## K18 Lethal Tachycardia Following a Low Dose of Clozapine

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The goal of this presentation is to report a case of lethal tachycardia that developed in a 99-year-old woman, who mistakenly received a low dose (50 mg) of clozapine.

This presentation will impact the forensic science community by showing how fatal cardiovascular side effect reported in association with clozapine may occur in very elderly patients even at low doses.

Clozapine is a well-proven antipsychotic agent with a wide atypical receptor profile. It is effective against both positive and negative symptoms, with sympatholytic, anticholinergic and antiserotoninergic side effects. It is particularly useful for the management of patients with schizophrenia who are either unresponsive to or intolerant of conventional antipsychotic agent. Use of clozapine is restricted to patients with treatment-refractory schizophrenia because of the drug's association with agranulocytosis, seen in about 1% of patients in the first year of treatment. Additional side effects that may occur with clozapine treatment include sleepiness, dizziness, seizures, pulmonary embolism and respiratory depression.

Recently, attention has focused on cardiovascular complications reported in association with clozapine. Cardiovascular side effects have been less commonly reported but have included orthostatic hypotension, tachycardia, electrocardiogram changes, myocarditis, and cardiomyopathy, which in some cases have resulted in the death of young people with no prior cardiac history.

Clozapine increases heart rate in the majority of patients and around 25% of individuals on therapeutic doses develop a mean increase of 10- 15 bpm. Seemingly, the main causes are anticholinergic vagal inhibition and an increase in circulating catecholamines caused by α-1 adrenergic blockade.

Major symptoms in severe clozapine overdose are altered states of consciousness, agitation, confusion, delirium, coma, convulsions, tachycardia, arrhythmias and respiratory depression.

A case will be presented of lethal tachycardia following a low dose (50 mg) clozapine administration, occurred in a 99-year-old woman, after a nurse mistakenly gave her another patient's drug.

Thirty minutes after the administration, the patient was conscious and vital signs were normal. Blood pressure was 118/61 mmHg, heart rate was 85 bpm. One hour later, the patient was still conscious, blood pressure was 108/58, and heart rate was 85 bpm. One hour later, blood pressure was 171/101, heart rate was 101 bpm. Because of deterioration in her spontaneous respiration, the patient was endotracheally intubated and artificial respiration was applied. Gastric lavage could not be performed. All attempts to reanimate the patient did not lead to the clinical improvement and she died due to cardiac arrest after three hours of intensive care. An autopsy was performed at the University Center of Legal Medicine in Geneva. External examination was unremarkable. Internal examination showed congestion of internal organs and pulmonary oedema. Neuropathological investigation was negative. Histological examination showed moderate generalized congestion and broncho-aspiration of foreign material. Toxicological tests included blood ethanol levels and screening for common drugs and illegal substances by gas chromatography and mass spectrometry. Toxicological analysis showed midazolam (blood concentration 40 µg/l), which was administered to the patient at the hospital, and clozapine (blood concentration 140 µg/l), whose level was consistent with the administration of a 50 mg dose of clozapine.

**Conclusion:** The cause of death was determined to be clozapine intoxication

**Adverse Drug Reaction, Clozapine, Tachycardia**

 ** Presenting Author*