

A case of iloperidone overdose in a 27-year-old man with cocaine abuse

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Abstract

Introduction: Iloperidone is a recently introduced antipsychotic medication. It is approved for the treatment of schizophrenia. There are no published reports of iloperidone overdosage, but there are eight cases that have been reported to the US Food and Drug Administration.

Case report: A case of a 27-year-old man who took 84 mg of iloperidone while also smoking cocaine is described. He developed a prolonged QTc (527 ms) without arrhythmias and respiratory failure with mandated respiratory support. He ultimately recovered without sequelae.

Discussion: The information regarding previous cases of toxicity on the US Food and Drug Administration website is incomplete. However, there were no fatalities due to iloperidone over-ingestion. Prolongation of the QTc may be a common feature.

Keywords

iloperidone, QT, QTc, overdosage, toxicity

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Introduction

Iloperidone (Fanapt®) is a new second-generation antipsychotic that is approved by the US Food and Drug Administration (FDA) for the treatment of schizophrenia.¹ It is not commonly used, and no cases of overdosage have been reported in the literature. We herein report a case of iloperidone overdosage.

Case presentation

A 27-year-old African-American male with a history of schizophrenia, asthma, and cocaine abuse presented to the hospital less than 1 h after intentionally overdosing on 84 mg of iloperidone after smoking crack cocaine to reduce the severity of the post cocaine nadir. There was no independent confirmation of the overdose medication or amount; however, the transient prolongation of the QTc (see below) seems to serve as independent validation of an overdose of some amount. The patient complained of some shortness of breath, but was not tachypneic, was awake and responsive but lethargic, and was tachycardic in 110s; vitals were otherwise stable and he had an oxygen (O₂) saturation of 89% on room air. Electrocardiogram showed a prolonged QTc interval of

527 ms. This dropped to 470 ms (essentially his normal) after 4 days without any arrhythmias. His baseline QTc interval was approximately 440 ms. Since he had a history of developing bronchoconstriction after smoking of cocaine, his respiratory status was a concern. He received intravenous (IV) fluids, oxygen by nasal cannula, nebulizer treatment, and IV steroids. Despite this, his O₂ saturation dropped to 78% while on oxygen. He ultimately required intubation and mechanical ventilation and was diagnosed with acute respiratory distress syndrome secondary to complications related to his comorbid conditions and the cocaine use. He eventually recovered without obvious sequelae.

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Table 1. Summary of information available in the package insert website.

	Mg ingested	Duration of ingestion	Highest reported QTc	Tachycardia	Hypotension	Sedation, lethargy	Extra-pyramidal symptoms	Fatality
1	576	All at once	–	–	–	–	–	–
2	438	4-day period	507	–	–	–	+	–
3	292	3-day period						–
4	48							–
Current case	84	All at once	527	+	–	+	–	–

While the package insert reports eight cases of overdose on iloperidone, only fragments of the cases are presented. Missing data are denoted by blank spaces.

Discussion

There are no published reports of iloperidone overdoses (PubMed search). There are eight known cases of overdoses in the US FDA clinical trials iloperidone database (Table 1) (product package insert: http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/022192lbl.pdf). While the presentation of these cases is fragmented and incomplete, there were no deaths or serious arrhythmias, even with ingestions exceeding 500 mg (Table 1).

The patient reported herein ingested 84 mg immediately before coming to the hospital. This is a dose only 3.5 times higher than the maximum recommended daily dose of 24 mg. In conjunction with this, he smoked crack cocaine. He had previously suffered respiratory failure after smoking cocaine and had previously required mechanical ventilation. Consequently, we believe the respiratory symptoms are probably not related to the iloperidone overdose. However, the initial lethargy and QTc prolongation are probably related to the iloperidone. Iloperidone is known to increase the QTc by a mean of 8.5–9 ms at therapeutic doses (16–24 mg/day).^{2,3} This is similar to the prolongation seen with ziprasidone (9.6 ms at 160 mg/day).^{2,3} The prolongation of QTc is dose-related, so that at 24 mg daily, the mean (range) QTc prolongation is 15.4 (13.4 to 36.0) ms.^{2,3} The observed increase of nearly 87 ms (nearly 2.4 times the maximum reported increase in QT studies) is compatible with the observed dose-related increase of QTc.² Animal studies reveal similar findings, but with a maximal prolongation observed even at very high doses (3 mg/kg caused a maximal QTc 42.7±10.2 ms prolongation in guinea pig hearts).⁴ Iloperidone is a potent inhibitor of the hERG protein (human *Ether-à-go-go-Related Gene*), a subunit of the potassium channel that mediates the inwardly repolarizing potassium current; so as the drug concentration increases, repolarization is delayed and QTc is prolonged.⁴

For this individual, his post ingestion course appears to be similar to the cases reported to the FDA (Table 1): with QTc prolongation without arrhythmia or hypotension, tachycardia, or sedation.

Cocaine use is associated with acute asthma exacerbations, more severe exacerbations with a higher incidence of necessity of assisted ventilation, and a higher prevalence of

new-onset bronchospasms.⁵ This patient had a previous history of that in the absence of iloperidone. However, it is possible that the iloperidone overdosage contributed to the respiratory distress.

Iloperidone is a strong alpha-2c receptor antagonist, which can prolong QTc, and delay cardiac repolarization. QTc prolongation can be noted at therapeutic dosage.² Excessive prolongation with the possibility of arrhythmia is probably the item of greatest concern in iloperidone overdosage.

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Declaration of conflicting interests

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Ethical approval

The University of Louisville's Human Subjects Protection Committee (IRB) has reviewed the case report and has determined that they do not need to approve it.

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Informed consent

The case report does not contain sufficient personal health information for anyone (other than the patient) to identify the subject of the case report. The authors have obtained a release from their University's Human Subjects Protection Committee.

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