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Ketogenic diet in pediatric patients with refractory focal status epilepticus

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Focal;
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Summary The ketogenic diet (KD) has been used as an alternative treatment for patients with refractory status epilepticus (SE).
Purpose: In this retrospective study we assess the efficacy and tolerability of the KD in patients with refractory SE.
Methods: Between March 1, 2010 and January 1, 2014, 10 patients who met the diagnostic criteria of refractory SE seen at our department were placed on the KD and followed for a minimum of 6 months.
Results: Ketonuria was reached within 2—4 days (mean 3 days) for all patients.

Seizures stopped in two patients and five patients had a 50—75% seizure reduction within 2—5 days (mean 2.5 days) following the onset of ketonuria and within 5—7 days (mean 5 days) following the onset of the diet. Three patients had a <50% seizure reduction and all of them had severe adverse events so the diet was discontinued. Seven patients remained on the diet for 6 months to 3 years (mean 1.5 years). In all seven patients within 4 months the seizures recurred, but their quality of life did not worsen. The frequency of the seizures consisted of weekly seizures in two, monthly seizures in two, occasional seizures in two, and isolated seizures in one. All of them kept a good tolerability of the diet.

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Conclusion: The KD is an effective and well-tolerated treatment option for patients with refractory SE. In patients with focal SE secondary to inflammatory or probably inflammatory diseases, the KD should be considered earlier in the course of the treatment.

Introduction

The ketogenic diet (KD) is a high-fat, low-carbohydrate, and adequate-protein diet (Stafstrom and Rho, 2004; Freeman et al., 2006; Kossoff et al., 2008; Caraballo and Vining, 2013). The ketogenic diet is now considered a safe and effective optional therapy not only for children but also for adults with intractable epilepsy (Stafstrom and Rho, 2004; Freeman et al., 2006, 2009; Kossoff et al., 2008; Caraballo and Vining, 2013; Neal et al., 2008, 2009; Caraballo et al., 2011). Interest in the diet has been increasing including for the emergency treatment of status epilepticus (SE) (Freeman et al., 2009; Neal et al., 2008, 2009; Caraballo et al., 2011; Bodenant et al., 2008; Wusthoff et al., 2010; Nabbout et al., 2010; Nam et al., 2011; Cervenka et al., 2011; Vaccarezza et al., 2012; Strzelczyk et al., 2013).

It has been suggested that the KD may be beneficial for seizure control in specific epileptic syndromes (Kossoff et al., 2008; Caraballo and Vining, 2013; Nangia et al., 2012). Over the last years, there has been a remarkable appearance in the concept of using dietary therapy for emergency management of pharmacoresistant seizures (Bodenant et al., 2008; Wusthoff et al., 2010; Nabbout et al., 2010; Nam et al., 2011; Cervenka et al., 2011; Vaccarezza et al., 2012; Strzelczyk et al., 2013; Nangia et al., 2012; Kossoff and Nabbout, 2013; Sort et al., 2013; Thakur et al., 2014).

Several publications have considered the benefits of the KD for SE (Bodenant et al., 2008; Wusthoff et al., 2010; Nabbout et al., 2010; Nam et al., 2011; Cervenka et al., 2011; Vaccarezza et al., 2012; Strzelczyk et al., 2013; Nangia et al., 2012; Kossoff and Nabbout, 2013; Sort et al., 2013; Thakur et al., 2014). The first report was of an adult patient with refractory focal SE, who responded well to the KD within seven days (Bodenant et al., 2008). Subsequently, more than 30 pediatric and adult patients with SE receiving diet therapy have been published (Bodenant et al., 2008; Wusthoff et al., 2010; Nabbout et al., 2010; Nam et al., 2011; Cervenka et al., 2011; Vaccarezza et al., 2012; Strzelczyk et al., 2013; Nangia et al., 2012; Kossoff and Nabbout, 2013; Sort et al., 2013; Thakur et al., 2014; O'Connor et al., 2014). They were treated with the KD, the modified Atkins diet, and the low glycemic index diet, and SE was secondary to different etiologies (Kossoff and Nabbout, 2013). Many of these patients had autoimmune or inflammatory diseases causing SE. Most of the patients were treated with the traditional KD using a ketogenic formula via nasogastric tube. When the diet was successful, it worked within 7–10 days (Kossoff and Nabbout, 2013).

In this study we evaluate the efficacy and tolerability of the KD in patients who met the diagnostic criteria of refractory SE.

Materials and methods

Between March 1, 2010 and January 1, 2014, 10 patients who met the diagnostic criteria of refractory SE were seen at our department. They were placed on the KD and followed for a minimum of 6 months.

The age of the patients ranged from 2 to 9 years (mean 5 years). The patients had no significant personal or family history, except two patients who had a nonspecific febrile illness that preceded the first seizures by 2–7 days and one who had a relative with epilepsy. The patients were followed over a period of 5 years. The electroclinical features of the patients are described in Table 1.

The patients mainly had repetitive and nearly continuous focal status epilepticus refractory to the conventional protocol treatment of SE, including intravenous benzodiazepines, phenytoin, sodium thiopental, corticosteroids, and gamma globulins. Cerebrospinal fluid (CSF) was normal in all patients. Extensive virologic investigations in blood, CSF, and urine were negative in all cases. In two patients, anti-NMDAR antibodies were searched for. The test was positive in one. Plasma lactate and pyruvate levels as well as plasma amino acid and urine organic acid chromatographies were normal. Magnetic resonance imaging (MRI) showed no white-matter hypersignal, but three cases had diffuse brain atrophy and one had an asymmetric hypersignal of the mesial temporal gray matter on both sides. One patient evidenced features compatible with hemimegalencephaly, two patients had focal cortical dysplasia, and in the three remaining patients the MRI was normal.

All patients received a 4:1 KD and glucose administration was removed, including from intravenous infusion. After 24 h of fasting, the patients were fed with a commercial preparation (KetoCal [KetoCal, SHS]). The diet was administered via a gastric tube. Urine ketosis was monitored daily with Labstix. No attempt was made to measure ketone bodies in plasma.

Results

Ten children (six boys and four girls) with a diagnosis of SE were placed on the KD as add-on to the use of more than one AED. Three patients received the diet during 1 week by nasogastric tube, but it was discontinued due to severe adverse effects. Of the remaining seven patients, who received the KD by nasogastric tube for 1–3 months, four continued to receive the same formula by oral administration and the other three were switched to the oral classic diet.

Treatment of the SE

Ketonuria was reached within 2–4 days (mean 3 days) in all patients.

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