



## Ghee Whiz! The Growing Evidence for the Benefits of the Modified Atkins Diet

### Use of the Modified Atkins Diet for Treatment of Refractory Childhood Epilepsy: A Randomized Controlled Trial.

Sharma S, Sankhyan N, Gulati S, Agarwala A. *Epilepsia* 2013;54:481–486.

**PURPOSE:** The aim of this study was to evaluate the efficacy of the modified Atkins diet in a randomized controlled trial in children with refractory epilepsy. **METHODS:** Children aged 2–14 years who had daily seizures despite the appropriate use of at least three anticonvulsant drugs were enrolled. Children were randomized to receive either the modified Atkins diet or no dietary intervention for a period of 3 months. The ongoing anticonvulsant medications were continued unchanged in both the groups. Seizure control at 3 months was the primary end point. Analysis was intention to treat. Adverse effects of the diet were assessed by parental reports (ClinicalTrials.gov Identifier: NCT00836836). **KEY FINDINGS:** Among a total of 102 children, 50 were in the diet group and 52 in the control group. Four children discontinued the diet before the study end point, and three children in the control group were lost to follow-up. The mean seizure frequency at 3 months, expressed as a percentage of the baseline, was significantly less in the diet group:  $59 \pm 54$  (95% confidence interval [CI] 44–74.5) versus  $95.5 \pm 48$  (95% CI 82–109),  $p = 0.003$ . The proportion of children with >90% seizure reduction (30% vs. 7.7%,  $p = 0.005$ ) and >50% seizure reduction was significantly higher in the diet group (52% vs. 11.5%,  $p < 0.001$ ). Constipation was the most common adverse effect among children on the diet (23, 46%). **SIGNIFICANCE:** The modified Atkins diet was found to be effective and well tolerated in children with drug-refractory epilepsy.

### Commentary

It has now been a decade since the modified Atkins diet (MAD), a less restrictive, outpatient-initiated version of the ketogenic diet (KD), was first published in the medical literature (1). Although still inducing ketosis, the MAD does not restrict protein, calories, or fluids—solely measuring daily carbohydrates and encouraging high fat intake. In the ten years since its introduction, there have been 27 articles published, reporting 355 children and adults. Results to date suggest similar efficacy but fewer side effects in comparison to the KD.

The scientific evidence behind the MAD is strong; however, until this article, there had not been any randomized and controlled trials to support its use. This is similar to the situation prior to 2008 for the classic KD, following which two studies, one blinded, were published (2, 3). The most widely publicized—a randomized and controlled study by Neal and colleagues from United Kingdom—tested the ketogenic diet (both the classic and the medium-chain triglyceride versions) versus 3 months of continued status quo anticonvulsants in children ages 2–16 years with refractory epilepsy (2). The randomization occurred following a 4-week baseline period for all children. As of the writing of this review, according to

Google Scholar, this publication has been cited 205 times in the literature in just 5 years, demonstrating its impact.

Perhaps seeking to replicate the fame and impact of this landmark study, Dr. Sharma and her colleagues from India utilized an essentially identical study design to evaluate the MAD in children ages 2–14 years with intractable epilepsy. There were some differences compared to the Neal study, primarily in regard to patient demographics: 78% were male, all from a single tertiary center, and a larger percentage (approximately half) had the diagnosis of Lennox-Gastaut syndrome (2). The study was completed successfully with a lower dropout rate than the Neal study; in fact, with a remarkable 8% discontinuation rate with MAD (versus 15% in the Neal KD study arm) (2).

The results certainly suggest both a similarity to the KD based on the Neal outcomes, as well as seizure improvement dramatically better than the control. The likelihood of > 50% seizure reduction at 3 months was 52% with the MAD versus 11.5% in the control group. Similarly, > 90% seizure reduction occurred in 30% versus 7.7%. This is similar, if not slightly better, than the Neal findings with the KD, in which they found 38% versus 6% (for > 50% seizure reduction) and 7% versus 0% (> 90% seizure reduction) (2). These studies can and should not be directly compared, and the high placebo rate in the current study is surprising, yet the results are intriguing. The MAD was very well-tolerated, with adverse effects primarily constipation, weight loss, and vomiting, as would be



expected for the KD. Adolescents were reported as having difficulty with the lack of rice and Indian wheat breads (*chapattis*); no comments were made about their opinions regarding ghee, cream, or oil. There have been prior attempts in India to use less fat and more carbohydrates (e.g., lower ratios) with the classic KD; a cultural taste for carbohydrates clearly exists there (4).

There are certainly some concerns about the ability to extrapolate these findings, primarily due to the single center in India with some cultural issues (including 44% vegetarian) and a high male percentage. Both this study and the Neal study, although randomized and controlled, had neither a placebo provided nor a blinded assessment. A perhaps more real-world control arm might have been the addition of a new anticonvulsant rather than no change to the current anticonvulsant regimen. However, the results are impressive and add further, now controlled, evidence to the benefits of the MAD.

After a decade of use, the MAD is here to stay. What role in the treatment of epilepsy does this modified ketogenic diet have to play? Most clear at this time is the treatment of adolescents and adults not typically offered the classic ketogenic diet due to its inherent restrictiveness and often need for hospitalization at initiation (5). From my personal communications, most adult epilepsy diet centers are primarily using the MAD. Dr. Sharma studied children as young as 2 years; however, we would suggest still using the classic KD in those under 10 years. Countries with large populations and limited dietitian availability, such as India, may be ideally suited for the MAD versus the KD, as stated in the Discussion section of this paper by its authors. The MAD has been used successfully in Honduras without dietitian support and can be maintained in adults solely by email, opening up opportunities for global telemedicine to remote regions with sparse resources (6, 7). Additionally,

the MAD may have a unique role in some idiopathic generalized epilepsies that may not be perceived as severe as other etiologies, including absence epilepsy and juvenile myoclonic epilepsy (8, 9).

by Eric Kossoff, MD

#### References

1. Kossoff EH, Krauss GL, McGrogan JR, Freeman JM. Efficacy of the Atkins Diet as therapy for intractable epilepsy. *Neurology* 2003;61:1789–1791.
2. Neal EG, Chaffe H, Schwartz RH, Lawson MS, Edwards N, Fitzsimmons G, Whitney A, Cross JH. The ketogenic diet for the treatment of childhood epilepsy: A randomised controlled trial. *Lancet Neurol* 2008;7:500–506.
3. Freeman JM, Vining EPG, Kossoff EH, Pyzik PL, Ye X, Goodman SN. A blinded, crossover study of the ketogenic diet. *Epilepsia* 2009;50:322–325.
4. Nathan JK, Purandare AS, Parekh ZB, Manohar HV. Ketogenic diet in Indian children with uncontrolled epilepsy. *Indian Pediatr* 2009;46:669–673.
5. Kossoff EH, Rowley H, Sinha SR, Vining EPG. A prospective study of the modified Atkins Diet for intractable epilepsy in adults. *Epilepsia* 2008;49:316–319.
6. Kossoff EH, Dorward JL, Molinero MR, Holden KR. The Modified Atkins Diet: A potential treatment for developing countries. *Epilepsia* 2008;49:1646–1647.
7. Cervenka MC, Terao NN, Bosarge JL, Henry BJ, Klees AA, Morrison PF, Kossoff EH. Email management of the Modified Atkins Diet for adults with epilepsy is feasible and effective. *Epilepsia* 2012;53:728–732.
8. Groomes LB, Pyzik PL, Turner Z, Dorward JL, Goode VH, Kossoff EH. Do patients with absence epilepsy respond to ketogenic diets? *J Child Neurol* 2011;26:160–165.
9. Kossoff EH, Henry BJ, Cervenka MC. Efficacy of dietary therapy for juvenile myoclonic epilepsy. *Epilepsy Behav* 2013;26:162–164.



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