**Ketogenic Diet Therapy for** **Drug-resistant Epilepsy and Cognitive Impairment in Children with Tuberous Sclerosis Complex**

**Objective:** We aimed to investigate the efficacy and safety of the ketogenic diet (KD) for drug-resistant epilepsy and cognitive impairment in children with tuberous sclerosis complex (TSC).

**Methods:** This study retrospectively enrolled 53 children with drug-resistant epilepsy or cognitive impairment caused by TSC from 10 hospitals from January 1, 2010, to December 31, 2020.

**Results:** 33 patients were male and 20 were female. 51 of 53 failed to be seizure-free with a mean of 5.0 (4 to 6) kinds of anti-seizure medications before KD. Although another 2 patients had achieved seizure freedom before KD, they still had psychomotor development delay and abnormal electroencephalogram. At 1, 3, 6, and 12 months after KD, there respectively remained 51 (100%), 46 (90.2%), 35 (68.6%), and 16 patients (31.4%) on the diet therapy. At the above time points, there were 26 (51.0%), 24 (47.1%), 22 (43.1%) and 13 patients (25.5%) had ≥50% reduction in seizures, including 11 (21.6%), 12 (23.5%), 9 (17.6%) and 3 patients (5.9%) with seizure free effect accordingly. In addition, 36 of the 51 patients (70.6%) with psychomotor retardation had cognitive and behavior improved. During KD, no serious side effects occurred in all patients. Gastrointestinal disturbance (20 of 53, 37.7%) and hyperlipidemia (6 of 53, 11.3%) were the main side effects.

**Conclusion:** KD is an effective and safe treatment for children with TSC-related drug-resistant epilepsy and cognitive impairment. KD can both reduce seizure frequency and improve cognition and behavior.

**Keywords:** Tuberous sclerosis complex; comorbidity; drug-resistant epilepsy; cognitive impairment; ketogenic diet; multi-center clinical trial; children