

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 medication; 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 ketogenic therapy (1).

The ketogenic diet is a high fat, restricted carbohydrate regime that has been used as a treatment for epilepsy since the 1920s; efficacy is demonstrated in prospective studies and a randomised controlled trial (5). It has been used successfully to treat seizures in TSC: of twelve ketogenic diet treated TSC children reviewed retrospectively, eleven had over 50% seizure reduction and five achieved seizure freedom for at least 5 months (6). Case reports are published of two young boys with TSC and refractory partial seizures who experienced seizure freedom after 2 months on the ketogenic diet with a third boy having significant reduction in drop attacks (7), and one adult with TSC who has successfully remained on dietary treatment for over 20 years (8). A more liberalized approach to ketogenic therapy, the low glycaemic index treatment, has also been successful in seizure management: a retrospective chart review of 15 TSC patients aged 1 to 20 years reported almost half to have over 50% seizure reduction after 6 months (9). The mechanism by which the diet may bring benefit is unclear; in a series of five ketogenic diet-treated TSC patients there was no evidence of dietary induced regression in tumour size or growth (10)

International consensus recommendations suggest that ketogenic therapy 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 (11). 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 the use of a ketogenic diet (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 during ketogenic therapy, it has been suggested that a diet may need to be continued for longer than the recommended two years in this group (12).

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