Ketogenic dietary therapy for Infantile Spasms

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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 (KD) is a high fat, restricted carbohydrate regime that has been used since the 1920s; KD efficacy in epilepsy has been demonstrated in many studies including randomised controlled trials in children (3,4) with a trial in infants currently in progress (5). Retrospective studies have shown this diet to be an effective and well-tolerated treatment for infantile spasms (6, 7, 8, 9), with one study reporting significant spasm improvements and less side effects when KD was used as an alternative first-line therapy to ACTH (10). Prospective studies also demonstrate KD efficacy in infantile spasms unresponsive to first line treatments. In a study of 104 infants, 64% had over 50% improvement in spasms after 6 months on KD, 29 of whom became seizure free (11). Another study reported 13 of 17 infants had over 50% seizure reduction after one month on KD, of whom 6 became seizure free, increasing to 11 after 3 months (12). 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 (13). However, one study of 22 children has questioned whether complete seizure response to KD can be achieved in highly refractive spasms (14).

A trial comparing efficacy and tolerability of KD with standard high-dose ACTH treatment for infantile spasms followed 101 infants (32 in a randomised trial and 69 in a parallel cohort) including those with and without prior vigabatrin treatment. Results showed similar electroclinical remission in ACTH and KD groups after 28 days but better tolerance in the KD group. The authors concluded that without prior vigabatrin treatment, ACTH should be first choice to achieve short-term seizure remission, however with prior vigabatrin, the KD was as effective as ACTH

with lower long-term relapse rate (15). A systematic review of KD efficacy in infantile spasms included 13 observational studies with results supporting benefit of the diet: out of a total 341 patients, a median of 65% experienced over 50% spasm reduction and 35% were spasm-free, although this fell to 10% with longer follow up data (16).

International consensus recommendations suggest that the KD 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 (17). Updated UK 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 KD (CG137, nice.org.uk). Practical guidelines and recommendations for specific KD use in infants have also been published (18).

Early KD use 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 (9). The KD can be initiated in infants maintained on breast milk (19) and, with careful screening, used safely in a neonatal intensive care setting (20). The most common reported side effects of the diet are gastro-intestinal disturbances especially constipation and reflux, altered lipid levels, renal stones and acidosis; most complications are transient and controlled with diet adjustment and monitoring (18). Short-term KD trials are unlikely to have any adverse effect on linear growth (21), however this may be more of a problem with longer-term use.

We therefore propose that infants with infantile spasms who have failed appropriate first-line treatment options are funded for an initial assessment of suitability for the KD. Evaluation after two or three months on diet is suggested to allow adequate assessment of benefit and appropriate fine-tuning of the dietary prescription to individual needs; earlier assessment after one month may be needed in infants on KD as first, second or third line treatment in view of the risks of uncontrolled seizures (18). Although it is often suggested that children with epilepsy who are benefiting from KD 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 diet treatment was tapered down after 8 months (22).

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