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Epilepsy

Non-pharmacological medical treatment in pediatric epilepsies☆

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ABSTRACT

The ketogenic diet is a high-fat, low-protein, low-carbohydrate diet that has been employed as a non-pharmacologic therapy for refractory epilepsy. Several multicenter and two randomized studies have demonstrated the efficacy of the ketogenic diet and the modified Atkins diet for children and adolescent with pharmacoresitant epilepsy. In order to facilitate patient tolerability and palatability, the diet protocols are gradually modified including changes in ratios of the fat versus non-fat components and the initiation of the diet with or without fasting. The modified Atkins diet is now used as an alternative diet. A randomized trial establishing the efficacy of the modified Atkins diet is now available. More recently, the low glycemic index diet seems to be used successfully for pharmacoresistant epilepsy but there are currently only open studies. Looking at the clinical efficacy of dietary treatments, the studies usually report a greater than 50% reduction in seizure frequency in about half of patients at 3 months under diet. Most of the patients who are responders to the ketogenic diet exhibited a decrease in seizure frequency within two months of treatment onset. Efficacy of the ketogenic diet has also been reported for teenager and adult patients. Dietary treatment of epilepsy should not be considered as a last chance treatment. It can be used during the investigation for epilepsy surgery even in case of structural abnormalities. In some epilepsy syndromes such as infantile spasms, myoclonic-astatic epilepsy and refractory status epilepticus, an early use seems helpful. The exact underlying mechanisms are unknown and remain a topic of active research.

Despite an increasing number of approved antiepileptic drugs (AED), approximately 20–30% of individuals appear to have pharmacoresistant epilepsy. The ILAE defined drug resistant epilepsy as failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom [1]. In case of pharmacoresistance, the management of children and adolescent is based on

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epilepsy surgery, dietary treatment including ketogenic diet (KD) and vagal nerve stimulation (VNS). All children and adolescents should be first adequately evaluated for epilepsy surgery. Then the use of KD and VNS should be discussed. However, KD should not be considered as a last treatment option. KD can be used during surgery investigation or if surgery is excluded. In some epilepsy syndromes with a particular efficacy has been suggested, the KD should be used earlier. VNS is typically used in refractory patient when surgery cannot be proposed.

1. Various types of ketogenic diets

The KD and other dietary treatment are now ''evidence-based-proved'' treatment for refractory epilepsy (Fig. 1) [2,3]. The ketogenic diet and the other dietary treatments should not be regarded as ''organic'' treatment of epilepsy. It is sometimes the request of some caregivers. It is important to state that the diets force the body to adapt to alternative intakes to provide adequate energy for the daily functioning (Fig. 2) requiring medical and trained dietician teams.

The original classical KD is based on a ratio of fat to carbohydrate and protein, usually 3:1 or 4:1. Fat is provided as long-chain triglycerides. Protein is kept to minimum requirements for growth, and carbohydrate sources are mostly limited to small portions of vegetables or fruit. The efficacy has been proved by several multicenter trials [4,5] and two randomized trial [2,3].

Forty to 50% of children under KD exhibit greater than 50% reduction in seizure frequency. Moreover, KD seems to exhibit a particular efficacy in some epileptic syndrome such as infantile spasms, Dravet syndrome, Lennox-Gastaut syndrome, myoclonic-astatic epilepsy [6,7]. There are more and more report of the use of KD in case of refractory status epilepticus [8–10]. The KD is also used to provide energy to the brain in some metabolism disorders regardless the patient exhibit seizure. The KD is used for its ability to counteract the brain energy disorders in case of GLUT1 deficiency syndrome and pyruvate dehydrogenase deficiency [6].

The modified Atkins diet (MAD) consists of a nearly balanced diet (60% fat, 30% protein, and 10% carbohydrates by weight), without any restriction of recommended daily calories according to patient age. In 2003, it was first suggested that this less restrictive form of KD may be effective to treat children and adults with epilepsy [11]. Less than 15 years later, there are many open studies and a randomized controlled trials that established the efficacy of MAD [3,11,12]. The MAD

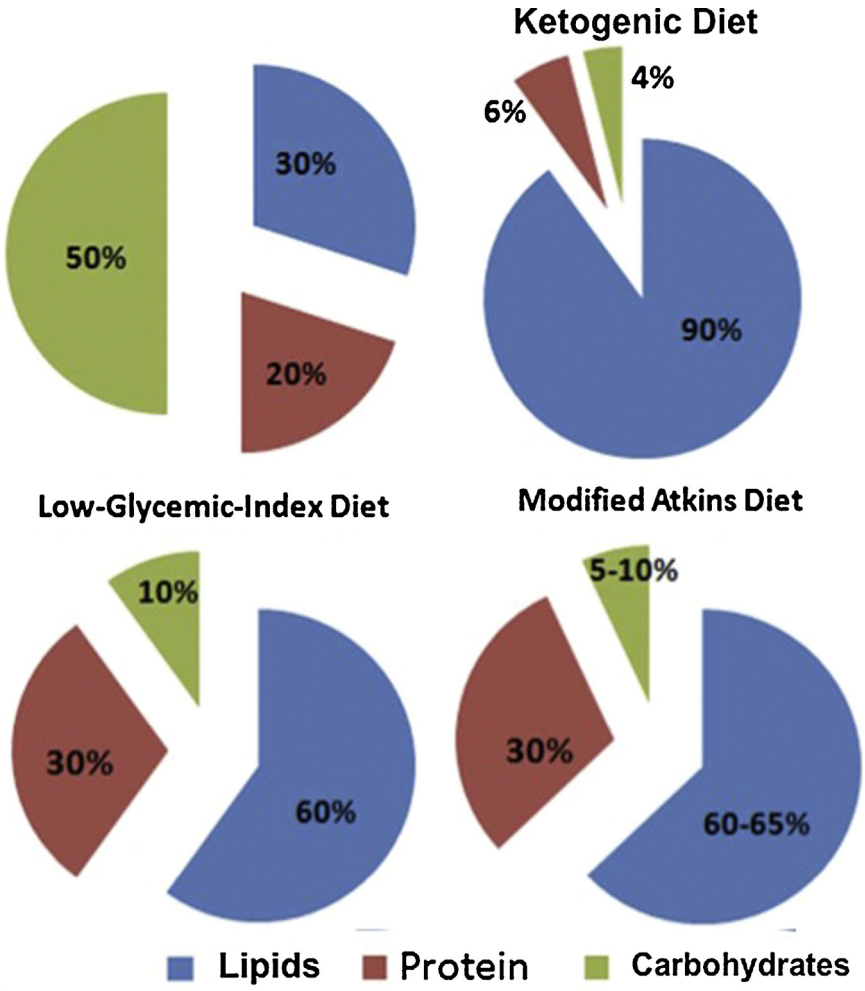

Fig. 1 – Percentage of carbohydrates, lipids and proteins on the regular diet, the Ketogenic Diet, the Low Glycemic Index Treatment and the Modified Atkins diet.

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