G96 Fatal Diabetic Ketoacidosis and Antipsychotic Medication

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After attending this presentation, attendees will understand the relationship between antipsychotic medications and the development of diabetes mellitus, diabetic ketoacidosis (DKA), and hyperosmolar syndrome.

This presentation will impact the forensic science community by demonstrating the relationship between antipsychotic medication administration and diabetes, and identifying those decedents most at risk. This understanding may affect the way that these deaths are certified, not only in terms of cause, but also manner, depending on the jurisdiction.

Schizophrenic and bipolar patients have been found to have an increased predisposition to the development of type 2 diabetes mellitus, independent of psychotropic medication administration, and after adjusting for other known risk factors. Within this susceptible population, however, poor glucose control, exacerbation of pre-existent diabetes mellitus, and new onset diabetes also have been widely described in association with the administration of certain antipsychotic medications, primarily second generation (atypical) antipsychotics, but, to a lesser degree, chlorpromazine, a low-potency first generation (typical) antipsychotic. This association has not usually been described with haloperidol, a high-potency first generation antipsychotic. The ushering in of these newer second generation (atypical) antipsychotic medications has rapidly rendered first generation antipsychotics all but obsolete due to the extreme efficacy of the former in treating psychotic symptoms, coupled with their greatly diminished negative motor and sexual side effects relative to the older medications. Their potential for sequelae of glucose dysregulation, however, has become a topic of much clinical literature review and analysis with recommendations for patient selection and monitoring. Theoretical mechanisms of dysregulation include insulin resistance, decreased insulin secretion, weight gain, hypertriglyceridemia, and elevated low-density lipoprotein cholesterol; however, a scientific consensus around mechanism has not been reached. While the atypical antipsychotics include quetiapine, clozapine, olanzapine, risperidone, aripiprazole, and ziprasidone, those that are thought to carry the highest risk for such metabolic side effects are clozapine, olanzapine, and quetiapine, with risperidone having the lowest.

In forensic practice, fatal diabetic ketoacidosis is the initial presentation of diabetes in some of these patients, who fall under the purview of the medical examiner due to their often precipitous and out-of-hospital deaths. This is the first large series describing such fatalities. Seventeen deaths were reported due to diabetic ketoacidosis in psychiatric patients treated with second generation antipsychotic medications.

Death certificates and toxicology data from January 2005 to December 2009 were searched for instances of diabetic ketoacidosis and hyperglycemia. The medical examiner records were reviewed which included the autopsy, toxicology, police, and medical examiner investigators' reports. Of all persons with DKA-related deaths (what is denominator/), 17 had a psychiatric history and were under current therapy with a second generation antipsychotic medication. The cause of death, contributing conditions, age, race, sex, co-morbidities, toxicology results, and BMI were extracted. Postmortem toxicologic analysis was performed on all decedents by the Forensic Toxicology Laboratory at the Office of Chief Medical Examiner. The decedents ranged in age from 32 to 57 years (average 48 years). There were fifteen men and two women. There were eleven Black, four Hispanic, and two White decedents. In all 17, the immediate cause of death was DKA. The psychiatric disorders included: ten schizophrenia, three bipolar/schizophrenia, two bipolar, and two major depression. The most frequent atypical antipsychotic medications were quetiapine and olanzapine (six each) followed by risperidone (three). Only one of the 17 had a medical history of diabetes. The decedent's BMI ranged from 20 to 60 (average 33). In 10 of these deaths, the use of the antipsychotic medication was recognized as the cause of death and the psychiatric disorder and/or medication were reflected in the cause and manner of death statements.

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