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.
Funding. Neurocrine Biosciences, Inc.

Quantifying Psychopathology in Rapid Readmissions

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Abstract

Psychiatric readmissions contribute to a significant cost and healthcare burden to physicians, hospitals, and the healthcare system as an entity. Furthermore, as part of the Affordable Care Act, the Centers for Medicare and Medicaid Services (CMS) began to reduce financial coverage to hospitals with overwhelming rehospitalization rates. The purpose of this study was to do a systematic analysis on inpatient psychiatric readmission data and identify co-morbidities and risk factors that lead to high readmission rates. The data collection includes 163 patients with a total of 348 readmissions over the span of 90 days at one inner-city hospital in the Chicagoland area. Study findings suggest that higher rates of readmission are linked to cocaine abuse in both male and female populations. Diagnosis of bipolar in females and schizoaffective disorder in male populations were the among the highest for readmission. Key social factors such as homelessness and low socioeconomic status were identified to contribute to a large proportion of psychiatric readmission burden. However, an overwhelming amount of information was missing due to unobtained labs and lack of current patient social history. By using this data as well as data from electronic medical records (EMRs) to further investigate and identify other features of at-risk patients, hospitals can potentially address these markers to lower readmission rates. Ultimately, a higher understanding of the patients' needs can be understood and can help develop standardized plans of care for prevalent psychiatric illnesses in these populations.

Prescription Stimulant Misuse and Abuse: Characterization of Exposures Managed by United States (US) Poison Centers

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Abstract

The National Poison Data System (NPDS), is the data warehouse for the 55 US regional poison centers. While the primary role of a poison center is to provide medical management to the public and healthcare providers, a standardized database is used to collect case data. These data are routinely used to evaluate drug safety, including characterization of prescription medication misuse and abuse. While an effective therapy for attention deficit/hyperactivity disorder (ADHD), prescription stimulant medications (RxStim) may be misused and abused, a behavior that has been noted as an emerging public health concern particularly in relation to polysubstance abuse. The objective of this study was to characterize intentional exposures to RxStim in patients age >12 y of age as managed by US poison centers from Jan 2015- 31 Dec 2019.

NPDS cases of intentional exposure to a RxStim in a patient >12 y managed from Jan 2015-Dec 2019 were included for analysis. Intentional exposures are defined in the NPDS manual as exposures that involve a purposeful action. These include intentional misuse, intentional abuse and intentional unknown cases. Intentional suspected suicide cases were excluded.

A total of 12,972 cases met inclusion criteria, of which 62.5% involved a male patient. Most patients were aged 13–19 y (34.7%) or 20–39 y (50.5%). Over one-half (53.3%) of cases were intentional abuse, 29.1% intentional misuse, and 17.6% intentional unknown. While most exposures were via oral route of administration (90.7%), 9.5% were via inhalation/intranasal and 2.4% via injection (multiple routes may be reported). Other substances in addition to a RxStim were involved in 48.2% of cases, including benzodiazepines (11.2%), alcohol (8.8%), marijuana (5.1%), cocaine (3.7%), methamphetamine (3.0%) and atypical antipsychotics (2.5%). The majority of cases resulted in significant medical outcome (60.3%). This included 39.3% with a moderate effect (medical attention indicated, not life-threatening), 6.1% major effect (life-threatening), 1.0% death and 14.0% lost to follow-up but judged as a potentially toxic exposure. Another 22.4% reported minimally bothersome effects. Admission to a healthcare facility was reported for 1 out of 3 cases and another 36.3% were treated/evaluated/released from a healthcare service. An average of 2.3 clinical effects were reported per exposure, the most common being neurological effects (53.2%; examples include agitation, drowsiness/lethargy, confusion, hallucinations/delusions, tremor), cardiovascular effects (50.8%; examples include tachycardia, hypertension), and gastrointestinal effects (9.4%; examples include vomiting, nausea).

RxStim misuse and abuse cases managed by US poison centers most often leads to significant medical outcomes which require medical attention. The role of these medications in polysubstance abuse is concerning and suggestive of needed strategies to address this increasingly important public health concern.

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Substance Use Trajectories: Nonmedical Use (NMU) of Prescription Stimulants via Non-Oral Routes of Administration Among Adults Recruited from Reddit

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