**Ketogenic diet for 134 cases of *SCN1A* related drug-resistant epilepsy**

**Objective:** We aim to investigate the efficacy and safety of ketogenic diet (KD) in *SCN1A* related drug-resistant epilepsy (DRE) and explore the relation between *SCN1A* genotype and KD efficacy.

**Methods:** This study retrospectively enrolled 134 children with DRE caused by *SCN1A* gene from 20 hospitals between January 1, 2010, to June 30, 2021.

**Results:** Of the 134 patients, 81 were boys and 53 were girls, including 64 patients of missense mutation, 23 patients of nonsense mutation, 21 patients of splicing mutation, 24 patients of frameshifting mutation,1 patient of synonymous mutation and 1 patient of frame-in mutation. At the 3rd month of KD, 97 patients (97/134,72.4%) had ≥50% seizure reduction, including 54 patients (54/134,40.3%) with seizure-free. Responders in missense, nonsense, splicing, frameshifting, synonymous, and frame-in mutation groups were respectively: 44 patients (44/64,68.8%), 18 patients (18/23,78.3%), 16 patients (16/21,76.2%), 17 patients (17/24,70.8%), 1 patient (1/1) and 1 patient (1/1). There was no statistical difference in KD efficacy of DRE caused by missense, nonsense, splicing and frameshifting mutation of *SCN1A* gene (*P*=0.81). In addition, 79 of the 108 patients (73.1%) with psychomotor retardation had cognitive function improved. There were no side effects in 48 patients (48/134,35.8%) during KD. Gastrointestinal discomfort (62/134,46.3%), infection (19/134,14.2%) and hyperlipidemia (16/134,11.9%) were relatively common.

**Conclusion:** KD is an effective and safe treatment for children with *SCN1A* related DRE, and there is no difference in the efficacy of KD in DER caused by missense, nonsense, splicing and frameshifting mutation of *SCN1A* gene.

**Key words:** *SCN1A* gene, Drug-resistant epilepsy, Ketogenic diet, Efficacy, Genotype, multi-center clinical trial, Dravet syndrome