

Ketogenic dietary therapy for Dravet syndrome

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Dravet syndrome (severe myoclonic epilepsy of infancy) was first described in 1978 (1). It is associated with a known genetic defect and is characterised by onset of prolonged seizures in the first year of life, often triggered by fever, then development of different seizure types over time with progressive neurological deficits (2). Anti-epileptic drugs (AEDs) are typically used as first line treatment but seizures are particularly resistant to medication with high likelihood of recurrent status epilepticus and need for further treatments; options include other AEDs or the ketogenic diet (KD) (3, 4). As failure of a first AED will significantly reduce likelihood of subsequent seizure freedom (5), there is growing support for dietary therapy. Dravet syndrome co-morbidities include intellectual disability and behavioural problems (3) and the NHS and social cost implications for supporting medical and educational needs can be considerable.

The KD is a high fat, restricted carbohydrate regime that has been used to treat epilepsy since the 1920s, newer and more liberal ketogenic therapies 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 (6,7,8). There are a number of positive reports of the specific benefit of KD in Dravet syndrome. In a retrospective study of 20 children from Argentina, 13 had over 50% reduction in seizure frequency and remained on the KD after one year (9). The same investigators re-evaluated 24 children, of whom 16 remained on the diet for a minimum of two years, all with greater than 50% seizure reduction including 2 who were seizure free (10). Another retrospective review from USA also reported that 13 of 20 Dravet syndrome children experienced over 50% seizure reduction on KD (11). An analysis of 32 Austrian children reported over 50% seizure reduction in 70% after 3 months and 60% after 12 months of KD treatment; these results were not significantly inferior to those in patients on the recommended Dravet first line AED combination so the authors concluded that the diet should be considered as an early treatment for this syndrome (12). Similar positive results were seen in two prospective trials of the KD in drug-resistant Dravet syndrome: 10 of 15 French children achieved over 75% seizure reduction after one month on KD (13); and 17 of 20 Chinese children achieved over 50% seizure reduction after 3 months on KD including 6 who were seizure-free, increasing to 10 after 6 months (14). Both studies reported additional positive benefits of the diet on behaviour disturbances (13) and questionnaire-assessed cognition (14), supporting similar findings in earlier study results (11). However the KD benefit on neuropsychological development is less conclusive and needs further study. A small retrospective study of Chinese Dravet Syndrome children reported that although developmental age subscores of 12 children increased after commencing KD, there was no significant difference between KD and non-diet groups in developmental quotient at the same age (15). The possibility of using the LGIT as an alternative dietary protocol was explored in 36 children and adolescents from South Korea with drug-resistant epilepsy; two became seizure free after 3 months on LGIT, both of whom had Dravet Syndrome (16)

International consensus recommendations suggest that KD should be strongly considered in a child with epilepsy who has failed two or three AEDs and could be offered earlier in particular syndromes such as Dravet syndrome (17,18). Updated 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 KD (CG137, nice.org.uk).

In view of these results and recommendations, we propose that children with Dravet syndrome 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 dietary prescription to a child's individual needs. If seizure control is improved, it is likely that AEDs would be reduced or discontinued after that time. The KD is usually continued for least two years if successful.

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