ICD-10 diagnoses and medications) was assessed during the 12-months following AAP initiation. Cohorts with and without EPS were defined. Demographics, clinical characteristics, and healthcare resource use and costs over 12 months following the first EPS claim (EPS) or randomly assigned index date (Non-EPS) were assessed.
Results. A total of 11,642 patients with schizophrenia were identified; 21.2% developed EPS in the 12-months following AAP initiation. EPS and Non-EPS cohorts included 2,295 (mean age 38, 61% male, CCI 0.6) and 5,607 (mean age 39, 57% male, CCI 0.7) patients, respectively. Over the 12-month post-index period, EPS cohort had significantly higher rates of all-cause (30.2% vs. 24.6%, p<0.001) and schizophrenia-related hospitalizations (22.5% vs. 12.9%, p<0.001) and schizophrenia-related emergency room visits (25.5% vs. 16.7%, p<0.001) compared to Non-EPS cohort. All-cause ($25,911 vs. $21,550, p<0.001) and schizophrenia-related healthcare costs ($12,134 vs. $6,230, p<0.001) were significantly higher in EPS vs. Non-EPS cohort.
Conclusions. In the 12 months following AAP initiation, over 20% of schizophrenia patients developed EPS, which was associated with increased healthcare resource utilization and costs. Treatment options that minimize EPS may reduce the economic burden of schizophrenia.
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Case History. A 32-year-old male presented to the emergency department (ED) for altered mental status (AMS). He has a documented history of anxiety but was never treated with prescription medications. No history of substance use was documented. He was self-medicating with concurrent use of tianeptine (atypical antidepressant with mu agonist properties,) phenibut (GABA mimetic) and etizolam (a benzodiazepine-like agent). During his stay, he was agitated and delirious with reports of visual hallucinations. Neuroimaging and lab studies were within normal limits, EEG showed no seizure activity. Over the course of his hospital stay, he was started on Depakote for agitation, a Valium taper for suspected benzodiazepine withdrawal and prevention of seizures, Seroquel for delirium, and baclofen for suspected GABAergic withdrawal symptoms. The patient's AMS improved and he was discharged on hospital day 10.
Conclusions. This case illustrates the difficulty managing poly-substance use/abuse and stresses the importance for physicians to screen for psychoactive agents purchased over the internet or over the counter to improve treatment outcomes. Continued discussions with patients regarding risks/benefits of use of such substances would be beneficial and help increase awareness.

Is this Withdrawal or Intoxication? Case Report Regarding Complications of Unregulated Use of Tianeptine, Etizolam, and Phenibut in the USA

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Abstract

Background. The internet allows easy access for the sales of psychoactive agents that are not regulated by the FDA. Some of those agents are used to help manage anxiety, depression and sleep, such as tianeptine, etizolam, and phenibut. These medications have the potential for abuse and potentially leading to altered mental status when intoxicated or withdrawing. This presents a challenge to clinicians who may not be aware of availability of such substances. Available literature has discussed the use of above substances individually, but how do you treat if there is use of more than one substance with different mechanisms of actions? Here we present a case of an adult male who has used all three agents simultaneously, leading to a hospital admission.

Safety of Using a Combinatorial Pharmacogenomic Test for Patients with Major Depressive Disorder in the GUIDED trial

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Abstract

Background. Pharmacogenomic testing has emerged to aid medication selection for patients with major depressive disorder (MDD) by identifying potential gene-drug interactions (GDI). Many pharmacogenomic tests are available with varying levels of supporting evidence, including direct-to-consumer and physician-ordered tests. We retrospectively evaluated the safety of using a physician-ordered combinatorial pharmacogenomic test (GeneSight) to guide medication selection for patients with MDD in a large, randomized, controlled trial (GUIDED).

Materials and Methods. Patients diagnosed with MDD who had an inadequate response to ≥1 psychotropic medication were randomized to treatment as usual (TAU) or combinatorial pharmacogenomic test-guided care (guided-care). All received combinatorial pharmacogenomic testing and medications were categorized by predicted GDI (no, moderate, or significant GDI). Patients and raters were blinded to study arm, and physicians were blinded to test results for patients in TAU, through week 8. Measures included adverse events (AEs, present/absent), worsening suicidal ideation (increase of ≥1 on the corresponding HAM-D17 question), or symptom worsening (HAM-D17 increase of ≥1). These measures were evaluated based on medication changes [add only, drop only, switch (add and drop), any, and none] and study arm, as well as baseline medication GDI.

Results. Most patients had a medication change between baseline and week 8 (938/1,166; 80.5%), including 269 (23.1%) who added only, 80 (6.9%) who dropped only, and 589 (50.5%) who switched medications. In the full cohort, changing medications resulted in an increased relative risk (RR) of experiencing AEs at both week 4 and 8 [RR 2.00 (95% CI 1.41–2.83) and RR 2.25 (95% CI 1.39–3.65), respectively]. This was true regardless of arm, with no significant difference observed between guided-care and TAU, though the RRs for guided-care were lower than for TAU. Medication change was not associated with increased suicidal ideation or symptom worsening, regardless of study arm or type of medication change. Special attention was focused on patients who entered the study taking medications identified by pharmacogenomic testing as likely having significant GDI; those who were only taking medications subject to no or moderate GDI at week 8 were significantly less likely to experience AEs than those who were still taking at least one medication subject to significant GDI (RR 0.39, 95% CI 0.15–0.99, p=0.048). No other significant differences in risk were observed at week 8.

Conclusion. These data indicate that patient safety in the combinatorial pharmacogenomic test-guided care arm was no worse than TAU in the GUIDED trial. Moreover, combinatorial pharmacogenomic-guided medication selection may reduce some safety concerns. Collectively, these data demonstrate that combinatorial pharmacogenomic testing can be adopted safely into clinical practice without risking symptom degradation among patients.

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A Combination of Olanzapine and Samidorphan in Adults with Schizophrenia and Bipolar I Disorder: Overview of Clinical Data

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Abstract

Objectives. Olanzapine effectively treats schizophrenia and bipolar I disorder (BD-I); however, its use is hindered by significant weight gain. A combination of olanzapine and samidorphan (OLZ/SAM) is in development to provide the efficacy of olanzapine while mitigating olanzapine-associated weight gain through opioid-receptor blockade. Here, we summarize OLZ/SAM clinical data.

Methods. The OLZ/SAM development program consists of 18 phase 1–3 clinical studies evaluating antipsychotic and weight mitigation efficacy of OLZ/SAM, along with pharmacokinetics, safety, and tolerability. Safety evaluation also included metabolic laboratory assessments.

Results. OLZ/SAM significantly improved psychotic symptoms (measured by Positive and Negative Syndrome Scale); improvements were similar to that observed with olanzapine vs placebo. OLZ/SAM resulted in significantly less weight gain than olanzapine. Additionally, 2 long-term phase 3 extension studies confirmed the durability of antipsychotic effect, as well as stabilization of weight and metabolic parameters in those continuing treatment. Supporting the potential use of OLZ/SAM in BD-I, OLZ/SAM or olanzapine resulted in bioequivalent olanzapine plasma concentrations, and OLZ/SAM did not affect lithium or valproate pharmacokinetics. OLZ/SAM treatment had no clinically relevant effects on ECG parameters (including QTc interval). OLZ/SAM and olanzapine safety were similar, except for reduced weight gain with OLZ/SAM; no additional safety risks were identified.

Conclusion. Data across 18 OLZ/SAM studies in >1600 subjects support an antipsychotic efficacy and safety profile for OLZ/SAM that is similar to olanzapine, with significantly less weight gain than olanzapine. OLZ/SAM is a potential new treatment for schizophrenia and BD-I patients needing efficacious long-term treatment with reduced risk of weight gain.

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