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Case Report

Modified Atkins Diet with slow reduction of carbohydrate

Amanda Gauthier [a], Nevena Simic [b], Kevin C. Jones [b], Rajesh RamachandranNair [b,*]

[a] Niagara Health, Welland, Ontario, Canada
[b] Comprehensive Pediatric Epilepsy Program, McMaster Children's Hospital, Hamilton, Ontario, Canada

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ABSTRACT

Typically, the amount of daily carbohydrate in the Modified Atkins diet (MAD) is restricted to 10–20 g from the beginning of the therapy. It is possible to gradually reduce the daily carbohydrate amount to this target to increase acceptability of the diet. We report the use of the MAD with slow carbohydrate reduction in a patient with Glucose Transporter 1 Deficiency, including results of neuropsychological assessments. Seizures were controlled at 45 g of carbohydrates daily. This case report illustrates that a liberalized form of MAD with slow reduction of carbohydrate may be a therapeutic option in some children with epilepsy. It is possible that other children with epilepsy could achieve seizure control at higher carbohydrate level than current MAD recommendations.

1. Introduction

The modified Atkins diet (MAD) is a liberalized form of the ketogenic diet (KD) utilized in the treatment of epilepsy [1]. The MAD is a practical option for older children and teenagers who may benefit from diet therapy for seizure control. Typically, the amount of daily carbohydrate in the MAD is reduced to 10–20 g from the beginning [1,2]; however, some patients may find it difficult to lower the carbohydrate content abruptly. We report the use of a liberalized version of the MAD with gradual reduction of carbohydrate to control seizures in a boy with glucose transporter type 1 (GLUT-1) deficiency.

2. Clinical report

A two-and-one-half-year-old boy presented with two convulsive episodes of unresponsiveness and associated body stiffness lasting 2–3 min. During one of the seizures, he was incontinent of urine. He also had two episodes with dystonic posturing of the right-sided limbs lasting several seconds with retained awareness. Subsequently, he developed multiple daily seizures with staring and unresponsiveness lasting up to 5–15 s. These episodes were not associated with automatisms or eye blinking. There was no history of exertional dystonia. Birth history was unremarkable. He walked independently at 18 months, but he was often described as "off balance." There was no family history of epilepsy. His neurological examination was normal except for a clumsy gait. His head circumference was 52 cm. EEG showed frequent generalized and bifrontal epileptiform discharges. Brain MRI did not reveal any parenchymal abnormalities and chromosomal microarray analysis was normal. Metabolic investigations were also normal. Targeted sequencing (using automated fluorescence dideoxy sequencing method), and deletion and duplication analysis (multiplex ligation-dependent probe amplification method) of SCL2A1 gene did not reveal any abnormality in 2012. Multiple anti-seizure medications did not control the seizures, and he developed headache consistent with features of migraine. In 2015, a next generation epilepsy genetic sequencing panel revealed a de novo heterozygous mutation in SCLC2A1 gene (p.Asp461_Ile463del), confirming the diagnosis of GLUT-1 deficiency. A cerebrospinal fluid analysis was not performed.

Following an assessment by our registered dietitian, blood investigations, and an ECG, the patient was initiated on a liberalized form of the KD as an outpatient in October of 2015. We used the principles of the MAD [1]: there were no restrictions of fat intake but minimum daily recommendations were provided. The appropriate amount of carbohydrate per day was prescribed. Initially, we decreased daily carbohydrate to 86 g (two-thirds of the pre-diet consumption). The patient was encouraged to increase the fat and protein intake, with minimum recommendations of 105-g fat and a maximum protein recommendation of 70 g per day. The patient was supplemented with vitamin D, calcium, and multivitamins. At the first stage, his home blood ketone levels were 1.3–3.1 mmol/L. One episode of hypoglycemia (2.9 mmol/L) was identified and responded readily to supplemental treatment with juice. After 2 weeks, the daily carbohydrate prescription was further reduced to 50 g, and suggestions were provided to increase recommended fat intake to maintain weight stability. It was

* Corresponding author at: Comprehensive Pediatric Epilepsy Program, McMaster Children's Hospital, 3A, 1280 Main St West, Hamilton, ON L8S4K1, Canada.
E-mail address: rnair@mcmaster.ca (R. RamachandranNair).

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recommended that daily carbohydrate intake be spaced out evenly throughout the day. Patient became seizure-free at this stage. A 3-day food record analysis showed an average intake of 47 g carbohydrate, 78.5 g protein, and 125.5 g fat per day. The calculated average ratio was 1:1. The 6-month blood investigations revealed low blood levels of selenium and zinc, which were corrected with supplementation. The patient developed six episodes of absence seizures within the next year; hence, the carbohydrate intake was further limited to 45 g per day. The patient remains seizure-free since then, with resolution of headache (Table 1). Home blood ketone levels ranged 0.5–1.5 mmol/L. Recent food record analysis data are as follows: 45–47 g carbohydrate per day (spread throughout the day), and average fat of 190 g per day with an estimated ratio of 1.2:1. Most recent lipid profile was normal. The patient has been off all anti-seizure medications for 10 months and the parents stopped home blood ketone level monitoring. The last three values of blood betahydroxybutyrate level in the hospital outpatient laboratory ranged from 0.34 to 0.55 mmol/L.

Neuropsychological assessment was done in September 2015 prior to diet initiation, and repeated in April 2016 and May 2019 to monitor cognitive development. At baseline, overall intellectual ability was below the 1st percentile, but the patient had a relative personal strength in his verbal reasoning skills, which were intact and age-appropriate. At follow-up, although still a relative strength, his verbal reasoning skills were more in line with the rest of his cognitive profile (i.e., very low). On the other hand, his mother reported improvement in the patient's attention and alertness and his adaptive functioning never declined and remained intact and age-appropriate.

Parental consent was obtained for this publication.

3. Discussion

This case suggests seizure freedom can be achieved at higher than standard carbohydrate levels by following an individualized approach to gradual carbohydrate reduction when compared to the traditional MAD, which allows only for 10–20 g of carbohydrate per day. It is unclear what level of ketosis is required in a patient with GLUT-1 deficiency. The classic KD is highly restrictive, which affects compliance. The MAD is increasingly being used in adolescents and adults with epilepsy. A 50–90% improvement in seizure control has been reported in four out of five children with trace to zero ketosis while following the MAD [1]. Though reasonable blood ketone levels were obtained during home monitoring, subsequent blood ketone levels were only modest. Nonetheless, the patient remained seizure-free. We suggest that in patients with seizures, seizure freedom could be a clinical marker for achieving the appropriate carbohydrate level of diet therapy as opposed to the amount of ketosis. It would be difficult to decide on the level of diet therapy vs ketosis in patients without seizures as a marker for improvement.

The rationale for choosing 10 g as the target daily carbohydrate intake in the MAD is unclear [2]. Centers vary in their practice of choosing initial carbohydrate amount and reduction in the MAD. A recent survey among the UK dietitians reported 72% of the centers advised patients to make initial dietary modifications (reducing dietary intake of high sugar foods and overall carbohydrates, over a 4- to 6-week period, before commencing a modified KD [3]. All UK centers (n = 18) provided a specific carbohydrate target (15–30 g per day) based on a predetermined weight in 67% of centers or 5% of the estimated total energy requirements in 28% of centers. One center calculated carbohydrates to provide between 10% and 20% of estimated total energy [3]. This means, for an older child requiring 1500 calories per day, daily carbohydrate would be 37.5–75 g. Authors from South Korea reported a different method of implementing the MAD: carbohydrates were restricted to 10 g per day initially, but were allowed to be increased by 5 g per day to a maximum of 10% carbohydrates per day by weight at intervals of at least 1 month, depending on tolerance [4]. One adult study reported the use of 50 g carbohydrate in their protocol for the MAD [5]. An inpatient protocol from Australia reduces carbohydrate over 2 weeks [6]. -Gradual titration of the classic version of the KD is practised in many centers where the ratio is advanced over several days or weeks [7,8].

A flexible patient-specific approach is often suggested, choosing an individualized treatment based primarily on specific dietary and lifestyle requirements, rather than on a rigid diet protocol. This can utilize one specific type of diet, but alternatively can use the principles of different or all forms of ketogenic therapies [9]. Ontario provincial guidelines for the management of drug-resistant epilepsy mention the use of individualized modifications to diet therapy [10]. Rapid lowering of daily carbohydrate intake can be difficult to implement in some patients on a MAD. A more gradual reduction in the amount of carbohydrates can be undertaken over days to weeks depending on individual tolerability and resultant seizure control. This is similar to the practice of gradual initiation of the classic KD [7,8]. Variable amount of medium chanin triglyeride oil can be added to any type of diet to increase the ketogenic potential [10]. In our patient, we combined the principles of the MAD and gradual titration method [1,6–8]. By this liberalized method, we were able to achieve seizure control at higher than standard daily carbohydrate intake. Slow reduction of carbohydrate in the MAD will allow the dietary team to identify the appropriate level of carbohydrate required for each patient. To our knowledge, this is the first report in English to outline a method of gradual reduction of daily carbohydrate intake using the MAD.

The clinical phenotype of our patient was consistent with GLUT-1 deficiency. Missing the mutation in the earlier genetic test was related to a reporting error by the laboratory. Patients with GLUT-1 deficiency in general require long-term treatment with the KD, and therefore the MAD may be an ideal option. A survey among families of children with GLUT-1 deficiency reported 31% of the patients were on the MAD [11], which is increasingly being used in GLUT-1 deficiency [12,13]. Many reports suggest at least some improvement in cognitive function following the KD [14]; however, a case series examining the cognitive outcome at 25 months reported no improvement in measures of the corresponding intelligence quotient [15]. Cognitive outcome may be related to earlier institution of KD as a therapy [14]. In our patient, the

Table 1
Seizure control in relation to carbohydrate reduction.

Time Period	Carbohydrate (Maximum-Prescribed)	Fat (Minimum-Recommended	Protein (Maximum-Recommended)	Ketosis	Seizure frequency
October 2015	NA	NA	NA	NA	4–5/week
Week 1–2	86 g	105 g	70 g	Blood 1.3–3.1 mmol/L Urine 16 mmol/L	1 /week
Week 3–46	50 g	120 g	98 g	Blood 1.3–3.8 mmol/L Urine 16 mmol/L	No seizures from Oct 28, 2015-Aug 2016. 6 seizures in late summer of 2016
Weeks 47 onwards	45 g	125	98 g	Blood 0.5–3 mmol/L Urine NA	Seizure free

NA: Not available/applicable.

neurocognitive status was already compromised at baseline but his adaptive functioning never declined and his subjective alertness and attention improved. Diet therapy was started at a later age of 7 years old in our patient, which may be the reason for lack of cognitive improvement.

4. Conclusion

A liberalized form of MAD with slow reduction of carbohydrate may be a therapeutic option in children with epilepsy. Hence, it is possible that some children could achieve good seizure control at higher carbohydrate level than current MAD recommendations, which in turn could improve compliance and ease of following the diet.

Declaration of competing interest

Authors have no conflict of interest relevant to this manuscript.
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