cognitive and neuropsychiatric problems commonly seen in TSC may be associated with poorly-controlled seizure activity (3) and will have considerable cost implications for health services. A child will need regular clinical review, ongoing medications (both routine and emergency) and input of other therapies. There may be frequent hospital admissions and full educational assessment and support is usually required. Non-pharmacological therapy options for the TSC child with refractory seizures should be explored as early as possible; these include surgery, vagal nerve stimulation and the ketogenic diet (KD) (1).

The KD is a high fat, restricted carbohydrate regime that has been used to treat epilepsy since the 1920s, newer and more liberal variants include the Modified Atkins Diet and Low Glycaemic Index Treatment (LGIT). Efficacy of these diets has been demonstrated in many prospective studies and randomised trials (5,6,7) and has also been reported in TSC. A retrospective review of twelve TSC children reported that eleven had over 50% seizure reduction on KD and five achieved seizure freedom for at least 5 months (8). Another group of twelve KD-treated TSC children have been reviewed: ten had over 50% seizure reduction after 3 months with improvements in cognition and behaviour in seven (9). Case reports are published of two young boys with TSC and refractory partial seizures who experienced seizure freedom after 2 months on KD with a third boy having significant reduction in drop attacks (10), and one adult with TSC who has successfully remained on dietary treatment for over 20 years (11). The LGIT 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 (12). The mechanism by which the diet may bring benefit is unclear; in a series of five KD-treated TSC patients there was no evidence of dietary induced regression in tumour size or growth (13).

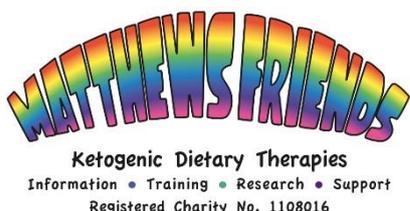
International consensus recommendations suggest that KD should be strongly considered in a child with epilepsy who has failed two or three AEDs, and may be particularly beneficial in certain epilepsy syndromes, including TSC (14). The UK NICE guidelines on management of the epilepsies in adults and children 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 KD (CG137, nice.org.uk, updated 2012).

In view of these recommendations, we propose that children with TSC who have failed appropriate AED therapy are funded for an initial assessment of suitability for ketogenic therapy. Children who start a diet will require a minimum of three 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 AEDs 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 KD, it has been suggested that a diet may need to be continued for longer than the recommended two years in this group (15).

## References:

1. Curatolo P, Jóźwiak S, Nabbout R; TSC Consensus Meeting for SEGA and Epilepsy Management (2012) Management of epilepsy associated with tuberous sclerosis complex (TSC): clinical recommendations. *Eur J Paediatr Neurol.* 16(6):582-6.
2. Overwater IE, Bindels-de Heus K, Rietman AB, et al (2015) Epilepsy in children with tuberous sclerosis complex: Chance of remission and response to antiepileptic drugs. *Epilepsia.* 56(8):1239-45.
3. Wang S, Fallah A (2014) Optimal management of seizures associated with tuberous sclerosis complex: current and emerging options. *Neuropsychiatr Dis Treat.* 10:2021-30.
4. Kwan P, Brodie MJ (2000) Early identification of refractory epilepsy. *N Engl J Med.* 342 (5):314-9.
5. 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.
6. 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.
7. 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.
8. Kossoff EH, Thiele EA, Pfeifer HH, et al (2005) Tuberous sclerosis complex and the ketogenic diet. *Epilepsia.* 46 (10):1684-6.
9. 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.
10. 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.
11. 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.
12. Larson AM, Pfeifer HH, Thiele EA (2012) Low glycemic index treatment for epilepsy in tuberous sclerosis complex. *Epilepsy Res.* 99(1-2):180-2.
13. Chu-Shore CJ, Thiele EA (2010) Tumor growth in patients with tuberous sclerosis complex on the ketogenic diet. *Brain Dev.* 32(4):318-22.
14. 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.
15. Martinez CC, Pyzik PL, Kossoff EH (2007) Discontinuing the ketogenic diet in seizure-free children: recurrence and risk factors. *Epilepsia.* 48(1):187-90.



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