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Ketogenic Dietary Therapies

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Ketogenic dietary therapy for Dravet syndrome

Dravet syndrome, also known as severe myoclonic epilepsy of infancy, was first described in 1978 and is associated with a known genetic defect (1). It is characterised by normal development prior to seizure onset occurring during the first year of life, with development of different seizure types and progressive neurological deficits. Anti-epileptic drug (AED) treatment is typically used as first line treatment for Dravet syndrome but seizures are particularly resistant to medication with high likelihood of recurrent status epilepticus and co-morbidities including intellectual disability and behavioural problems (2). In view of this prognosis and the impact of on-going intractable seizure activity on long-term cognitive and behavioural function, Dravet syndrome will have considerable cost implications for NHS services with need for regular visits to hospital and medications; full educational assessment and support is also usually required. Children with Dravet's syndrome will frequently require addition of second line treatments for seizures; options include further AEDs or the ketogenic diet (2). As failure of a first medication will significantly reduce likelihood of subsequent seizure freedom (3), there is growing support for use of dietary therapy.

The ketogenic diet is a high fat, restricted carbohydrate regime that has been used as a treatment for epilepsy since the 1920s; efficacy has been demonstrated in many prospective studies and a randomised controlled trial (4). There have been a number of positive reports of its benefits in Dravet syndrome. In a retrospective study of 20 children, 13 remained on the ketogenic diet after one year (65%), all 13 had over 50% reduction in seizure frequency (5). The same investigators re-evaluated 24 children with Dravet

syndrome of whom 16 remained on the diet for a minimum of two years (66%), all 16 had greater than 50% seizure reduction including 2 who were seizure free (6). Another retrospective review found similar efficacy results (13 of 20 children experienced over 50% seizure reduction on the ketogenic diet, 6 over 90% reduction) with additional benefits on alertness, cognition and behaviour (7). A prospective trial of 15 Dravet syndrome children with uncontrolled seizures despite many AEDs reported that 10 (66%) achieved over 75% seizure reduction after one month on the ketogenic diet with additional positive impact on behaviour disturbances (8). An analysis of 32 children with Dravet syndrome reported over 50% seizure reduction in 70% after 3 months and 60% after 12 months of ketogenic diet treatment (9); these results were not significantly inferior to those in patients on the recommended Dravet first line AED combination so the authors recommended the diet should be considered as an early treatment for this syndrome (9).

International consensus recommendations suggest that the ketogenic diet 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 (10,11). Recently updated 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).

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 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 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 ketogenic diet is usually continued for least two years if successful.

1. Dravet C (2011) Dravet syndrome history. Dev Med Child Neurol. 53(2):1-6.

2. Wirrell EC (2016) Treatment of Dravet Syndrome. Can J Neurol Sci. 43(3):S13-8.

3. Kwan P, Brodie MJ (2000) Early identification of refractory epilepsy. N Engl J Med. 342(5):314-9.

4. 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.

5. Caraballo RH, Cerosimo RO, Sakr D, et al (2005) Ketogenic diet in patients with Dravet syndrome. Epilepsia 46(9):1539–44.

6. Caraballo RH (2011) Nonpharmacologic treatments of Dravet syndrome: focus on the ketogenic diet. Epilepsia 52(2):79-82.

7. Laux L, Blackford R (2013) The ketogenic diet in Dravet syndrome. J Child Neurol. 28(8):1041-4.

8. Nabbout R, Copioli C, Chipaux M, et al (2011) Ketogenic diet also benefits Dravet syndrome patients receiving stiripentol: a prospective pilot study. Epilepsia 52(7):e54-7.

9. Dressler A, Trimmel-Schwahofer P, Reithofer E, et al (2015) Efficacy and tolerability of the ketogenic diet in Dravet syndrome: comparison with various standard antiepileptic drug regimen. Epilepsy Res. 109:81-9.

10. 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.

11. Veggiotti P, Burlina A, Coppola G, et al (2011) The ketogenic diet for Dravet syndrome and other epileptic encephalopathies: An Italian consensus. Epilepsia 52(2): 83-9.