

spontaneous diuresis and renal function. Treatment duration ranged between 16 and 155 h, with a median of 27 h. We did not detect any complications associated with the technique, such as infection or catheter malfunction (Table 1).

In this sample of patients, we found that CFPD with a dual catheter system for RRT was easy to implement, efficient, and safe due to the absence of associated complications.

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Ketogenic diet as a therapeutic option in refractory epilepsy[☆]



Dieta cetogénica como opción terapéutica en la epilepsia refractaria

Dear Editor:

Refractory epilepsy (RE) is defined as epilepsy with poor seizure control despite treatment with anticonvulsant

medication. It accounts for 25%–30% of epilepsy cases, and poses a significant therapeutic challenge from a medical perspective.^{1–6} One of the effective therapeutic alternatives for RE is the ketogenic diet (KD).^{1–6} The KD consists of a diet rich in fat and low in protein and carbohydrate aimed at increasing the levels of ketone bodies.^{1–6} Several theories have been proposed to explain its mechanism of action, none of them conclusive.^{1–3,6}

Despite the popularity the diet has achieved in the past twenty years, there is still no consensus on how the KD must be managed to achieve maximum efficacy

Table 1 Characteristics of the patients under study.

Patient (number)	Genetic cause	Sex	Age of onset	No. seizures/day	Status epilepticus before diet	Total number of AEDs used before diet	Other previous non-AED treatment
1	Dravet syndrome	♂	3–6 months	>50	Yes	5	γ globulin
2	Dravet syndrome	♂	3–6 months	<10	Yes	7	None
3	Rett syndrome	♀	3–6 months	>50	No	9	ACTH
4	SCN2A encephalopathy	♂	<1month	>50	No	7	None
5	Dup 15q13.3 multifocal encephalopathy	♂	4 years	<10	Yes	3	Prednisolone
Patient (number)	Structural cause	Sex	Age of onset	No. seizures/day	Status epilepticus before diet	Total number of AEDs used before diet	Other previous non-AED treatment
6	Thalamic infarction	♂	4 years	20–50	No	7	γ globulin
7	Extensive malformation of cortical development in both hemispheres	♂	3–6 months	20–50	No	5	ACTH

♂, male; ♀, female; ACTH, adrenocorticotrophic hormone; Dup, duplication; AED, antiepileptic drug.

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with minimum side effects and to make its use more widespread.²

The aim of our study was to assess the clinical efficacy, tolerability, degree of parental satisfaction and side effects of patients with RE treated with the KD.

We conducted a descriptive retrospective analysis of epileptic patients treated with a KD in our hospital in the past three years.

We evaluated the efficacy of the KD based on the percent reduction in the frequency of seizures (>75%, 74%–50%, <50%, and no response). We considered that patients had a good response when they experienced a seizure reduction of 50% or more compared to baseline.

We assessed parental satisfaction by means of a survey, asking their level of satisfaction (poor, fair, good, excellent).

We included a total of seven patients (six male and one female).

The onset of epilepsy occurred before age 6 months in all patients except patients 5 and 6, who had onsets at around 4 years of age.

The aetiology was genetic in five patients: two had Dravet syndrome (patients 1 and 2), one had Rett syndrome (patient 3), one a SCN2A mutation (patient 4) and one a 15q13.3 microduplication (patient 5). Two patients had lesional epilepsy, caused by a perinatal thalamic infarction in one (patient 6) and extensive malformation of cortical development involving both hemispheres in the other (patient 7).

All patients had received appropriate treatment with several antiepileptic drugs (AEDs) and shown no response prior to the introduction of the KD (3–5 AEDs [43%], 6–8 AEDs [43%] and >9 AEDs [14%]; Table 1).

The patients that showed the best response, with a 75% or greater reduction in seizure frequency, suffered from various genetic anomalies (two had Dravet syndrome, one a mutation in the SCN2A gene, and one a 15q13.3 microduplication). The patients that had the worst outcomes, remaining seizure-free for less than one week, suffered from Rett syndrome and bilateral thalamic infarction.

Patients who had a past history of status epilepticus (28.56%) did not experience it again after the introduction of the diet. Status epilepticus was also not documented in patients that had not experienced it before.

The overall degree of satisfaction of the families was good. The reason for discontinuing the diet was family choice in two patients and progressive ineffectiveness despite an initial good response in the others.

The most frequently observed side effects were vomiting (42.85%) and insomnia. However, four patients (three of them with a 3:1 diet ratio) did not experience any adverse effects (Table 2).

The KD is effective for treatment of refractory epilepsy, although its effects are only temporary in most patients; out of the seven patients presented here, only one continues with the ketogenic diet, and the effectiveness was temporary after an initial reduction of 50% in more than 70% of patients.^{1–6} Patients with genetic mutations benefited most from the diet, especially patients with Dravet syndrome, who achieved a reduction in seizures of 75% or greater.^{2,4–6}

Patients in whom the KD was introduced earlier and after trying fewer AEDs responded better than patients in whom the diet was introduced several years after the onset of

Table 2 Summary of study outcomes.

Patient ^a	Diet ratio	Cognitive outcome	Sleep	Reduction in number of seizures	EEG	Status epilepticus after TX	Time seizure-free	Side effects	Duration of TX (months)	Reason for discontinuation	General satisfaction
1	3:1	Mild improvement	Worsening	>75%	No changes	No	1 month	Vomiting, irritability, insomnia	13	Subsequent ineffectiveness ^b	Very satisfied
2	3:1	Marked improvement	Marked improvement	>75%	No changes	No	1 month	Vomiting	9	Not completed	Satisfied
3	3:1	Mild improvement	No changes	<50%	No changes	No	1 week	None	12.5	Subsequent ineffectiveness ^b	Moderately satisfied
4	4:1	No changes	No changes	>75%	No changes	No	3 months	None	4	Subsequent ineffectiveness ^b	Moderately satisfied
5	4:1	No changes	Worsening	>75%	Not performed	No	None	Vomiting, constipation, changes in eating patterns	2	Family rejection	Dissatisfied
6	3:1	No changes	No changes	<50%	No changes	No	None	None	3	Family rejection	Dissatisfied
7	3:1	Marked improvement	No changes	50–75%	No changes	No	3 months	None	12	Subsequent ineffectiveness ^a	Satisfied

EEG, electroencephalogram; TX, treatment.

^a Patients numbered consistently with the previous table.

^b Initial effectiveness with recurrence/worsening of seizures over time.

epilepsy and after trying multiple antiepileptic drugs (>6 AEDs).

The side effects were similar to those described in the literature,^{2,6} with vomiting being the most frequent complication.⁶ None of the side effects led to discontinuation of the diet.² We found fewer side effects in association with the 3:1 diet ratio.

Although this is a retrospective study with a small sample, we can conclude that the KD is efficacious for the treatment of RE. However, more randomised studies are needed to improve its implementation and prevent complications.

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Gaucher disease: Enzyme replacement treatment initiated at pediatric age; 20-year experience[☆]



Enfermedad de gaucher: tratamiento enzimático sustitutivo iniciado en la edad pediátrica. Experiencia de 20 años

Dear Editor:

Gaucher disease (GD) is caused by deficiency of the enzyme acid beta-glucosidase (GBA).¹ The currently accepted classification is: type 1 (non-neuropathic) (GD-1), type 2 (acute neuropathic) (GD-2) and type 3 (chronic neuropathic). Since 1994, enzyme replacement treatment (ERT) has been available in Spain. Due to the limited long-term safety and efficacy experience with ERT, it was of interest to describe the experience in a tertiary pediatric hospital in which, this treatment started being used as soon as it was available.

The evolution of 7 patients with GD (5 GD-1 and 2 GD-2) treated within the past 20 years in Hospital Infantil La Fe (Valencia) was retrospectively described. The diagnosis was confirmed by glucocerebrosidase activity in leukocytes (GAL) and by mutations in the GBA gene.

At diagnosis, and yearly thereafter, weight, height, BMI, hepatomegaly–splenomegaly degree, hemogram, hemostasis, chitotriosidase, chemokine ligand 18 (CCL18) and spine densitometry were assessed. Abdominal magnetic resonance imaging (MRI) was performed to assess liver and spleen volumes, calculating the multiples of their normal volumes (MNV).² In patients with bone involvement, MRI of long bones was performed. ERT was administered by iv infusion for 2 h, every 2 weeks at a 60 UI/kg dose in patients with GD-1.

Table 1 shows evolution of the 5 patients with GD-1. Age at diagnosis ranged between 22 months and 11 years. In every case, bone marrow aspiration showed Gaucher cells. Genetic analysis showed that 3 of the patients carried the mutation N370S in heterozygosis and 2 the mutation L444P. Every patient showed hepatosplenomegaly and anemia. The initial hepatomegaly was 1.9–3.5 times MNV, and splenomegaly was 9–65 times MNV. One patient presented with lesions of bone infarction and two had Erlenmeyer-flask shaped femurs. GAL ranged from 0.26–2.87 nM/mg prot.h (lower than 8% of control GAL in every case). Patients 1 and 2 received treatment with alglucerase from 1995 to 1998 and with imiglucerase thereafter. Every patient improved his/her weight and height, hemoglobin and platelets count. ERT reduced the hepatic volume up to 3 times and that of the spleen 4–15 times. These improvements occurred mainly during the first 12–24 months of treatment. The patients did not need blood transfusions. In 2009, due to the 6-month shortage of imiglucerase,³ 2 patients started taking miglustat. Both patients showed an increase in chitotriosidase and CCL18; both biomarkers returned to normal values when ERT was reintroduced at previous doses. These patients did not show hematologic or bone involvement and no modification

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