Ketogenic dietary therapy for Epilepsy with Myoclonic Atonic seizures (Doose syndrome)

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Doose syndrome, also known as epilepsy with myoclonic-atonic seizures (previously myoclonic astatic epilepsy), is a rare epileptic encephalopathy that was first described in 1970 (1). Onset is in early childhood typically following a febrile seizure and evolving to multiple seizure types such as myoclonic, GTCS, atonic (causing drops/astatic seizures), episodes of non-convulsive status epilepticus, with development of multiple generalised seizure types including periods of status epilepticus; cognitive prognosis is variable (2). Although anti-seizure medication (ASM) is the usual first-line treatment, in about two thirds' seizures are well controlled with overall good prognosis while in the remainder seizures remain refractory to medications and have significant cognitive consequences. Cognitive prognosis is variable even in those responding to medications. Doose syndrome is frequently refractory to medication, up to 5% cases may have underlying GLUT1 deficiency and ketogenic dietary therapy (KDT) is increasingly being recognised as one of its most efficacious treatments (2, 3, 4).

KDT is a high fat, restricted carbohydrate regime that has been used to treat epilepsy since the 1920s and includes the stricter Classical ketogenic diet (CKD) and Medium Chain Triglyceride (MCT) diet, and less restrictive Modified Atkins diet (MAD) and Low Glycaemic Index Treatment. Randomised trials have reported efficacy of all types of KDT (5, 6, 7, 8, 9), which has a 'relative risk' of 3.16 of achieving seizure freedom, and 5.80 of over 50% seizure reduction, compared to the usual care of children with medication-resistant epilepsy (10).

There are many reports of the beneficial effects of KDT for children with Doose syndrome. A study from Argentina reported on 11 children on CKD: all of the six who followed this for 18 months had over 50% seizure reduction including two who became seizure free and discontinued ASMs (11). A long-term follow-up study by the same investigators included 38 Children with Doose syndrome, of whom 11 (29%) became seizure free on CKD (12). A French multi-centre study retrospectively reviewed 50 children with Doose syndrome (47 on CKD and 3 on MAD), reporting 54% to be seizure free after 6 months or longer on KDT with 86% experiencing over 70% seizure reduction after 2 months. Early diet treatment significantly resulted in seizure remission and was correlated with a better cognitive outcome (13). A review of 30 Doose syndrome children on MAD who were observed for a mean of 19 months reported 25 (83%) of 30 patients had a seizure reduction of 50% or more with 14 (47%) seizure-free, concluding MAD could be used as a KDT option to the more restrictive CKD (14). Another review of nine Doose syndrome children on KDT reported that seven became seizure free within several weeks of starting a diet and were able to discontinue all ASMs: four were on MAD, two on CKD, and one started on MAD but needed to transition to CKD to achieve full seizure freedom (15). An earlier review of 27 children with epilepsy on KDT, of whom nine had Doose syndrome, also found that some patients saw additional seizure benefits by switching from MAD to the stricter CKD (16).

Other studies have examined outcomes in patients following different treatments for Doose syndrome including diet and medications, although KDT was generally only used after failure of many ASMs. A review of 81 children from Japan included 26 who were treated with KDT (CKD or MCT diet) of whom 15 (58%) became seizure free (17), and a review of 23 children from USA included 10 on KDT of whom three became seizure free (18). A large retrospective review from three major USA centres identified 166 children with Doose syndrome of whom KDT (CKD or MAD) was used as a second or third treatment option in 19% and ultimately used in 57%. Of those who were on diet, 79% had greater than 50% seizure reduction, significantly greater than response to the first three ASMs, with 57% achieving seizure freedom (2). In all three studies, the authors concluded KDT to be the most effective treatment in controlling seizures.

Most studies indicate that the drops which are most troublesome causing injuries and myoclonic seizures respond well to KDT. International consensus recommendations suggest that KDT should be used early in the course of epilepsy management in children with certain specific conditions, including Doose syndrome (19). UK guidelines on management of epilepsy also suggest KDT should be considered under the guidance of a tertiary epilepsy specialist in certain childhood-onset epilepsy syndromes including Doose syndrome (nice.org.uk:ng217). We therefore propose that Doose syndrome children who have failed appropriate ASM therapy are funded for an initial assessment of KDT suitability, with diet ideally followed for a minimum of 3 months 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 ASMs would be reduced or discontinued after that time. KDT is usually continued for least two years if successful.

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