Patient is a 3 year old male who had neonatal hypoglycaemia and confirmed homozygosity for the GSD Type IIIa gene. Patient was commenced on the KD at 8 months of age when progression of his GSD resulted in severe cardiomyopathy. The following outlines the transition onto the KD and clinical findings between 8-22 months

Method

Standard dietetic treatment was provided from birth to maintain euglycaemia along with placement of a percutaneous endoscopic gastrostomy. Continuous 24 hour feeding was required due to unsuccessful bolus feeding. A modified KD incorporating MCT fat - which has been noted to further aid ketosis was commenced at 8 months with a ketogenic ratio of 0.5:1 building to 1:1 within 2 weeks. Ketones and blood sugar levels were closely monitored with a threshold of 2.6 mmol/L of glucose and ketones >1 mmol/L before hypoglycaemia intervention was required.

Results

Prior to the KD, there was a high glucose infusion rate (GIR) of 9.75 mg glucose/kg/minute. After initiation of the KD, the GIR reduced initially to 5.8 mg glucose/kg/minute, with a gradual increase of MCT fat from 6% to 28% and the GIR further reduced to 2.73 mg glucose/kg/minute. There were no episodes of hypoglycaemia and ketones ranged from 1–2.9 mmol/L. Echocardiographs showed a significant improvement in cardiac function with a cardiac output reduction of 13.7 to 39 mmHg.

Discussion

The KD was trialled as an alternative treatment. It resulted in the reduced intake of carbohydrate and the subsequent reduction of glycogen build-up within cardiac muscle. Ketones were used as an alternative fuel source and euglycaemia was maintained.

Conclusion

The KD should be considered as an alternative treatment for GSD Type IIIa where standard intervention is not effective.
Epilepsies in children represent a heterogeneous group of disorders and syndromes with different etiology, severity, prognosis and treatment. Early diagnosis, accurate recognition of underlying etiologies leads to more effective management and treatment and improve overall health and quality of life. Genetic testing is very important in the cases of therapy-resistant seizures. The purpose of study was to recognize the possible reason of failed AED treatment and to find the ways to overcome it.

Methods 45 patients with different forms of epilepsy aged from 3 months to 16 years not the candidate for surgical treatment have been studied. The long duration EEG, high resolution MRI, blood biochemical tests, blood level lactate and ammonia, amino acid, organic acid and disturbance of fatty oxidation by TMS, genetic investigations (mtDNA and exome sequence), measurement of autoantibodies to NR2 and GluR1 in blood serum by ELISA were performed to these children.

Results The respiratory chain disorders confirmed by mtDNA sequence were found in 11 children. Metabolic epilepsies discovered in patients have the following origins: two with glutaric aciduria type1, one – glutaric aciduria type2, one with propionic aciduria, one with methylmalonic aciduria, one with Gaucher’s disease type3, two patients with glycogenosis type 9, two patients with ceroid lipofuscinosis type 2 and 6, lysosomal storage disorders in 3 cases.

Genetic epilepsies with mutation in genes SCN8A (two patients), GRIN2A, KCNMA1, SRPX2, SCN9A, ACO2, ARHGEF9, 15q11.2q13.3, TSC-4 patients were revealed. In other cases with normal MRI the reason of pharmacoresistant seizures was not discover yet. The elevated level of autoantibodies to glutamate NR2 and GluR1 receptors were found in children of these groups. But in patients with metabolic epilepsies the elevation level of autoantibodies to NR2 was in 4 to 7 times higher in comparing with children with genetic epilepsies. In children with metabolic disorders and energy metabolism disorders we use the specific therapy (special diet, L-carnitine, vitamins, enzyme replacement therapy etc) in cases which it possible, avoid valproic acid in treatment of children with mitochondrial disorders and glutaric acidurias, as well we use the phenytoin in patient with potassium channel mutation SCN8A. These treatment management led to reduction in seizures frequency or even to seizures remission in some cases.

Conclusions The recognition and diagnostic of underlying etiologies of intractable seizures improve the treatment management in many cases. The excessive NMDA transmission might be the part of pathogenesis of seizures in children with inborn error of metabolism.