Efficacy, retention rate and influencing factors of ketogenic diet therapy in children with refractory epilepsy: a retrospective study

Jue Shen, Tiejia Jiang, Feng Gao, Kewen Jiang.

Affiliations below.

DOI: 10.1055/a-1942-2447

Please cite this article as: Shen J, Jiang T, Gao F et al. Efficacy, retention rate and influencing factors of ketogenic diet therapy in children with refractory epilepsy: a retrospective study. Neuropediatrics 2022. doi: 10.1055/a-1942-2447

Conflict of Interest: The authors declare that they have no conflict of interest.

This study was supported by Zhejiang Provincial Education Department Foundation of China, Y201737746

Abstract:

Aim This study aimed to evaluate the efficacy and retention rate of a ketogenic diet (KD) and assess factors that influence the efficacy of KD therapy in children with refractory epilepsy (RE). Methods We retrospectively studied the efficacy and retention rate of 56 RE children who accepted KD therapy from January 2013 to December 2019. Patients who had a ≥50% reduction in seizure frequency were defined as responders. The retention rate was calculated as the proportion of children who continued KD/the total number of children who were followed up at the time of enrollment. We also analyzed the effects of different factors (such as gender, KD initial age, KD duration, the type of epilepsy syndrome, and others) on the efficacy of the KD. Results (1) The efficacy rates for the KD at 3, 6, 12, and 18 months were 51.8%, 53.6%, 39.2%, and 23.2%, respectively. (2) The retention rates for the KD at 3, 6, 12 and 18 months were 100%, 69.6%, 41.1% and 23.2%, respectively. (3) There was no correlation between efficacy and gender, epilepsy onset age, the type of epilepsy syndrome, EEG improvement, or the number of antiseizure medications (ASMs), while cranial magnetic resonance imaging (MRI) abnormalities, KD duration, and KD initial age affected its efficacy at three months. Conclusion (1) KD therapy for refractory childhood epilepsy was effective and produced a high retention rate. (2) MRI abnormalities and the initial age and duration of KD influenced its short-term efficacy in RE children.

Corresponding Author:

Affiliations:
Efficacy, retention rate and influencing factors of ketogenic diet therapy in children with refractory epilepsy: a retrospective study

Jue Shen¹, Tiejia Jiang¹, Feng Gao¹, Kewen Jiang²,³

¹Department of Neurology, Children’s Hospital, School of Medicine, Zhejiang University, Hangzhou, China
²Department of Biobank, Children’s Hospital, School of Medicine, Zhejiang University, Hangzhou, China, ³Department of Neurobiology, Key Laboratory of Medical Neurobiology of Ministry of Health of China, Zhejiang Province Key Laboratory of Neurobiology, School of Medicine, Zhejiang University, Hangzhou, China

The highest academic degree of Kewen Jiang is a doctorate degree, while the other three authors have master’s degrees.

Correspondence to: Kewen Jiang, MD
3333 Binsheng Road, Binjiang District, Hangzhou City (310052), P.R. China
Email: jiangkw_zju@zju.edu.cn

Abstract

Aim This study aimed to evaluate the efficacy and retention rate of a ketogenic diet (KD) and assess factors that influence the efficacy of KD therapy in children with refractory epilepsy (RE). Methods We retrospectively studied the efficacy and retention rate of 56 RE children who accepted KD therapy from January 2013 to December 2019. Patients who had a
≥50% reduction in seizure frequency were defined as responders. The retention rate was calculated as the proportion of children who continued KD/the total number of children who were followed up at the time of enrollment. We also analyzed the effects of different factors (such as gender, KD initial age, KD duration, the type of epilepsy syndrome, and others) on the efficacy of the KD. **Results** (1) The efficacy rates for the KD at 3, 6, 12, and 18 months were 51.8%, 53.6%, 39.2%, and 23.2%, respectively. (2) The retention rates for the KD at 3, 6, 12 and 18 months were 100%, 69.6%, 41.1% and 23.2%, respectively. (3) There was no correlation between efficacy and gender, epilepsy onset age, the type of epilepsy syndrome, EEG improvement, or the number of antiseizure medications (ASMs), while cranial magnetic resonance imaging (MRI) abnormalities, KD duration, and KD initial age affected its efficacy at three months. **Conclusion** (1) KD therapy for refractory childhood epilepsy was effective and produced a high retention rate. (2) MRI abnormalities and the initial age and duration of KD influenced its short-term efficacy in RE children.

**Key words** ketogenic diet, refractory epilepsy, efficacy, retention rate, influencing factors

**Introduction**

According to the definition from the International League Against Epilepsy (ILAE), refractory epilepsy (RE) describes individuals “whose seizures fail to respond to at least two antiseizure medications (ASMs) (whether as monotherapies or in combination)”.\(^1\) Approximately 20%-30% of epileptic children treated with effective ASMs eventually...
develop drug-resistant epilepsy and need to seek other treatment.  Ketogenic diet (KD), a high-fat, low-carbohydrate, and protein-restricted diet, was developed over 90 years in the United States and then promoted and used worldwide. Increasing evidence  suggests that KD is an effective therapeutic option for refractory epileptic seizures, and its effectiveness, safety, and tolerability in drug-resistant epilepsy have been documented in children.  It is hypothesized that a KD exerts antiepileptic effects by affecting ketone bodies, neuronal function, neurotransmitter release, ion channels, and the mechanistic target of rapamycin (mTOR) pathway and drives immunological adjustments. Compared to ASMs, the advantages of KD therapy are obvious.  The diet treatment led to seizure-free status among 15%-27.6% of drug-resistant epilepsy patients  and was also shown to reduce the overall usage of ASMs in a previous report.  In addition, KD treatment has no adverse effects on the cognition and behavior of children with epilepsy and seems to be beneficial to neurobehavioral development in children with drug-resistant epilepsy.  Nevertheless, there are still some limitations of KD therapy. KD is not an ordinary diet that causes a series of adverse effects, especially metabolic acidosis in the initial phase and chronic stage, and may affect the growth of children.  The other limiting factor is that it is difficult to maintain therapy for various reasons, especially in adolescents and adults.  In summary, it is thought that the KD could be a valuable option for children with drug-resistant epilepsy. However, the correlative factors associated with the efficacy of the KD in RE patients have not yet been determined. In the present study, we retrospectively reviewed clinical observations of the efficacy and retention rate of a KD in RE patients in a single center in Hangzhou, China, and evaluated the influencing factors affecting its therapeutic efficacy.
Materials and methods

The data of the drug-resistant epilepsy children who received KD treatment with the following inclusion and exclusion criteria were collected retrospectively at the Department of Pediatric Neurology, Children’s Hospital of Zhejiang University School of Medicine, China, from January 2013 to December 2019. Inclusion criteria: (1) met the 2010 International League Against Epilepsy (ILAE) criteria for refractory epilepsy and (2) underwent no previous KD treatment. Exclusion criteria: (1) not suitable for the KD or had contraindications for KD treatment, such as a deficiency in pyruvate carboxylase, in the transport or oxidation of fatty acids or ketone bodies, exhibited a mitochondrial disease and (2) dropped out in the first three months of dietary therapy due to various reasons, such as poor family compliance, social circumstances, parents with difficulties in preparing for KD, and severe adverse effects. All of the patients initiated KD therapy in the hospital for seven days and then were followed up at the outpatient clinic for over one year.

The modified Johns Hopkins protocol was used to initiate KD therapy after excluding unsuitable cases. The initial ketogenic ratio was 2:1 (fat: carbohydrates plus protein), while the target ratio was 3:1 (under one year of age) or 4:1 (over one year). KD therapy was administered for at least three months, and no drug adjustments were permitted during the first three-month period. The recommended calories provided to these patients were 75% of the daily requirement for healthy peers. Supplementation with potassium citrate, multivitamins, minerals, and calcium without sucrose and lactose was provided in the daily diet. All patients were hospitalized for one week and closely monitored for efficacy and
potential side effects. The seizure frequency, nutritional status, the number of ASMs, cognitive function, and physical examination were followed up once per month in the first half of the year after discharge and every three months in the latter half. Electroencephalogram (EEG) monitoring was performed every three months. The intelligence quotient (IQ) of the participants was measured using the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV) or Denver Development Screen Test (DDST) according to their age. To minimize the adverse effects of KD therapy, the patients in our cohort were carefully supervised by the neurologist after initiation. The KD team distributed educational literature about the KD one by one to the subjects. When they suffered some discomfort, our clinical dietitians and pediatric neurologist were available for phone calls or WeChat if needed.

The principal measure of efficacy was the reduction in seizure frequency according to Engel grading: grade I, no seizures; grade II, a 90-100% reduction; grade III, a 50%-90% reduction; and grade IV, a <50% reduction. The efficacy rate= number of children reaching (grade I + grade II + grade III)/total number of children enrolled × 100%. Patients who had a ≥50% reduction in seizure frequency were defined as responders, and the others were defined as non-responders. The retention rate—i.e., the proportion of children who continued KD/the total number of children who were followed up at the time of enrollment—was calculated at 3, 6, 12, and 18 months.

We performed statistical analyses using SPSS for Mac, version 21.0. Univariate analyses (Chi-square test, Mann-Whitney test) and multivariate analyses (logistic regression analyses) were used to evaluate the factors associated with KD therapy in patients with refractory
epilepsy. All potential predictor variables were included in multivariate models. A p-value of <0.05 was considered statistically significant. This study was approved by the Ethics Committee of the Children’s Hospital of Zhejiang University School of Medicine, China (2019-IRB-152). Written informed consent for publication of clinical details was obtained from the patient’s parents or legal guardians.

Results
We retrospectively screened data from 63 patients who were diagnosed with drug-resistant epilepsy and received KD treatment at the Department of Pediatric Neurology, Children’s Hospital of Zhejiang University School of Medicine, China, from January 2013 to December 2019. In seven patients, the parents decided not to continue further treatment in the first three months of dietary therapy for different reasons (2 due to economic reasons, 2 due to poor compliance, and 3 due to difficulties in preparing for KD). Finally a total of 56 RE patients (38 males and 18 females) were included in our cohort (Figure 1), and the details of their general characteristics are presented in Table 1. The median epilepsy onset age and KD initial age were six months (ranging from 1-131 months) and 28 months (ranging from 3-156 months), respectively. The median KD duration was six months (ranging from 3-54 months). Half of the RE patients (28 cases) were diagnosed with West syndrome, while another half were diagnosed with other epileptic syndromes, including Dravet syndrome (8/56, 14.3%), Lennox-Gastaut syndrome (LGS) (4/56, 7.1%), and unclassified drug-resistant epilepsy (11/56, 19.6%), etc (Table 1). The most frequently detected seizure types were epileptic spasms, focal seizures, and generalized tonic-clonic seizures. The most commonly used drugs
were valproate, topiramate, levetiracetam, and clonazepam. We noted that 29 patients (51.8%) showed abnormal cranial MRI scans, of whom 16 patients exhibited focal lesions and 13 patients demonstrated developmental abnormalities. All 56 children manifested EEG abnormalities, including abnormal background and/or interictal epileptiform discharges, which were consistent with the characteristics of different epilepsy syndromes.

Thirty patients (53.6%, 30/56) and 22 patients (39.2%, 22/56) achieved an over-50% reduction in their seizure frequency at six and 12 months, respectively. Thirteen patients (23.2%) continued on the KD and experienced more than a 50% seizure reduction at 18 months, including 12.5% (7/56) at grade I and 10.7% (6/56) at grade II according to the Engel scale (Table 2). The efficacy rates for KD at 3, 6, 12, and 18 months were 51.8%, 53.6%, 39.2%, and 23.2%, respectively, and the total control rates were 8.9%, 8.9%, 12.5%, and 12.5%, respectively.

The retention rates for the KD at 3, 6, 12 and 18 months were 100%, 69.6%, 41.1%, and 23.2%, respectively, and no one withdrew from the KD therapy within three months. Of the 56 patients, 17, 16, and 10 patients withdrew during the periods of 3-6 months, 6-12 months, and 12-18 months, respectively. The two common causes for withdrawal were unresponsiveness to KD therapy (22 cases) and side effects (14 cases). Due to our careful selection and supervision, no severe adverse effects were observed in our group. In the present study, the primary minimal and reversible side effects included gastrointestinal adverse effects and respiratory tract infection. In the first two weeks, a total of 18 children suffered from nausea or vomiting. After adding the nausea medication, changing the KD ratio, or changing the diet frequency, all gastrointestinal symptoms improved. Finally, 12
(21.4%) patients withdrew due to gastrointestinal adverse effects (4 with nausea, 8 with vomiting), and 2 (3.6%) patients dropped out due to respiratory tract infection from three months to six months.

All RE patients were treated with a KD for at least three months, so we evaluated the correlative factors affecting the short-term efficacy of KD treatment. Fifty-six patients were divided into two groups after 3 months treatment: 29 patients who had an over-50% reduction in their seizure frequency were considered the responder group, and the other 27 patients were considered the non-responder group. The univariate and multivariate analyses of the clinical data for the responder and non-responder groups regarding KD therapy addition are shown in Table 3. The most common types of epilepsy syndromes in both groups were West syndrome (11 cases in responder group vs 17 cases in non-responder group), Dravet syndrome (5 cases in responder group vs 3 cases in non-responder group), and LGS (3 cases in responder group vs 1 cases in non-responder group). There were 17 patients with improved EEG background or reduced interictal epileptiform discharges in the responder group and 11 patients in the non-responder group. The duration and age at initiation of KD treatment in the responder group were significantly higher than those in the non-responder group (median KD duration: 11 months vs 3 months, P < 0.05; median KD initial age: 35 months vs 26 months, P < 0.05). The number of patients with abnormal brain MRI manifestations in the responder group was also higher than that in the non-responder group (20 vs 9, P < 0.05). Multivariate regression analysis indicated that MRI abnormality, KD duration, and initial age with respect to the KD affected its efficacy at three months (P < 0.05). There were no significant
differences in epilepsy onset age, gender, cognitive dysfunction, the type of epilepsy syndrome, EEG improvement, or the number of ASMs between the two groups.

**Discussion**

The present study provided evidence for the benefits of KD therapy in drug-resistant epilepsy patients, with efficacy rates at 3, 6, 12, and 18 months of 51.8%, 53.6%, 39.2%, and 23.2%, respectively. These results were in agreement with those of previous workers, which ranged from 35% to 85%, indicating that the ketogenic diet was an optional treatment method for children with drug-resistant epilepsy. The retention rate in previous study groups ranged from 20% to 80% at six months and from 10% to 60% at twelve months and was significantly related to overall clinical teamwork, the educational level of parents, and the efficacy of KD therapy. The data in our report were consistent with the literature, as 69.6% and 41.1% of patients maintained their special diet at six and twelve months in our cohort, respectively, and 23.2% still adhered to KD therapy one and a half years later. In our cohort, two common reasons for discontinuing trials were poor curative effects and adverse reactions. In the report by Riantarini I et al., 22 (19%) patients withdrew from KD due to side effects, and Cai et al. found that nearly half of their patients discontinued the diet due to a lack of efficacy. Wibisono and other scholars reported similar conclusions. Herein, we also demonstrated that poor curative effects and side effects were the two most common factors affecting retention rate as they relate to dietary therapy.

The potential factors underlying a successful outcome of KD therapy are still unknown. We attempted to identify some influencing factors that affected the efficacy of short-term KD
therapy because 17 patients had ceased their KD therapy after three months in our study. We noted no significant differences in epilepsy onset age or gender between the two groups, as was also reported by Feng et al. Cognitive dysfunction or the number of ASMs also did not predict a reduction in seizure frequency in our study. The previous data showed a favorable response to the KD in infantile spasms, Doose syndrome, Dravet syndrome, and LGS. However, some other investigators, such as Sariego et al., studied 60 children with refractory epilepsy who received KD therapy and found that the efficacy of treatment was not related to the etiology of epilepsy. They thus concluded that KD therapy appeared to work equally well for any etiology of epilepsy. In our cohort, the type of epilepsy syndrome also exerted no effect on reducing seizures after short-term KD treatment.

Our results demonstrated that the duration of dietary therapy was related to KD efficacy, and therefore, a longer duration of KD might be useful as a predictive factor of seizure reduction. Although the previous data demonstrated that children with a successful response at three months were more likely to achieve success at 12 months of KD therapy and 13% of epilepsy children terminated their KD after three months, there were still some cases that led to a successful outcome after three months. We also showed that one patient ultimately experienced an over 90% reduction in seizure frequency at six months even if he experienced ineffective KD therapy at three months. Thus, for the patients who exhibited an unsuccessful response to the diet at three months, we need to evaluate all aspects to decide whether to continue or halt treatment. In a Korean cohort, investigators compared the prognoses between short-term (8 months) and conventional long-term (>2 years) trials in IS patients and found that the short-term trials achieved similar outcomes and recurrence rates and less growth
disturbance relative to the longer-term trials. Kossoff recommended that the KD be continued for 3-6 months if unsuccessful. Such analyses require additional studies in the future to determine the minimal and longest duration of KD therapy. Lemmon reported that the efficacy of the KD was independent of age at initial KD in LGS patients. On the other hand, we found that a higher KD initial age predicted more favorable outcomes for KD treatment, which indicated that KD therapy is an alternative choice of treatment even for RE patients who have suffered seizures over a lengthy period of time.

MRI abnormalities were another factor associated with a favorable outcome in the present study. Some investigators demonstrated that KD treatment was more effective for patients with focal lesions, especially children with cerebral cortex dysplasia and tuberous sclerosis complex. As mentioned above, a KD exerts antiepileptic effects by various pathways; the effect of KDs on the mTOR pathway makes them effective for children with TSC. The beneficial effect of KD treatment in children with epilepsy combined with cerebral cortex dysplasia may be due to the effect of ketones, which are produced in the process of KD therapy and play an important role in the formation of myelin in the brain. In our cohort, the main MRI abnormalities included focal lesions and developmental abnormalities. We supposed that the reason why the efficacy of KD in children with MRI abnormalities was higher than that in children without abnormalities may be due to the effect of ketones on the formation of myelin in the brain. However, other researchers arrived at the opposite conclusion. Kang and colleagues uncovered no significant differences in the seizure remission rate with KD therapy between patients with MRI-negative and MRI-
positive drug-resistant infantile spasms. Further evidence is therefore required to better understand the relationship between MRI findings and the efficacy of the KD.

There are several limitations to our study. First, we only calculated factors affecting the short-term efficacy of KD therapy because 17 patients ceased their dietary therapy due to poor curative effects or other reasons. Further study is needed to evaluate the potential correlative factors that influence the long-term efficacy of KD therapy. Second, this was a single-center retrospective study with a small sample size and short follow-up period, which may lead to a potential for selection bias. We chose children who underwent follow-up for more than three months, which also led to selection bias. Prospective control studies with sufficient sample sizes and longer follow-up periods are needed to improve the conclusions. Third, self-reporting by parents increased the subjective error in seizure detection and could also affect the observation.

**Conclusion**

In conclusion, we demonstrated herein that a KD could be a successful treatment for children with drug-resistant epilepsy. We found that the higher the initial age was, the longer the duration of KD and that abnormal MRI findings predicted more favorable outcomes of KD therapy. We suggest that it is necessary to reevaluate and then decide whether to continue or halt treatment for patients who exhibit an unsuccessful response to KD therapy at three months. However, additional studies are required to corroborate these findings.

**Acknowledgments**
We would like to thank all volunteers for their participation in the survey. This study was supported by a Grant from the Zhejiang Provincial Education Department Foundation of China (Y201737746).

**Conflict of Interest**

The authors declare no conflicts of interest.

**References**


2. Garcia-Penas JJ. Epilepsy, cognition and ketogenic diet. Rev Neurol 2018; 66(S01): S71-S75


Figure 1. The flowchart of the participants’ recruitment process
Table 1. Clinical characteristics and seizure syndromes of enrolled refractory epilepsy patients

<table>
<thead>
<tr>
<th>age</th>
<th>cases</th>
<th>West</th>
<th>Dravet</th>
<th>LGS</th>
<th>unclassifie</th>
<th>other</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1y</td>
<td>14</td>
<td>10</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1-3y</td>
<td>22</td>
<td>13</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>3-6y</td>
<td>13</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>&gt;6y</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>total</td>
<td>56</td>
<td>28</td>
<td>8</td>
<td>4</td>
<td>11</td>
<td>5</td>
</tr>
</tbody>
</table>

West: West syndrome; Dravet: Dravet syndrome; LGS: Lennox-Gastaut syndrome.

Table 2. Retention rate and efficacy in refractory epilepsy patients with different ketogenic diet durations

<table>
<thead>
<tr>
<th>KD duration</th>
<th>Total cases</th>
<th>Engel Grade</th>
<th>Retention rate</th>
<th>Efficacy rate</th>
<th>Control rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>56</td>
<td>I 5 II 7 III 17 IV 27</td>
<td>100%</td>
<td>51.8%</td>
<td>8.9%</td>
</tr>
<tr>
<td>6 months</td>
<td>39</td>
<td>I 5 II 8 III 17 IV 9</td>
<td>69.6%</td>
<td>53.6%</td>
<td>8.9%</td>
</tr>
<tr>
<td>12 months</td>
<td>23</td>
<td>I 7 II 6 III 9 IV 1</td>
<td>41.1%</td>
<td>39.2%</td>
<td>12.5%</td>
</tr>
<tr>
<td>18 months</td>
<td>13</td>
<td>I 7 II 6 III 0 IV 0</td>
<td>23.2%</td>
<td>23.2%</td>
<td>12.5%</td>
</tr>
<tr>
<td>total</td>
<td>56</td>
<td>I 7 II 6 III 17 IV 26</td>
<td>/</td>
<td>53.6%</td>
<td>12.5%</td>
</tr>
</tbody>
</table>

KD: ketogenic diet; Total cases: numbers of refractory epilepsy patients who continued KD therapy at that time; The retention rate: the proportion of children who continued KD therapy at that time/the total number of children who were followed up at the time of enrollment; The efficacy rate: number of children reaching (grade I + grade II + grade III)/total number of children enrolled × 100%; Control rate: number of children reaching grade I/total number of
children enrolled × 100%.

Table 3. Analysis of the influencing factors of ketogenic diet (KD) in patients with refractory epilepsy at 3 months.

<table>
<thead>
<tr>
<th>factors</th>
<th>Responder group n (%)</th>
<th>Non-responder group n (%)</th>
<th>Univariate p-value</th>
<th>Multivariate p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>22 (75.9)</td>
<td>16 (59.3)</td>
<td>0.18</td>
<td>0.60</td>
</tr>
<tr>
<td>female</td>
<td>7 (24.1)</td>
<td>11 (40.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seizure onset age, months, median (range)</td>
<td>7 (1-131)</td>
<td>6 (1-44)</td>
<td>0.19</td>
<td>0.40</td>
</tr>
<tr>
<td>KD initial age, months, median (range)</td>
<td>35 (4-156)</td>
<td>26 (3-92)</td>
<td>0.03</td>
<td>0.04</td>
</tr>
<tr>
<td>KD duration, months, median (range)</td>
<td>11 (3-54)</td>
<td>3 (3-38)</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Epilepsy syndromes, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>West syndrome</td>
<td>11 (37.9)</td>
<td>17 (63.0)</td>
<td>0.29</td>
<td>0.91</td>
</tr>
<tr>
<td>Dravet syndrome</td>
<td>5 (17.3)</td>
<td>3 (11.1)</td>
<td></td>
<td>0.78</td>
</tr>
<tr>
<td>Lennox-Gastaut syndrome</td>
<td>3 (10.3)</td>
<td>1 (3.7)</td>
<td></td>
<td>0.48</td>
</tr>
<tr>
<td>Others</td>
<td>10 (34.5)</td>
<td>6 (22.2)</td>
<td></td>
<td>0.90</td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>------------------------</td>
<td>------------------------</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>Abnormal MRI</td>
<td>20 (69.0)</td>
<td>9 (33.3)</td>
<td>0.01</td>
<td>0.03</td>
</tr>
<tr>
<td>EEG improvement</td>
<td>17 (58.6)</td>
<td>11 (40.7)</td>
<td>0.09</td>
<td>0.84</td>
</tr>
<tr>
<td>Cognitive dysfunction, n</td>
<td>21 (72.4)</td>
<td>20 (74.1)</td>
<td>0.89</td>
<td>0.39</td>
</tr>
<tr>
<td>Antiepileptic drugs &gt;=3</td>
<td>27 (93.1)</td>
<td>26 (96.3)</td>
<td>0.59</td>
<td>0.69</td>
</tr>
</tbody>
</table>

MRI: magnetic resonance imaging; EEG: electroencephalogram; univariate analyses were confirmed by the chi-square or Mann-Whitney test.
Drug-resistant epilepsy patients who accepted ketogenic diet therapy were screened (n=63)

include in final analysis (n=56)

7 were excluded due to discontinue the diet in less than three months:
- economic reasons (n=2)
- poor compliance (n=2)
- parents with difficulties in preparing for diet (n=3)

divided into two groups according to the efficacy of ketogenic diet treatment at three months

Responder (≥50% reduction in seizure frequency) (n=29)

Non-responder (<50% reduction in seizure frequency) (n=27)