

# NEUROLOGIC IMPROVEMENT AFTER A HYPERCALORIC DIET IN TWO PATIENTS WITH PANTOTHENATE KINASE-ASSOCIATED NEURODEGENERATION

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## ABSTRACT

Pantothenate kinase-associated neurodegeneration (PKAN), caused by a mutation in the PANK2 gene, is a degenerative neurological disorder characterized by iron accumulation in the basal ganglia. As the disease progresses, patients experience increased energy needs that must be supplied by their diet. We present a case report of 2 siblings with neurodegeneration, 1 of them with malnutrition. After a 2 week calorie dense diet and with increasing body weight, an improvement of movement and functional limitations was observed as well as a reduction of 4 and 3 points respectively in the Barry Albright dystonia scale.

## BACKGROUND

Pantothenate Kinase-Associated Neurodegeneration (PKAN) is a rare neurological disorder caused by a mutation of the gene PANK2. The resulting metabolic defect affects the production of coenzyme A, which – among others- might interfere with lipid metabolism. The clinical expression is characterized by dystonia, cognitive impairment and Parkinsonism and is attributed to a primary lesion in the Globus pallidus consisting of a circumscribed gliosis surrounded by an accumulation of iron. However, the origin and mechanism of this lesion is not fully defined. With an onset usually before 10 years of age, the disease follows a progressive course.<sup>1</sup>

Weight loss frequently occurs during the late state of PKAN as progressive oromandibular dystonia contributes to a decline of nutritional status. In addition, patients with PKAN need an average of 8% more calories than normal to meet their basal energy demands. Apart from other metabolic deviations like a defective production of myelin precursors and an increased level of serum lactate, data suggest that these patients have higher resting energy needs.<sup>2,3</sup>

Here, we present a report of 2 genetically confirmed cases from the Dominican Republic showing that a hypercaloric diet may not only improve the general health in PKAN, but also the neurological status.

## CASE PRESENTATION

We present on 2 patients, both brothers, belonging to a cohort of genetically confirmed patients all suffering from the same missense mutation of the PANK2 gene (c.680 A>G, p.Y227C). Both individuals were subjected to a hypercaloric diet for 2 weeks. A balanced diet at the rate of 50 kcal/kg and 1.8 g/kg of protein, 30% fat, 53% carbohydrate and fiber intake of 30g per day had been calculated. As a nutritional supplement, Ensure® Plus, was added to their diets. Having received informed consent, this procedure was carried out as an individual therapeutic measure, in an emergency situation and without additional medication or other interventions.

The first patient was a 28 year old male with disease manifestations at 10 years of age. He was severely underweight, even though a gastric tube had been inserted due to extreme dysphagia. Initial BMI was 13.3 and increased to 14.3 after the diet. Likewise, the initial brachial perimeter was measured at 27 mm and increased to 28 mm. Waist circumference was maintained at 66 cm. Neurologically, there was severe oropharyngeal dystonia with almost complete anarthria, and swallowing was nearly impossible due to permanent tongue protrusion and mouth contractions. His neck and trunk presented important dystonic pulling and bending. The extremities were severely affected with increased tone, making it impossible for him to perform repetitive

movements, to grasp and to write as well as to stand and walk without assistance.

The second patient was a 24 year old male with disease manifestations at the age of 10. He could still swallow, but with some difficulty. His initial BMI was at the lower level of normal (18.8) and increased to 19.4 after the diet. His initial brachial perimeter was 31 cm and increased to 33 cm. The waist circumference was maintained at 74 cm. His neurological status was slightly better than in his brother's: using tricks, he was able to eat independently, but with minor complications and accompanied by occasional choking. He could pronounce some words, but not speak in coherent sentences because of mouth contractions and tongue protrusion. Trunk and cervical dystonia were moderate to severe with occasional bending and pulling. In spite of moderate involvement of arms and hands, he was able to grasp with some difficulty. Walking was impaired because of increased tone and occasional freezing, and he usually needed some assistance.

In both patients, the dystonia of the neck and trunk improved by 4 and 3 points respectively on the Barry-Albright scale (**Table 1**). We also saw some improvement in swallowing liquids in the first patient, but only while using the gastric tube. We saw some improvement in the second patient in grasping and walking. Both patients reported a reduction of their occasional painful cramps. The Barry-Albright scale however was not able to represent these changes.

## CONCLUSIONS

An improvement in patients suffering from neurodegenerative disease with a calorie dense diet is confirmed by early results of a trial in amyotrophic lateral sclerosis.<sup>4</sup> Improvements in this condition have mainly been attributed to improved energy balance.<sup>5</sup> Although we cannot be sure whether the neurologic improvement of our 2 cases is due to a similar effect, a hypercaloric diet might improve patients' conditions.

Since lipid metabolism appears to be widely affected in PKAN,<sup>3</sup> a calorie-rich diet might not only be of value in advanced cases with apparent malnutrition, but also in earlier stages of this metabolic disease. If our preliminary findings can be replicated in larger samples, a hypercaloric diet may be regarded as an uncomplicated though palliative measure to help PKAN patients, especially in those living in developing countries who are at increased risk of poor nutrition, due to their low socio-economic status.<sup>6</sup>

## ACKNOWLEDGEMENT

We thank the Dr. Juan Taveras Foundation (CEDIMAT, Santo Domingo) for financial support.

## References

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**Table 1:** BMI and scores on the Barry Albright dystonia scale before and after 2 weeks of a hypercaloric diet

	Patient 1 (male, 28 years)		Patient 2 (male, 24 years)	
	Before diet	After diet	Before diet	After diet
BMI	12.94	13.88	18.72	19.37
BAD scale total	22	18	20	17
Eyes	2	2	1	1
Mouth	4	4	4	4
Neck	4	2	4	2
Trunk	4	2	3	2
Upper extremities	4	4	4	4
Lower extremities	4	4	4	4

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