

# Extreme Dose In Acute Zolpidem Intoxication

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## Abstract

Zolpidem is a benzodiazepine-receptor-1-agonist and serves as a short-acting hypnotic agent for the treatment of insomnia and anxiety.

Intoxications with Zolpidem, most in suicidal intent, are benign in the first place but can cause CNS and respiratory depression.

Signs and symptoms are dose-regulated and exacerbated by co-ingestion of other CNS or respiratory depressants. Most clinical manifestations are somnolence, dizziness, amnesia, vomiting, ataxia and visual hallucinations with full recovery.

We report a unique case of a man presenting in our Emergency Room with the highest recorded blood concentration (8.4 µg/ml) of Zolpidem and furthermore survived the overdose.

## INTRODUCTION

Zolpidem is an imidazopyridine derivate with strong sedative, myorelaxant and anticonvulsant properties. It has high affinity to the omega-subtype of the benzodiazepine-receptor 1 and serves as an agonist. It has been introduced as a short-acting hypnotic agent mainly for the treatment of insomnia. An excellent safety profile is shown for several years of clinical usage. Therapeutically oral doses of 5 to 60 mg per day have been administered (1).

In the literature several intoxications with Zolpidem are described, mostly in suicidal intents. Primary effects of Zolpidem overdose involve CNS and respiratory depression. Signs and symptoms are dose-regulated and exacerbated by co-ingestion of other central or respiratory depressants. Many studies showed that oral benzodiazepine overdose rarely causes respiratory failure that requires mechanical ventilation (2). In all reported cases except in one the Zolpidem overdose included other medications that could explain the respiratory failure (3).

Most Mono-intoxications resulted in somnolence, dizziness, amnesia, vomiting, ataxia and visual hallucinations with full recovery (4,5).

Regarding cardiovascular complications hypotension was observed and in one case a 14-year-old female developed sinus tachycardia following the ingestion of 100 mg of Zolpidem (5,6). We report a unique case of a man presenting in our Emergency Room with the highest recorded survived

overdose and blood concentration of zolpidem.

## CASE REPORT

A 68-year old male was brought to our Emergency Room in coma, intubated and ventilated. The emergency doctor, who was on the ambulance, reported that the patient was found in his flat after the police pried up the door. The patient registered for his funeral the night before on the answering machine of a local sepulchral company who informed the police. Initially found was a spontaneously breathing patient without any reaction to speech or pain. Due to the obscurity and genesis of the situation the emergency doctor decided for intubation and mechanical ventilation. No signs of intoxication were found, e.g. empty packages.

Due to the records of our hospital we got to know in the emergency department that the past medical history was significant for coronary artery disease, status post bypass-operation, arterial hypertension, diabetes mellitus type II and cerebral apoplexy. On presentation, blood pressure was hypertensive with 190/100 mmHg and pulse rate was 85/min. The physical examination was significant for a decreased level of consciousness with a Glasgow Coma score of 3. Blood glucose was 10.1mmol/l, creatinkinase 60.41 umol/l (<3,17µmol/l) and myoglobin 1822 µg/l (<106 µg/l) as a result of laying on the floor for several hours. Myoglobin was later elevated up to 10097ug/l. In a brain MRI a structural cause of the coma could be ruled out. A toxicological screening was taken and appeared positive for Zolpidem in a concentration of 8.4 µg/ml (blood).

Flumazenil was administered and the patient was stabilized in our Intensive Care Unit (ICU). We abstained from orogastric lavage. The patient became more and more responsive and had a Glasgow Coma Scale of 10 and a Zolpidem blood-concentration of 0.11 µg/ml 24 hours after admission to our clinic. When the patient got back to be oriented he delineated plausible that he had taken 200 tablets of 10 mg Zolpidem (total amount of 2 g). 72h after admission the patient was referred to the psychiatric clinic for further therapy.

### **DISCUSSION**

To our knowledge this case reports the highest blood concentration of zolpidem to date. Furthermore it is the second reported case where the respiratory depression is attributed exclusively to zolpidem overdose. The highest reported dose so far was reported by Lichtenwalner and Tully (7) describing a fatality involving Zolpidem with post mortem blood concentrations of 7.9 µg/ml.

Disturbances of consciousness can be successfully treated with flumazenil. After ingestion of a potentially life-threatening amount of poison a gastric lavage could be considered if it can be performed within one hour after ingestion. The elimination half time of zolpidem is about 2.4 hours (8).

In conclusion our case supports the position of the long held view that Zolpidem single-drug poisonings are generally benign and could be survived in high doses with supportive care.

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