Ketogenic dietary therapy for Dravet syndrome

Written by:

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

Dravet syndrome (DS), also known as 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 therapy, 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, 5). As failure of a first AED will significantly reduce likelihood of subsequent seizure freedom (6), there is growing support for dietary therapy. DS 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), with many prospective studies and randomised trials showing efficacy of all diets (7, 8, 9). There are many positive reports of the specific benefit of KD in DS, including smaller retrospective studies from Argentina and USA (10, 11, 12) and a larger review from China which found KD to be effective in over half of the 60 DS children at 12, 24 and 48 weeks of diet therapy (13). An analysis of 32 Austrian children reported over 50% seizure reduction in 70% after 3 months and 60% after 12 months on KD; these results were not significantly inferior to those in patients on the recommended DS first line AED combination so the authors concluded that the diet should be considered as an early treatment for this syndrome (14). Similar positive results were seen in two prospective trials of the KD in drug-resistant DS: 10 of 15 French children achieved over 75% seizure reduction after one month on KD (15); 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 (16). 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 DS (17). A recent meta-analysis on efficacy of KD in DS included seven studies involving 167 patients and found 63%, 60% and 47% of responder patients achieved over 50% seizure reduction after 3, 6 and 12 months respectively, concluding KD to be a safe treatment option for DS with mostly acceptable adverse effects, although further larger studies were recommended (18).

Additional positive benefits of KD on behaviour disturbances and questionnaire-assessed cognition in DS children have been reported (12, 13, 15, 16) but the benefit on neuropsychological development is less conclusive and needs further study. A small retrospective Chinese study 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 (19).
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 DS (20, 21). 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 DS children 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 at least two years if successful.

References: