

Characterisation of Depressive Symptoms in Huntington's Disease and of the Pharmacological Treatment for Depression: patterns, trends and Statistical Analysis of Enroll-HD Dataset

Background: Huntington's Disease (HD) is a rare autosomal dominant genetic disorder characterised by a triad of motor, psychiatric and cognitive symptoms. Among the psychiatric manifestations, depression is very common and may appear several years prior to motor symptoms, correlating with suicide and resulting in higher rates of premature death in HD. Although the symptoms and signs of HD are distressing, depression and suicidal ideation are treatable conditions. Clinical guidelines are lacking due to the dearth of specific data for tailored approaches in HD.

Objective: The aim of this study was to describe the pharmacological treatments of depression in Huntington's Disease and compare the results with current clinical practices using Enroll-HD an international disease register of HD.

Methods: The methods used in this study included the examination of the quality of the data provided by Enroll-HD, the characterisation of the drug treatments and of the participants presenting symptoms of depression using customised Excel tools. Analysis was carried out using One-Way ANOVA and Chi-Square tests; a mixed model was utilised to evaluate factors influencing depression scores over time and, the logistic regression technique was used to assess factors influencing depression scores and those associated with suicide using SPSS version 26.

Results: The analysis of the data indicated that it was of satisfactory quality. The characterisation of participants with depressive symptoms demonstrated a prevalence of 23.4% of depression using the HADS scale (N=3,910). There was a high frequency of the use of other agents rather than traditional serotonergic drugs to treat depression in HD affected individuals when compared to the HD non-affected control group. When evaluating depression over time, results showed that it decreased gradually. The logistic regression tests indicated that younger subjects, with no history of involuntary movements or irritability and an absence of motor signs were most likely to bring their depression scores down to a less depressed level when compared to older subjects. Alcohol abuse, HD category (Enroll-HD), TFC score, motor score, disease stage, independence scale and history of cognitive impairment were all factors associated with death by suicide.

Discussion: The statistical analyses provided valuable insights about the management of depression in the context of HD. An aspect worth mentioning in this study is the use of antipsychotics as an alternative for treating depression, as their multiple actions may benefit HD patients by treating more than one symptom (chorea, sleep disturbances, weight loss) and also in terms of reduction of side-effects, drug interactions, polypharmacy and preserving cognitive function by reducing the anticholinergic burden in the long term. Additionally, both logistic regression analyses generated results that provide preliminary evidence for a profile of patients who are more likely to see a reduction in the symptoms of depression and of those who may be at risk the of committing suicide.

Conclusion: The present study has gone some way towards enhancing the understanding of depression in HD and has provided preliminary ideas and starting points for the development of further and powerful clinical trials. Patients suffering with HD have multiple needs, and, consequently, require multifaceted tailored care. Although HD and depression in HD remain as complex topics and still face several challenges, the hope that new clinical approaches may significantly improve the consequences of HD in patients' activities of daily living and ultimately maximize their quality of life, motivates studies like this present one.