G35 Antipsychotic Polypharmacy: Lessons to be Learned From Forensic Toxicological Screening

Lisa F. Michaelsen, MD, Department of Forensic Medicine, Brendstrupgaardsvej 100, Aarhus N, 8200, DENMARK; Ingrid Rosendal, MSc, and Jørgen B. Hasselstroem, PhD, Department of Forensic Toxicology, Aarhus University, Brendstrupgaardsvej 100, Aarhus N, 8200, DENMARK; Birgitte Brock, MD, PhD, Department of Clinical Farmacology, Aarhus Universityhospital, Noerrebrogade 44, Aarhus C, 8000, DENMARK; and Annie Vesterby, MD, DMSc, Institute of Forensic Medicine, University of Aarhus, Brendstrupgårdsvej 100, 8200 Aarhus N, DK-8000, DENMARK*

After attending this presentation, attendees will understand the challenge of medical treatment of psychiatric patients with several drugs and the importance of the forensic autopsy in psychiatric patients dying suddenly

This presentation will impact the forensic science community by showing an example of what can be revealed from routine forensic toxicological screening and toxicological interpretation and how it can help understanding drug intoxication in psychiatric patients.

The prevalence of antipsychotic polypharmacy among schizophrenic patients is high and increasing internationally although a considerable difference in prescription practices exists. To estimate the overall risk of polypharmacy for the patient, pharmacodynamics, pharmacokinetics, as well as pharmacogenetics (how genetic differences influence patient's response to drugs) also have to be taken into consideration.

A 62-year-old schizophrenic man treated with several antipsychotic drugs died suddenly and unexpectedly. Beside his psychiatric diagnose he was once hospitalized with atrial flutter and ventricular extrasystoles (VES). No cause of death was found. The autopsy was performed and blood samples were taken from the femoral vein in accordance with standard procedures. Toxicological screening revealed the following: a lethal concentration of sulpiride (4,6mg/kg blood), concentrations of amitriptyline (0,43mg/kg blood) and the active metabolite nortriptyline (1,1mg/kg blood) were in levels where symptoms of lethal intoxication are seen, clozapine (1,3mg/kg blood), zuclopenthixole (0,16mg/kg blood) and procyclidine (1,2mg/kg blood) were found in concentrations where symptoms of intoxication are seen, levomepromazine (0,13mg/kg blood) and metoclopramide (0,13mg/kg blood) were both found in therapeutic concentrations. Alcohol was not detected in blood or urine.

Histology showed a simple pneumonia and slightly myocardial fibrosis. The cause of death was stated to be intoxication due to polypharmacy with several drugs. The manner of death was accident. All drugs were found to have been prescribed in recommended doses, and findings at the crime scene did not disclose intended intake or overdose.

The high drug concentration could according to toxicological interpretation not be explained by hepatic metabolic interactions, whereas pharmacodynamics may have played a role; the influence of potential pharmacogenetics was not examined.

Sulpiride is poorly absorbed from the gastrointestinal tract leading to low bioavailability of 25-35%. The patients constipation may have increased the absorption of sulpiride and thereby his serum concentration.

Metoclopramide was prescribed to the patient due to complaints of nausea, a well known symptom of intoxication of the drugs he was treated with. Metoclopramide which share side effects with antipsychotics is; however, not recommended in combination with other antipsychotic drugs. A majority of the drugs this patient was treated with share prolonged QT-interval and cardiac arrhythmia as side effects among others. This, in combination with the history of atrial flutter and ventricular extrasystoles, gives a high risk of cardiac arrhythmia. Furthermore, sulpiride is not recommended in combination with other drugs that may cause prolonged QT interval

This study presents this case illustrating that the potential fatality of polypharmacy in psychiatric patients should be considered and explored. Furthermore, it will reveal hypotheses of how this patient, treated with medication in recommended doses, could reach these high serum concentrations.

Antipsychotic Polypharmacy, Drug Intoxication, Psychotropic Drugs

 ** Presenting Author*