



The Importance of Nutritional Control and Diet Care in Huntington's Disease

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The first descriptions of chorea, from the Greek word “dance”, date back to the middle ages. The condition “Saint Vitus dance” was initially considered a curse, and was named so, because afflicted individuals were “cured” when they touched churches, which enshrined Saint Vitus relics [1]. In 1872, Dr. George Huntington published a report entitled “On chorea”, where he characterized the Huntington's disease (HD) as a genetic condition, which specifically causes degeneration in neurons of the striatum, resulting in a triad of symptoms, and also including emotional alterations and motor impairments [2]. The genetic defect underlying this autosomal dominant pathology, is a CAG triplet expansion (≥ 36 repeats), located in exon 1 of the HTT gene, which encodes the huntingtin in protein [3,4]. Aggregates formation in the cytosol and nucleus, leads to a generalized atrophy of the brain due to the presence of the mutated protein (polyQ). This mutated protein presents a modified folding, which produces a dominant effect on gain of function; and although it is widely expressed in brain neurons, and is ubiquitous in the body; its functionality still remains unknown [5].

HD has an estimated prevalence in Europe and the USA of 5-10 cases per 100,000 worldwide [6], and the symptoms begin about halfway through the average human lifespan (30-50 years of age), progressive and continuously evolving (15-20 years) until the end of the disease, which coincides with the end of life by dementia and death, or in some cases, suicide [7,8]. Despite the fact that scientific community has performed therapeutic advances in slowing the disease progression down and relieved suffering in the patients, a definitive treatment has not emerged yet [9].

Although HD is considered primarily a neurological disorder, in addition to neuronal degeneration and motor modifications, the patient has to face a drastic weight loss-proportional to the size of the CAG triplet expansion [10]. Low weight and unintentional weight loss ($> 10\%$ within the last 3-6 months) are frequent during all phases of the disease and its etiology is multifactorial [11-13]. Moreover, the weight is influenced by severe digestive alterations, dysphagia and eating disorders.

Neurological physicians describe that the first signs of the disease are very mild and may include small changes in personality or character. Forgetfulness, clumsiness and erratic movements of the fingers or toes may be a sign. Often, during these early stages of the disease, individuals do not visit any doctor, and may take several years

until a medical diagnosis is made. The disease manifests itself very slowly. If family medical record exits a predictive genetic diagnosis could be done. However, in the absence of genetic follow up because a *de novo* mutation occurs, the delay in the diagnosis could be longer. The estimated probability that a new penetrant HD allele (≥ 36) could arise, in a male carrying a high normal allele (27-35 CAG repeats) during the paternal transmission due to the instability of the repeats, ranges from 1/6,241 to 1/951 [14].

As HD progresses, brief, abrupt, irregular, unpredictable, non-stereotyped movements; in milder cases the patient often shows restlessness and clumsiness. These movements affect various body parts, and interfere with speech, swallowing, posture and gait [15]. Moreover, constant movement increases energy expenditure and requires following a high calorie diet [16]. In advance stages, when oral diet may not provide for the patient's nutritional needs and due to cachexia, enteral feeding must be considered [17]. Not only before the symptoms appear, but also throughout the duration of the disease, nutritional aspects and diet care in individuals diagnosed with HD should be followed, by specific healthcare professionals. Recommendations are provided by limited guidelines, which are focused on specific instructions in the early, middle and advance stages of the disease, for patients, families and caregivers.

The research related to HD's diet is limited; however dietary interventions in HD asymptomatic carriers have been described in a close connection with the subsequent onset of the disease. One observational study has reported that high consumption of dairy products has a two-fold increased risk of phenoconversion [18]. Also, higher baseline uric acid levels are associated with slower HD progression, which potentially suggests that rich purines food could be beneficial in an HD's diet [19]. Moreover, in a global perspective, Mediterranean diet does not have impact on HD onset, although higher caloric intake is associated with a risk of phenoconversion [20]. On the other hand, recently, a Spanish multicenter dietary intake study has reported that an adequate dietary intake prevents against weight loss in patients with advanced HD, but it is not associated with better functional state [21]. However, the information related to diet and HD's phenoconversion is limited, being not definitive enough to allow a specific conclusion. The small number of studies and their no replications lead us to carefully consider those outcomes.

Metabolic aspects such as glucose and lipid profiles, control weight, nutrient absorption could represent key factors in the quality of life for patients with HD, being heavily influential in morbidity and mortality. For example: length of hospital care, severity of the disease and efficiency of the pharmacological therapies; representing clinical relevance for its potential contribution to the symptoms, treatment and influence on the course of the disease. Studies on diet and energy expenditure in pre-manifest HD carriers may provide knowledge for interventions to modify specific components of the diet that may delay the onset of the disease. Additionally, research should include the study on the patient status after the onset, when the nutritional control and diet care become even more essential.

The ongoing and future research should be focused on a treatment approach, which would include peripheral alterations and also central pathologies in HD, setting up the basis for a more effective therapeutic strategy; the maintenance of a healthy nervous system is closely linked to the metabolic health.

The support of the importance of nutritional control and diet care in Huntington's disease will be provided by the Journal of Nutritional Medicine and Diet Care. The journal will constitute a platform for the interaction between the experts around the world, and will aim at spreading scientific discoveries, and major milestones in the field not only of HD, but also of a wide range of neurological syndromes (eg. Alzheimer disease, Down syndrome and Friedreich ataxia), which evolve in parallel with the metabolic alterations.

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