

doctors had hated him and put him on Lithium as a form of punishment. He claims that Lithium, as a result, has significantly affected him negatively and also damaged his nerves. This led the authors to explore the significance of use of Lithium in people with schizoaffective disorders and also bipolar affective disorders. We also discuss the disease course in the patient and his clinical response to use of various psychotropic medications.

CONCLUSIONS: The case exemplifies the negative effects of Lithium when used as a mood stabilizer in patient population that is susceptible to its adverse effects due to various factors.

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Heroin Dependence as an Enantiopathy to Quetiapine-Induced Restless Leg Syndrome

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ABSTRACT: Introduction: Use of heroin in self-management of Restless Leg Syndrome (RLS) has not heretofore been described. Such a case is presented.

METHODS: Case study: This 29 years old right handed male presented with a long history of major depressive disorder, generalized anxiety disorder and opioid dependence. The Patient felt compelled to take quetiapine since was the only drug found to be effective in controlling racing thoughts, Major Depressive Disorder with psychotic features. Prior to use of quetiapine the patient never experienced RLS. Quetiapine in doses ranging from 25 mg to 300 mg a day precipitated severe RLS whereby he was forced to move his leg all night long leading to poor sleep quality. The RLS was unresponsive to Gabapentin and Benzotropine, however it was eliminated with a variety of opioids including hydrocodone, buprenorphine, buprenorphine/naloxone. Particularly sensitive to heroin, 1/2 twenty dollar bag, self-administered IV prior to sleep eliminated the RLS immediately, but when injected more than four hours before sleep it had no effect. RLS acted only when induced with quetiapine, since he wished to continue quetiapine to control his mood, he felt compelled to self-

medicate with heroin to stop RLS side effects. He showed no other signs of extrapyramidal symptomatology or evidence of any other movement disorder.

RESULTS: Abnormalities in physical examination: General: Abundance of tattoos on body and face. Cranial Nerve (CN): CN I: Alcohol Sniff Test: 7 cm (anosmia). CN II: Anisocoria OD 5 mm OS 2 mm. Motor Examination: drift testing: right pronator drift. Cerebellar: Finger to Nose: end point dysmetria bilaterally. Low amplitude high frequency tremor in both upper extremities on extension. Sensory Examination: decreased graphesthesia in both upper extremities. Reflexes: 3+ knee jerks, absent ankle jerks, positive jaw jerk, bilateral palmo-mental reflex is present.

DISCUSSION: This patient has a long history of quetiapine use due to his major depressive disorder with psychotic features and subsequent self-administration of IV heroin reportedly to reduce the symptoms of quetiapine-induced RLS. Heroin elevates dopamine levels in forebrain by blocking inhibitory GABA interneurons near the ventral tegmental area, leading to activation of mesocorticolimbic dopaminergic neurons (Nakagawa 2008, Steidl 2011). The time frame of opioid administration has a critical impact on its efficacy in improving RLS symptoms. However, the drug's effects only up to 3 to 6 hours (Buchfuhrer 2012). In this case administration of heroin more than 4 hours before sleep would not alleviate the RLS symptoms. Patient chose the time of injection, not for hedonic pleasure of heroin, but rather to prevent RLS symptoms. In those with heroin dependence, the possibility that is a result of self-medication of underlying movement disorder warrants additional investigation. In those with RLS who are unresponsive to other treatment modalities, a trial of opioids maybe worthwhile.

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Predictors of Tardive Dyskinesia in Psychiatric Patients Taking Concomitant Antipsychotics

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ABSTRACT: Background: Tardive dyskinesia (TD) is typically caused by exposure to antipsychotics, is often irreversible, and can be debilitating. TD symptoms can increase the social stigma of patients with comorbid psychiatric disorders, negatively impact quality of life, and potentially increase medical morbidity and mortality.

An increased risk of developing TD has been associated with factors such as older age, female sex, underlying mental illness, and long-term use and higher doses of antipsychotics. The association of TD with the use of typical versus atypical antipsychotics has also been evaluated, with mixed results. To date, predictive models assessing the joint effect of clinical characteristics on TD risk have not been developed and validated in the US population.

STUDY OBJECTIVE: To develop a prediction model to identify patient and treatment characteristics associated with the occurrence of TD among patients with psychiatric disorders taking antipsychotic medications, using a retrospective database analysis.

METHODS: Adult patients with schizophrenia, major depressive disorder, or bipolar disorder who were taking oral antipsychotics, and who had 6 months of data prior to the index date were identified from Medicaid claims from six US states. The index date was defined as the date of the first claim for an antipsychotic drug after a claim for the underlying disorder but before TD diagnosis. A multivariate Cox prediction model was developed using a cross-validated version of the least absolute shrinkage and selection operator (LASSO) regression method to improve prediction accuracy and interpretability of the model. The predictive performance was assessed in a separate validation set via model discrimination (concordance) and calibration.

RESULTS: A total of 189,415 patients were identified: 66,723 with bipolar disorder, 68,573 with depressive disorder, and 54,119 with schizophrenia. The selected prediction model had a clinically meaningful concordance of 70% and was well calibrated ($P=0.46$ for Hosmer–Lemeshow goodness-of-fit test). Patient's age at index date (hazard ratio [HR]: 1.03), diagnosis of schizophrenia (HR: 1.73), dosage of antipsychotic at index date (up to 100 mg/day chlorpromazine equivalent; HR: 1.40), and presence of bipolar and related disorders (HR: 1.16) were significantly associated with an increased risk of TD diagnosis. Use of atypical antipsychotics at index date was associated with a modest reduction in the risk of TD (HR = 0.94).

CONCLUSIONS: This study identified a group of factors associated with the development of TD among patients with psychiatric disorders treated with antipsychotics. This may allow physicians to better monitor their patients receiving antipsychotics, allowing for the prompt identification and treatment of TD to help maintain quality of life.

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Long-term Outcomes with Aripiprazole Lauroxil for the Treatment of Schizophrenia: A 2-Year, Phase 3, Multicenter Extension Study

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ABSTRACT: Background: One of the challenges in schizophrenia long-term trials is that clinical outcomes are often confounded by covert nonadherence to prescribed oral antipsychotics. This is a post hoc analysis (>2 years) of the symptoms and illness trajectory of patients treated with the long-acting injectable (LAI) antipsychotic aripiprazole lauroxil (AL). As adherence to LAIs can be monitored, these data could assess outcome trajectories unaffected by medication discontinuations that may occur with oral antipsychotics.

METHODS: The efficacy and safety of once-monthly AL (441 or 882 mg) for the treatment of schizophrenia were previously demonstrated in a phase 3 trial, followed by a 52-week, long-term safety study of two AL doses (441 or 882 mg once monthly; patients continuing from the phase 3 study remained on their fixed AL dose [NCT01626456]), after which patients could enroll in a second long-term extension study. Patients entering the second long-term study continued on their fixed AL dose, with a variable follow-up period of up to 128 additional weeks (NCT01895452). In this post hoc analysis, the extension studies were combined to provide continuous outcome data over 2 years' follow-up. The 12-week assessment visit (rather than the first visit) in the first extension study was chosen as the baseline to account for patients entering this study with variable AL exposure histories (with/without prior AL exposure). We report on the trajectory of symptoms and illness severity for >2 years (up to 112 weeks) after the 12-week visit using the Positive and Negative Syndrome Scale (PANSS) total and Clinical Global Impression–Severity (CGI-S) scale scores. Course of illness was measured as the difference in PANSS and CGI-S scale scores within dose