Abstract

Background. Chorea is a prominent motor dysfunction in Huntington's disease (HD). Deutetrabenazine, a vesicular monoamine transporter 2 (VMAT2) inhibitor, is FDA-approved for the treatment of chorea in HD. In the pivotal, 12-week First-HD trial, deutetrabenazine treatment reduced the Unified Huntington's Disease Rating Scale (UHDRS) total maximal chorea (TMC) score versus placebo. ARC-HD, an open-label extension study, evaluated long-term safety and efficacy of deutetrabenazine dosed in a response-driven manner for treatment of HD chorea.
Methods. Patients who completed First-HD (Rollover) and patients who converted overnight from a stable dose of tetrabenazine (Switch) were included. Safety was assessed over the entire treatment period; exposure-adjusted incidence rates (EAIRs; adverse events [AEs] per person-year) were calculated. A stable, post-titration time point of 8 weeks was chosen for efficacy analyses.
Results. Of 119 patients enrolled (Rollover, n=82; Switch, n=37), 100 (84%) completed ≥1 year of treatment (mean [SD] follow-up, 119 [48] weeks). End of study EAIRs for patients in the Rollover and Switch cohorts, respectively, were: any AE, 2.6 and 4.3; serious AEs, 0.13 and 0.14; AEs leading to dose suspension, 0.05 and 0.04. Overall, 68% and 73% of patients in Rollover and Switch, respectively, experienced a study drug–related AE. Most common AEs possibly related to study drug were somnolence (17% Rollover; 27% Switch), depression (23%; 19%), anxiety (9%; 11%), insomnia (10%; 8%), and akathisia (9%; 14%). Rates of AEs of interest include suicidality (9%; 3%) and parkinsonism (6%; 11%). In both cohorts, mean UHDRS TMC score and total motor score (TMS) decreased from baseline to Week 8; mean (SD) change in TMC score (units) was –4.4 (3.1) and –2.1 (3.3) and change in TMS was –7.1 (7.3) and –2.4 (8.7) in Rollover and Switch, respectively. While receiving stable dosing from Week 8 to 132 (or end of treatment), patients showed minimal change in TMC score (0.9 [5.0]), but TMS increased compared to Week 8 (9.0 [11.3]). Upon drug withdrawal, there were no remarkable AEs and TMC scores increased 4.4 (3.7) units compared to end of treatment.
Conclusions. The type and severity of AEs observed in long-term deutetrabenazine exposure are consistent with the previous study. Efficacy in reducing chorea persisted over time. There was no unexpected worsening of HD or chorea associated with HD upon deutetrabenazine withdrawal.
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Challenges in Treating Tardive Dyskinesia: Assessing the Impact of Virtual Medical Education

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Abstract

Introduction. Tardive Dyskinesia (TD) refers to abnormal, involuntary, choreoathetoid movements of the tongue, lips, face, trunk, and extremities and is associated with long-term exposure to dopamine-blocking agents, such as antipsychotic medications. Once established, these movements usually persist. The movements are disfiguring and can bring unwanted attention to affected individuals. When severe, especially if the respiratory muscles are affected, the movements can be disabling, limit activity, and reduce quality of life. The prevalence is 7.2% in individuals on newer antipsychotics who have never been exposed to older neuroleptics. Until recently, there were no effective treatments for TD. In recent years, many new treatments have been investigated for the treatment of TD, including valbenazine, deutetrabenazine, and branched chain amino acids. Valbenazine first, followed by deutetrabenazine are FDA approved to treat TD. A virtual broadcast was developed to assess the ability of continuing medical education (CME) to improve awareness of the recognition and treatment of TD among psychiatrists.
Methods. The virtual broadcast (May 9, 2020) consisted of a two-hour, live-streamed discussion between two expert faculty. Impact of the educational activity was assessed by comparing psychiatrists' responses to four identical questions presented before and directly after activity participation. A follow-up survey was sent to all participants six-weeks post-activity to measure performance in practice changes. A chi-square test was used to identify significant differences between pre- and post-assessment responses. Cohen's *d* was used to calculate the effect size of the virtual broadcast.
Results. Activity participation resulted in a noticeable educational effect among psychiatrists (n=621; d=6.12, P<.001). The following areas showed significant (P<0.05) pre- vs post-educational improvements: recognition of movements in patients with TD, rate of TD in SGA exposed patients, treatment options for TD (on and off-label), and treatment of TD using VMAT inhibitors. Additionally, 54% of psychiatrists reported a change in practice performance as a result of the education received in the activity, including utilization of a standard scale to evaluate movement disorders and educate patients and family members about potential for TD, how to recognize symptoms, and when to treat.
Conclusions. The results indicated that a CME-certified two-hour virtual broadcast was effective at improving knowledge among psychiatrists for the recognition and treatment of TD. This knowledge also resulted in positive changes in practice performance post-activity. Future education should continue to address best practices in the diagnosis, treatment and management of patients with TD, as there remains an increased need for tailored CME among psychiatrists.
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Quantifying Psychopathology in Rapid Readmissions

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