

CLINICAL FEATURES AND SEVERITY OF CLOZAPINE POISONING

Just S, Ackermann W, Deters M, Prasa D, Hentschel H

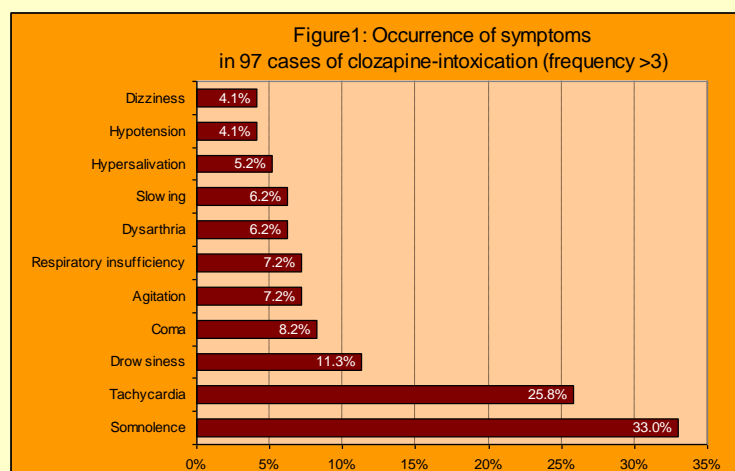
Poisons Information Centre Erfurt, Nordhäuser Straße 74, D-99089 Erfurt, Germany

Objective

The aim of the retrospective study was to analyse clinical features and severity of clozapine poisoning cases reported to the Poisons Information Centre (PIC) Erfurt over an eleven-year period. Additionally, we demonstrate a typical course after ingestion of a potentially lethal dose in March 2012.

Case series PIC Erfurt 2001 - 2011

<u>Number of cases:</u>	97 single drug ingestions (2001 to 2011)
<u>Patients:</u>	87 (89.7%) adults, 10 (10.3%) children
<u>Dose:</u>	0.4 - 285 mg/kg and 0.1 to 67-fold DDD, respectively
<u>Reason of poisoning:</u>	47 (48.5%) suicide attempts, 32 (33.0%) accidental ingestions, 4 (4.1%) adverse effects, 14 (14.4%) unknown cause
<u>Severity of poisoning:</u>	17 (17.5%) without symptoms, 59 (60.8%) minor, 13 (13.4%) moderate, 8 (8.3%) severe symptoms ¹

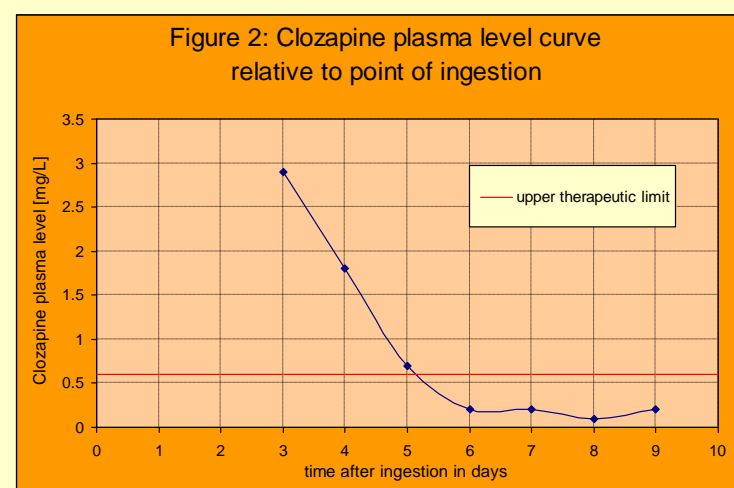


Laboratory findings:

Clozapine plasma level from 2.9 mg/L on day 3 to 0.2 mg/L on day 9 (see figure 2)
Therapeutic plasma level: 0.35 – 0.6 mg/L
Increased pancreas enzymes:
lipase 87 U/L (day 3), 1307 U/L (peak on day 5), 833 U/L (day 9), amylase 775 U/L (day 6), 545 U/L (day 9)

Treatment and further course:

- About 18 hours after ingestion the patient was admitted to emergency department because of increasing loss of consciousness and agitation. She presented with sopor in reduced general condition.
- Gastric decontamination was not performed.
- Initially diazepam and physostigmine were given.
- On day 3 the patient was intubated and artificially ventilated. Clozapine plasma level of 2.9 mg/L, still highly toxic, correlated with persistent cerebral depression, recurrent seizures and tachycardia.
- Supportive therapeutic measures like infusions of sodium bicarbonate, sedatives, electrolytes, glucose, diuretics, antibiotics and physical cooling were applied.
- On day 6 clozapine plasma level declined below upper therapeutic limit. The patient was extubated and was cardiopulmonary stable with normal neurological status.
- On day 9 she was transferred to psychiatric department.



Case report PIC Erfurt

<u>Patient:</u>	14 year-old female
<u>Dose:</u>	3000 mg clozapine (approximately 62.5 mg/kg)
<u>Time of admission:</u>	18 -20 hours after ingestion

Clinical features:

- **CNS:**
sopor, agitation, recurrent seizures
- **Cardiac monitoring:**
initial heart rate 140-155 beats/min, persistent tachycardia, normal blood pressure
- **Others:**
reduced general condition, aspiration pneumonia with decreasing oxygen saturation, high fever (nearly 40 °C), rhabdomyolysis with transient renal failure

Conclusion

- Symptoms and severity of clozapine poisoning cases in our study confirmed the results of a 13 year retrospective study in Switzerland². A minor exceeding of therapeutic dose could induce severe symptoms, especially in non-adapted individuals.
- Important poisoning symptoms after clozapine overdose are cerebral depression with drowsiness, somnolence to coma, but also agitation. Cardiac symptoms such as tachycardia are very often seen. Respiratory insufficiency occurs frequently.

References

1. Persson H, Sjöberg G, Haines J, Pronczuk de Garbino J. Poisoning Severity Score. Grading of Acute Poisoning. *J Toxicol Clin Toxicol* 1998; 36:205-213.
2. Krämer I, Rauber-Lüthy C, Kupferschmidt H, Krähenbühl S, Ceschi A. Minimal dose of severe poisoning and influencing factors in acute human clozapine intoxication: a 13-year retrospective study. *Clin Neuropharmacol*. 2010; 33(5):230-234.