to the HLA typing results. HLA typing results were also compared to the tag SNP rs1061235 results to calculate the false positive rate.
Results. There was 100% concordance between our real-time PCR results and expected results based on HLA typing. 89 sample results for tag SNP rs1061235 were compared to HLA typing results. 75/89 samples had a rs1061235 variant, but 31/75 (41%) samples did not have the HLA-A*31:01 type, thus defining the false positive rate of the tag SNP for our population. We theorized there would be a small subset of rare HLA-A types that would interfere with the assay and we tested the three types available to us. We confirmed that 3 of the HLA types (HLA-A*31:04, 31:12, and 31:16) result falsely positive due to sequence homology with 31:01. There is no known literature indicating whether these rare HLA-A*31 subtypes are associated with cutaneous adverse reactions. These 3 HLA types and the other suspected interfering HLA types have limited frequency data sets and are expected to occur rarely in our patient population; we expect these HLA types make up less than 0.003% of the our population. Our assay specificity for the validation is >99%.
Conclusions. Our custom real-time PCR assay for detection of HLA-A*31:01 is significantly more specific than the commonly used tag SNP rs1061235. Clinicians considering carbamazepine therapy for their patients will have a better understanding of cutaneous adverse reaction risk and can make improved personalized treatment decisions. This quick, cost effective assay allows more patients in need of carbamazepine treatment to benefit from its use.
Funding. Genomind, Inc.

Can Low Dose Sertraline Cause Serotonin Syndrome in Pediatric Patients? 2 Case Reports

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Abstract

Background. Serotonin syndrome is a potentially life-threatening condition associated with increased serotonergic activity in the central nervous system. Serotonin syndrome is underreported complication of pharmacotherapy. The Hunter Criteria for serotonin syndrome (SS) are fulfilled if the patient has taken a serotonergic agent and has one of the following symptoms: 1) spontaneous clonus, 2) inducible clonus and agitation or diaphoresis, 3) ocular clonus and agitation or diaphoresis, 4) tremor and hyperreflexia, 5) hypertonia, or 6) temperature above 38 C and ocular clonus or inducible clonus.
Method. Patient A was a 16-year-old Caucasian male with history of major depressive disorder, social anxiety and OCD who presented to the emergency room with multiple complaints: twitching of bilateral cheeks, intermittent tremor of his hands and feet, mental fogginess/confusion, stuttering when attempting to speak, agitation, profuse sweating and headache. 3 weeks prior, his sertraline dose was increased from 25mg daily to 50 mg daily. His physical exam was remarkable for elevated blood pressure and heart rate as well as hyperreflexia noted on patellar reflex testing. No significant abnormalities were noted on routine labs. He was told his symptoms were likely due to medication side effects. The patient was discharged with instructions to decrease his sertraline dose from 50 mg to 25 mg daily and follow up with his outpatient psychiatrist. 2 days later the patient was seen at the outpatient child psychiatry clinic and he was advised to taper off sertraline completely by taking 12.5mg daily for 3 days before cessation. After stopping the medication, the patient's symptoms resolved.
Patient B was a 16-year-old female with generalized anxiety disorder and major depressive disorder who presented to the general pediatric clinic with progressively worsening hand tremors and body shaking since her Zoloft dose was increased from 25mg to 50mg daily. She also felt it was more difficult to hold objects. At the physical exam she had an elevated heart rate to 93 and elevated blood pressure to 182/75. Her deep tendon reflexes were 4+ bilaterally. Upon consultation with child psychiatry, the patient was recommended to taper off sertraline. After the discontinuation of sertraline, her symptoms resolved.
Result. These 2 patients developed mild to moderate symptoms of serotonin syndrome with low doses of sertraline. Symptoms resolved after the discontinuation of the SSRI.
Discussion. In the pediatric patient population, serotonin syndrome can develop even with lower doses of an SSRI. To avoid a missed diagnosis, clinicians should familiarize themselves with the Hunter Criteria for serotonin syndrome. It is also vital to educate parents and caregivers about the toxicities of SSRIs, including serotonin syndrome, so they may monitor treatment and take appropriate action if needed.

Phase 3 Safety and Tolerability Results of the Combination Olanzapine and Samidorphan in Patients with Schizophrenia: The 1 Year ENLIGHTEN-2-Extension

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Abstract

Objective. Combination olanzapine and samidorphan (OLZ/SAM) is in development for treatment of schizophrenia and bipolar I disorder and is intended to provide the antipsychotic efficacy of olanzapine while mitigating olanzapine-associated weight gain. This 52-week open-label extension study (NCT02873208; ENLIGHTEN-2-EXT) in schizophrenia assessed the safety and tolerability of OLZ/SAM. Methods: Patients completing the 24-week, randomized,

https://doi.org/10.1017/S1092852920002473 Published online by Cambridge University Press