G91 A Fatality Due to Atomoxetine - The First Known Case

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The goal of this presentation is to alert the forensic community to the first known fatality associated with Atomoxetine, a non-stimulant medication utilized for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).

This presentation will impact the forensic community and/or humanity by alerting forensic scientists and the medical community of the potentially deadly combination of atomoxetine and paroxetine and to inform them of the first known fatality due to atomoxetine.

Attention Deficit Hyperactivity Disorder (ADHD) is a diagnosed condition in which a child exhibits symptoms of inattention, hyperactivity, and impulsivity. As these behaviors are part of most developing children at one time or another, the diagnosis requires that such behavior be demonstrated to a degree that is inappropriate for the person's age. Diagnostic guidelines exist to aid clinicians in determining if the symptoms displayed represent ADHD or are just part of normal development. This diagnosis can be quite controversial amongst physicians, with some feeling that the diagnosis is fictitious and over-used and others who feel that it is a medically justified disorder and have documented improvement in children with treatment. This paper serves to provide basic information on ADHD, without bias towards one view or the other.

Treatment for ADHD includes behavioral therapy and medication management. Stimulants are typically the class of medication used for ADHD treatment, and include amphetamine, methylphenidate, and dextroamphetamine. These medications work on the dopamine receptor. Atomoxetine is the first and only non-stimulant medication approved by the FDA for the treatment of ADHD in children, adolescents, and adults. Atomoxetine works differently than the stimulants in that it is a norepinephrine reuptake inhibitor. Evidence to date indicates that over 70 percent of children with ADHD who take Atomoxetine manifest significant improvement in their symptoms. Over 2 million prescriptions have been filled since the FDA approved it in 2002. It is not a controlled substance like the amphetamines; therefore refills may be phoned in, rather than having to pick up a refill prescription in person.

Because it is a relatively new medication, postmortem blood and tissue levels are not well established. Prior to this case, there have been no known fatalities associated with the use of the medication. There have been deaths due to other factors (motor vehicle accidents, hanging, etc) where atomoxetine has been identified, but in low levels. One factor in the lack of information regarding postmortem levels is that not all the toxicology laboratories have the atomoxetine standard to run the samples against.

This case is a 17-year-old male with a history of ADHD, depression and one prior suicide attempt with medications. His social history is negative for alcohol and tobacco use, but positive for prior recreational marijuana use. At the time of his death, he had not used marijuana in approximately one year. He presented to a psychiatrist in January 2004 with complaints of difficulty sleeping, indifference towards school, anxiety and depressed mood. At the time of that presentation, he was taking escitalopram, quetiapine, and lamotrigene. He was diagnosed with Bipolar disorder and ADHD and the plan was to begin a trial of atomoxetine and taper and stop the lamotrigene. He was also placed on zolpidem, 10 mg each evening. Several days later, he attempted suicide with the zolpidem after relationship problems. He had not shown any suicidal ideations prior to that. His atomoxetine dose was increased from 40 mg to 80 mg three weeks from the initial visit and he was instructed to stop the lamotrigene. Three weeks later, the depression was reportedly improved, his aggression reduced and overall affect seemed "more flexible." At the time of his death, his medications consisted of atomoxetine, paroxetine, quetiapine, lamotrigene, and zolpidem. He was found face down in a wooded area near his home, approximately 22 hours after last being seen alive.

Autopsy findings reveal a well-developed male with pulmonary edema and no evidence of natural disease. There were a few abrasions on the face that were consistent with the terminal fall and body position. Toxicologic examination of postmortem blood from the inferior vena cava, just above the iliac bifurcation, revealed an atomoxetine level of 16 mg/L and a small amount of paroxetine (less than 0.10 mg/L). The liver level of atomoxetine was 240 mg/kg and paroxetine of <5 mg/kg. These levels of atomoxetine are markedly higher than any levels published to date.

The presence of both the atomoxetine and paroxetine complicates the toxicologic picture, as they are both metabolized by the cytochrome P450 2D6 enzyme. It has been documented that co-administration of other 2D6 inhibitors with atomoxetine can increase serum atomoxetine levels threeto fourfold. In one documented non-fatal overdose of atomoxetine alone, the patient developed seizures and a prolonged QTc, but was medically managed and survived. Because of the co-administration of these two medications and the lack of suicidal ideations or suicide notes, the manner of death is undetermined. The cause of death is atomoxetine and paroxetine poisoning.

Atomoxetine, Attention Deficit Hyperactivity Disorder, Paroxetine

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