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Ketogenic Dietary Therapies

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Ketogenic dietary therapy for Infantile Spasms

Infantile spasms, also known as West syndrome, was first reported in 1841 and affects approximately 1 in 2000 infants (1). It typically presents within the first year of life as spasm-type seizures and an EEG abnormality known as hypsarrhythmia; neuro-developmental delay is frequently seen from a young age. In approximately two thirds of affected infants, the syndrome will be associated with a detectable underlying neurological abnormality (2) and many cases of infantile spasms will progress into another epilepsy syndrome.

First-line treatment options for infantile spasms are adrenocorticotropin hormone (ACTH), oral prednisolone or vigabatrin; the latter being particularly effective at treating spasms associated with tuberous sclerosis (1, 2). These treatments will successfully control seizures in many cases but have significant side effects that limit their duration of use. Alternative anti-epileptic drugs (AEDs) are often used if first-line treatments are unsuccessful, however with more limited success. Continued intractable seizure activity in an infant will impact on long-term cognitive and behavioural outcomes, with considerable cost implications for health services due to need for regular clinical review, hospital treatment, medications and support of other therapies. All other treatment options for this syndrome should therefore be explored as early as possible.

The ketogenic diet is a high fat, restricted carbohydrate regime that has been used since the 1920s; efficacy in epilepsy has been demonstrated in many studies including a randomised controlled trial (3). Retrospective studies have shown this diet to be an effective and well-tolerated treatment for infantile spasms (4, 5, 6, 7, 8), with one study reporting significant spasm improvements and less side effects when the diet was used as an alternative first-line therapy to ACTH (9). Three prospective studies have also been published which demonstrate efficacy of the ketogenic diet in infantile spasms unresponsive to first line treatments. In a study of 104 infants, 67 (64%) had over 50% improvement in spasms after 6 months on a ketogenic diet, 29 of whom became seizure free (10). Another study reported 13 (76%) of 17 infants had over 50% seizure reduction after one month on the ketogenic diet, of whom 6 became seizure free, this increased to

11 seizure free after 3 months (11). Similar results were found in a further group of 20 infants of whom 70% had over 50% seizure reduction after 3 months on the diet (12).

The most common reported side effects of the diet in these studies were gastro-intestinal disturbances especially constipation and reflux, altered lipid levels, renal stones and acidosis; most complications were transient and could be controlled with diet adjustment and monitoring. Short-term trials of the ketogenic diet are unlikely to have any adverse effect on linear growth (13), however this may be more of a problem with longer-term use.

International consensus recommendations suggest that ketogenic dietary 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 such as infantile spasms (14). Recently updated NICE guidelines on management of the epilepsies also recommend children 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).

Early use of the ketogenic diet in infants is recommended: a review of outcomes in 115 children with a range of epilepsy syndromes, over half with infantile spasms, found significantly more infants under 18 months of age achieved seizure freedom when compared to those over 18 months, this difference was even greater when infants under 9 months of age were examined separately (8).

We therefore propose that infants diagnosed with infantile spasms who have failed appropriate first-line therapy are funded for an initial assessment of suitability for ketogenic dietary therapy. Those 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 an infant's individual needs. Although it is often suggested that children with epilepsy who are benefiting from ketogenic dietary therapy continue this for at least two years, duration of treatment could be shorter in patients with infantile spasms who become seizure-free; one study reported no adverse effect on seizure outcomes and less risk of growth disturbances when treatment was tapered down after 8 months (15).

1. Kossoff EH (2010) Infantile spasms. Neurologist 16(2):69-75.
2. Hancock EC, Osborne JP, Edwards SW (2008) Treatment of infantile spasms. Cochrane Database Syst Rev. CD001770.
3. 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.
4. Kossoff EH, Pyzik PL, McGrogan JR, et al (2002) Efficacy of the ketogenic diet for infantile spasms. Pediatrics 109(5):780-3.

5. Rubenstein JE, Kossoff EH, Pyzik PL, et al (2005) Experience in the use of the ketogenic diet as early therapy. J Child Neurol. 20(1):31-4.

6. Eun SH, Kang HC, Kim DW, Kim HD (2006). Ketogenic diet for treatment of infantile spasms. Brain Dev. 28(9):566-71.

7. Caraballo R, Vaccarezza M, Cersósimo R, et al (2011) Long-term follow-up of the ketogenic diet for refractory epilepsy: multicenter Argentinean experience in 216 pediatric patients. Seizure 20(8):640-5.

8. Dressler A, Trimmel-Schwahofer P, Reithofer E, et al (2015) The ketogenic diet in infants--Advantages of early use. Epilepsy Res. 116:53-8.

9. Kossoff EH, Hedderick EF, Turner Z, Freeman JM (2008) A case-control evaluation of the ketogenic diet versus ACTH for new-onset infantile spasms. Epilepsia 49(9):1504-9.

10. Hong AM, Turner Z, Hamdy RF, Kossoff EH (2010) Infantile spasms treated with the ketogenic diet: prospective single-center experience in 104 consecutive infants. Epilepsia 51(8):1403-7.

11. Pires ME, Ilea A, Bourel E, et al (2013) Ketogenic diet for infantile spasms refractory to first-line treatments: an open prospective study. Epilepsy Res. 105(1-2):189-94.

12. Kayyali HR, Gustafson M, Myers T, et al (2014) Ketogenic diet efficacy in the treatment of intractable epileptic spasms. Pediatr Neurol. 50(3):224-7.

13. Numis AL, Yellen MB, Chu-Shore CJ, et al (2011) The relationship of ketosis and growth to the efficacy of the ketogenic diet in infantile spasms. Epilepsy Res. 96(1-2):172-5

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. Kang HC, Lee YJ, Lee JS, et al (2011) Comparison of short- versus long-term ketogenic diet for intractable infantile spasms. Epilepsia 52(4):781-7.