



CASE STUDY 3: NINA

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## KETOGENIC DIET, THE RECIPE AGAINST DESAFÍOR CHILDHOOD REFRACTORY EPILEPSY.

The control of childhood refractory epilepsy is one of the most complex medical challenges in paediatric neurology. It is a very disabling disease with a great impact on the quality of life, both of the patient and of their entire family.

In addition, we must not forget, the health expenditure generated by this pathology due to multiple treatments, hospital admissions, specialty consultations and multidisciplinary sessions.

We present the case of a patient from our unit who after years of multiple treatments, manages to control her epilepsy thanks to starting a KD.. The good control of their crises, allows improvement of the behavioral and motor state of these patients and consequently, an improvement of other associated pathologies such as gastroesophageal reflux and nutritional status.

### Patient profile

Girl of 10 years and 6 months, in follow-up in our unit from 4 months for connatal multicystic encephalopathy that occurs with:

- Cerebralpalsy spastic-dyst or nica tetraparesis of left predominance
- Secondary refractory epilepsy
- Disorder of the development of intelligence
- Moderate malnutrition. Carrier of percutaneous endoscopic gastrostomy (PEG)

### Background:

During pregnancy, Nina's mother had gestational maternal arterial hypertension. She was induced at 38 weeks due to severe pre-eclampsia however after a failed induction Nina was born by a caesarean section. At birth Nina's Apgar test showed 9/10/10 to 1/5/10 minutes of life respectively.

No incidents occured in the perinatal period. No neonatal jaundice occured and the extended neonatal metabolic screening was normal. Nina was exclusively breastfed.

### FAMILY HISTORY:

- A 35-year-old father. Psoriasis, treated with immunomodulators. No toxic habits, no other health incidents.
- Mother of 35 years. No previous pregnancies. Gestational arterial hypertension. Vitiligo and autoimmune hypothyroidism. No toxic habits.
- No other family history of interest.

### Clinical Assessment:

The patient at 4 months of age is evaluated for the first time in our center, after referral by her primary care pediatrician for difficulty in acquiring developmental milestones. In the first consultation of Neuropediatrics, there was little cephalic control, as well as axial hypotonia and microcephaly. She does not present a social smile or persecution with his gaze. It also associates convergent strabismus of the left eye. It does not show dysmorphic features or other alterations noteworthy to exploration.



Given these findings, an expanded study is requested including: Complete blood analysis (blood count, general profile, liver profile, renal profile, ferric profile, celiac profile, thyroid, as well as vitamins, trace elements and autoimmunity. It includes TORCH serologies), brain magnetic resonance and tandem mass study to rule out possible metabolopathy.

In the following months, the Nina presents an unfavorable evolution from the psychomotor point of view. She initiates clonal movements of the left lower limb and spasticity of both lower limbs. A requested imaging study of objective multicystic encephalomalacia, together with anodyne blood analysis and negative metabolic study, leads to a diagnosis of cerebral palsy of the spastic tetraparesis type of left predominance. Possible anoxic encephalopathy or previous infarction in the territory of bilateral middle cerebral artery in perinatal period.

In this context, multidisciplinary follow-up of the patient by: Neurology, Maturation, Early Care, Ophthalmology, Child Rehabilitation and Pediatric Gastroenterology begins from this moment. From the neurological point of view, the patient presents unfavorable evolution during the first years of life. At 10 months of age, she began myoclonus of the left lower limb increasingly frequent, subsequently associating palpebral myoclonus and hyper extension of the upper limbs. In the study of electroencephalogram (EEG), paroxysms of a complex tip-wave type at high amplitude in right temporo-parieto-occipital regions are objectified. It therefore begins with anticomyceal treatment (firstly, with alproic V-acid at standard doses).

For the next 2 years, she maintains a secondary epilepsy that is difficult to control. It requires treatment with multiple associated antiepileptics in different combinations and in increasing doses (Alproic V Acid, Levetiracetam, Lamotrigine, Piracetam, Clobazam, Clorazepam) without finding a satisfactory response to the control of seizures. In total, it has required up to a total of 4 simultaneous antiepileptics without good control.

In multiple reviews, the patient maintains generalized epileptic seizures with continuous electrical activity. In addition, due to the use of multiple treatments and high doses, her parents observed a worsening of Nina's general condition and found her more disconnected with the environment. This situation was a great professional challenge, causing repeated visits to the Emergency Department by the family and great anguish.

From the nutritional point of view, she was exclusively breastfed until 7 months of age. Complementary feeding was initiated without incident. She maintained an acceptable nutritional status until 15 months of age, after which, due to the evolution of basic disease, she began with greater spasticity and crisis of difficult control, presenting difficulties to cover caloric-protein requirements; nutritional support with hypercaloric formulas began at this time.

During the following months, she maintains a state of moderate malnutrition, with progressive deterioration at the neurological and nutritional level, starting with severe oropharyngeal dysphagia, so that at 2 years of age a percutaneous endoscopic gastrostomy is performed. From this moment, she begins being fed via her PEG with habitual feeding and supplements presenting favorable nutritional evolution.

At 8 years of age she maintains refractory secondary epilepsy that motivates numerous hospital admissions and outpatient reviews for treatment adjustment and reversal of epileptic status.

## Dietetic Intervention

Given the unfavorable situation, at this time the possible realization of KD as a treatment is raised from Child Neurology consultations, so a multidisciplinary consultation is carried out with Neurology and Paediatric Nutrition, and the family is proposed as a therapeutic option for refractory epilepsy.

The family accepts and carries out initial study, as well as training of the parents, starting KD with 3:1 ratio with good tolerance and acceptance. Ketonemia levels are maintained in an adequate range without relevant side effects and normal blood glucose at all times.

The evolution of the patient after 2 years of initiation of KD is very favorable. A decrease in antiseizure treatment is achieved, requiring only monotherapy with Levetiracetam; after a new consultation begins a withdrawal regimen and can be completely suspended.

## Clinical Outcome

At present, she is with total absence of crisis. She also has a noticeable improvement in both her cognitive-behavioral and motor state (appreciated by parents and specialists), even allowing her to wander with the help of a Bipedestador, among other advances.

Refractory or drug-resistant epilepsy is epilepsy that, despite a correct diagnosis, presents an unsatisfactory control of seizures despite the appropriate use of antiepileptic drugs, alone or in all possible combinations and at maximum tolerable doses. This type of epilepsy occurs in up to 30% of patients. The KD, despite being a well-known treatment, has now opened up as a new path in the treatment of refractory epilepsy, achieving promising results. This diet is based on the state theory of anabolism by metabolic fasting thanks to ketosis. For this, a diet rich in fats and with the lowest possible contribution of carbohydrates must be carried out, maintaining the necessary protein intake.



In a state of fasting, our greatest energy source is found in fatty acids, which will be transformed into ketone bodies and these will serve as our beta precursors for obtaining ATP through beta-oxidation in the mitochondria.

There are multiple theories about its mechanism of action at the brain level, although, to this day, none are conclusive. Among them we find: increased production of glutamate and GABA, activation of K channels with hyperpolarization effect of synaptic membrane, increased levels of cerebral ATP as a membrane stabilizer, among others. But in addition to the antiepileptic effect of ketone bodies, its direct neuroprotective effect stands out due to its antioxidant capacity. It has been observed in this type of epilepsy, one of up to 50% in frequency of crisis in 40-50% of patients and, a reduction of 90% or total disappearance up to 30% of children with secondary refractory epilepsy.

The design of this type of diet is based on the ketogenic capacity of each macronutrient. So, a classic KD is one in which 90% of the energy consumed comes from fats, with a minimum amount of carbohydrates and proteins. This should be individualised in each case and assess the possible existence of harmful effects. An attempt is made to maintain a level of ketonemia between 2-5 µmol/L. In addition, taking into account the swallowing and digestive disorders that affect these type of patients, we can make this diet with natural foods, with special formulas or through preparations for the parenteral route. These facilities allow the adherence and maintenance of this diet to be improved.

Despite this, many patients feel it is “difficult” to manage the diet, cook and adapt foods etc., assuming this a handicap for its use and maintenance in some patients. This difficulty can be overcome more easily in patients with enteral imentation devices.

## Learning Points

In the case of our patient it has been evident that the use of the diet has allowed an important cognitive-behavioral improvement but, in addition, it has allowed maintenance without crisis, also achieving the withdrawal of pharmacotherapy.

But perhaps the most interesting thing to emphasize is that the fact that the patient is a carrier of PEG, allows them to establish a diet more easily and precisely thanks to the formula used (Ketocal), which adapts perfectly to the nutritional needs of the patient maintaining the proper range of ketosis, adequate levels of macro and micronutrients and allowing simple use by the family, which means a better adherence to it and the achievement of such good results.

We therefore propose that the use of exclusive gastrostomy feeding with a specific formula facilitates the fulfillment and achievement of the objectives, allowing control of epilepsy, improving the quality of life, reducing the number of consultations to emergency services, hospital admissions, medical visits and complementary examinations both at the psychomotor level and the rest of the associated symptoms. Nor assuming in any case, an added complexity for the family and caregivers.

Therefore, we propose the initiation of diet in refractory epilepsy early in those patients with a probe or gastrostomy, since it entails little family repercussion and numerous benefits in the control of these patients.

## References

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