Ketogenic dietary therapy for Doose syndrome

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Doose syndrome, also known as myoclonic astatic epilepsy (MAE) or epilepsy with myoclonic-atonic seizures, is a rare type of generalised epilepsy that was first described in 1970 (1). Onset is usually before the age of five years and multiple different seizure types develop including periods of non-convulsive status epilepticus in some children (2) Appropriate anti-epileptic drug (AED) therapy is usually used as an initial treatment for MAE, however failure of a first medication to control seizures will significantly reduce the likelihood of subsequent seizure freedom (3). International consensus recommendations suggest that the ketogenic diet (KD) should be strongly considered in a child with epilepsy which has failed to respond to two or three AEDs (4). 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 KD (CG137, nice.org.uk).

The KD is a high fat, restricted carbohydrate regime that has been used as a treatment for epilepsy since the 1920s; efficacy of this type of dietary therapy has been demonstrated in many prospective studies and randomised trials (5, 6, 7). The diet has been shown to be particularly beneficial in MAE where seizures are often resistant to AEDs. One study from Argentina reported on 11 children with this syndrome: of six who remained on the KD after 18 months, all had over 50% seizure reduction including two who became seizure free and discontinued AEDs (8). A long-term follow-up study by the same investigators included 38 children with MAE of whom 11 (29%) were seizure free on KD (9). A French multi-centre study retrospectively reviewed 50 children with severe MAE, reporting 54% to be seizure free after 6 months or longer on KD 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 (10).

An alternative more liberal type of KD is the modified Atkins diet (MAD). A review of 30 children with MAE who were observed for a mean of 19 months on MAD 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 an option to the more restrictive KD (11). Another review of nine children with MAE on dietary therapy reported that seven became seizure free within several weeks of starting a diet and were able to discontinue all AEDs: four were on MAD, two on traditional KD, and one started on MAD but needed to transition to KD to achieve full seizure freedom (12). An earlier review of 27 children with epilepsy, of whom nine had a MAE diagnosis, also found that some patients saw additional seizure benefits by switching from MAD to the stricter KD (13).

Other studies have examined outcomes following different treatments for MAE including diet and medications, although KD was generally only used after failure of many AEDs. A review of 81 children from Japan included 26 who were treated with KD of whom 15 (58%) became seizure free (14), and a review of 23 children from USA included 10 who received KD of whom three became seizure free (15). A recent large retrospective review from three major USA centres identified 166 children with MAE of whom diet therapy was used as a second or third treatment option in 19% and ultimately used in 57%. Of those who received diet therapy, 79%, had greater than 50%

seizure reduction, significantly greater than response to the first three AEDs, with 57% achieving seizure freedom (16). In all three studies, the authors concluded diet therapy to be the most effective treatment in controlling seizures.

It is clear that KD is increasingly being recognised as one of the most efficacious treatments for MAE (17, 18). We therefore suggest that children with this syndrome should be given the chance to try diet therapy early in the course of their epilepsy with those who have failed appropriate AEDs funded for an initial assessment of suitability for a KD. Children who start the diet will require a minimum of three months on treatment to allow adequate assessment of benefit and appropriate fine-tuning of the ketogenic 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 least two years if successful.

References:

1. Doose H, Gerken H, Leonhardt R, et al (1970) Centrencephalic myoclonic-astatic petit mal. Clinical and genetic investigation. Neuropadiatrie 2(1):59-78.
2. Bergqvist AG (2012) Myoclonic astatic epilepsy and the use of the ketogenic diet. Epilepsy Res. 100(3):258-60.
3. Kwan P, Brodie MJ (2000) Early identification of refractory epilepsy. N Engl J Med. 342 (5):314-9.
4. 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.
5. 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.
6. Sharma S, Sankhyan N, Gulati S, Agarwala A (2013) Use of the modified Atkins diet for treatment of refractory childhood epilepsy: a randomized controlled trial. Epilepsia 54(3):481-6.
7. Lambrechts DA, de Kinderen RJ, Vles JS, et al (2017) A randomized controlled trial of the ketogenic diet in refractory childhood epilepsy. Acta Neurol Scand. 135(2):231-9.
8. Caraballo RH, Cersósimo RO, Sakr D, et al (2006) Ketogenic diet in patients with myoclonic-astatic epilepsy. Epileptic Disord. 8(2):151-5.
9. 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.
10. Stenger E, Schaeffer M, Cances C, et al (2017) Efficacy of a ketogenic diet in resistant myoclono-astatic epilepsy: A French multicenter retrospective study. Epilepsy Res. 31:64-9.
11. Wiemer-Kruel A, Haberlandt E, Hartmann H, Wohlrab G, Bast T (2017) Modified Atkins diet is an effective treatment for children with Doose syndrome. Epilepsia 58(4):657-62.
12. Simard-Tremblay E, Berry P, Owens A, et al (2015) High-fat diets and seizure control in myoclonic-astatic epilepsy: A single center's experience. Seizure 25:184-6.
13. Kossoff EH, Bosarge JL, Miranda MJ, et al (2010) Will seizure control improve by switching from the modified Atkins diet to the traditional ketogenic diet? Epilepsia 51(12): 2496–9.
14. Oguni H, Tanaka T, Hayashi K, et al (2002) Treatment and long-term prognosis of myoclonic-astatic epilepsy of early childhood. Neuropediatrics 33(3):122-32.
15. Kilaru S, Bergqvist AG (2007) Current treatment of myoclonic astatic epilepsy: clinical experience at the Children's Hospital of Philadelphia. Epilepsia 48(9):1703-7.
16. Nickels K, Kossoff EH, Eschbach K, Joshi C (2021) Epilepsy with myoclonic-atonic seizures (Doose syndrome): Clarification of diagnosis and treatment options through a large retrospective multicenter cohort. Epilepsia 62 (1):120-7.
17. Kelley SA, Kossoff EH (2010) Doose syndrome (myoclonic-astatic epilepsy): 40 years of progress. Dev Med Child Neurol. 52(11):988-93.
18. Mulligan JE, Mandelbaum DE (2011) Myoclonic astatic epilepsy and the role of the ketogenic diet. Med Health R I. 94(5):127-30.

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