

# Loperamide Dependency: A Case Report

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## Case Report

### Abstract

**Background:** Loperamide is used as an antidiarrheal drug and is available over-the-counter. It cannot pass the blood-brain barrier and it does not have a considerable abuse potential. It can lead to dangerous cardiac arrhythmia.

**Case Report:** Herein, we report a 35-year-old man with a 13-year history of abusing opioids who had undergone detoxification for four times during this period. He underwent detoxification for using 200 mg loperamide daily with anticholinergic agents, clonidine, non-steroidal analgesics, and diazepam. No evidence of arrhythmia was seen in the patient.

**Conclusion:** Tolerating high doses of loperamide could be dangerous and increases the risk of fatal cardiac arrhythmias.

**Keywords:** Loperamide; Addiction; Cardiac arrhythmia

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## Introduction

Loperamide is used as an antidiarrheal drug which is available over-the-counter since the Food and Drug Association (FDA) has reported it to be safe. In contrast to other  $\mu$ -receptor agonists, loperamide specifically affects the myenteric gastrointestinal network.<sup>1</sup> This drug affects the peripheral  $\mu$  receptors, inhibiting its passage through the blood-brain barrier, which in turn prevents evident cerebral symptoms;<sup>2</sup> and theoretically does not have a potential to be abused.

The treatment dose of this drug is 2-8 mg daily.<sup>2</sup> In common doses, loperamide has very few side effects. In less than 5% of the patients, constipation, abdominal cramps, nausea, and dizziness occur.<sup>3</sup> Respiratory depression and paralytic ileus are among the dangerous side effects of loperamide seen in children.<sup>4</sup> Despite the low theoretical abuse potential of this drug, several reports are available regarding its abuse and consequent cardiac complications in some of them.<sup>1,5</sup> In most reports, the patients had used doses of less than 200 mg. Herein, we report a 35-year-old man who was dependent to loperamide and used 200 mg of this drug daily. The consent of the patients was obtained for reporting his case.

## Case Report

A 35-year-old married educated man referred for loperamide withdrawal relief. His first referral was 10 years back for opioids withdrawal. He was diagnosed as having anxiety disorder (Axis I) and narcissistic personality disorder (Axis II) based on diagnostic psychiatric assessments, the Millon Clinical Multiaxial Inventory (MCMI), and the Diagnostic and Statistical Manual of Mental Disorders-5<sup>th</sup>-Text Revision (DSM-IV-TR). He stated that he started using opium at the age of 22 and was able to quit it using diphenoxylate, clonidine, and tramadol. After his relapse during the first visit at age 25, and during the detoxification process with clonidine and baclofen, loperamide was prescribed for him to treat diarrhea. Diarrhea was controlled using 6 mg of loperamide and the drug was tapered and discontinued during one month.

Three years later, the patient referred for detoxification because of using 40 acetaminophen codeine pills daily and 200 diclofenac sodium

pills daily. He started using these medications one year back and their use had increased during the past three months.

No liver complications were seen in routine evaluations. The abuse was controlled with 16 mg buprenorphine and it was tapered and discontinued during two weeks. At this time, the patient complained of insomnia, abdominal cramps, and a little diarrhea. Accordingly, he was prescribed 10 mg dicyclomine (three times daily), 25 mg trimipramine every night, and 2 mg loperamide after each loose stool pro re nata (PRN) and the symptoms were controlled.

Six years later, the patient had experienced hyperprolactinemia because of dexamethasone overdose following a headache and had been treated with bromocriptine. Because of being worried about this situation, he had used loperamide for boosting his mood. However, he again referred for using 100 loperamide 2 mg tablets daily during the past two months.

Physical examination as well as electrocardiography and echocardiography evaluations showed no abnormality. He had mild depression and was prescribed nortriptyline 25 mg, biperiden 2 mg, dicyclomine, and ibuprofen 400 mg tablets, and 2 atropine 0.5% oral drops (all three times daily).

Diazepam 5 mg (three times daily) and half a 0.2 mg tablet of clonidine (twice a day) were added to the mentioned medications because of limbs twitches. At this time, the patient had no diarrhea and perspiration and had defecations 3-4 times daily. Detoxification ended after 15 days and the patient became asymptomatic. All medications except nortriptyline were discontinued after 15 days. The patient had no complications after 12 months of follow-up.

## Discussion

Loperamide decreases the bowel movements and is used for symptomatic treatment of diarrhea.<sup>6</sup> For this purpose, 4 mg loperamide is initially prescribed and in case diarrhea persists, 2 mg is prescribed after each loose stool. In any case, the dose should not exceed 16 mg per day. This dosage is usually adequate for 48 hours. If diarrhea persists 4-8 mg of loperamide is prescribed for a maximum of 10 days.<sup>6</sup> This drug is also used for symptomatic treatment of addiction but even for this purpose, the dosage

should not exceed 16 mg.<sup>7</sup> Although loperamide is a peripheral  $\mu$ -receptor agonist and does not pass the blood-brain barrier, and is not considered to be addictive; our patient used 200 mg of loperamide daily for lifting his mood and did not experience any cardiac or respiratory complications. He was treated during 15 days without prescribing opioid agonists by managing the symptoms of withdrawal.

In a recent web-based study, loperamide was used for a wide spectrum of symptoms related to opioid abuse and some even called it the "methadone of the poor". The mean consumption was 70-100 mg per day. Most participants stated that the effect of loperamide was "acceptable" to "excellent". However, most participants doubted its analgesic and euphoric effects. Most of them supported the potency of loperamide for control of withdrawal symptoms. The most common complications of this drug were constipation, dehydration, and other gastrointestinal complications.<sup>8</sup>

In another study, three patients were described who had used loperamide. These cases were 14-25-year-old men and had diarrhea due to phobic and anxiety disorders and since they were worried about not having access to the toilet when they were out, they had abused loperamide. During psychotherapy, amitriptyline and venlafaxine were prescribed for two of the patients and one underwent psychotherapy alone, and the problem of all three patients was resolved and loperamide was discontinued.<sup>9</sup> The amount and duration of abusing loperamide was not stated in the mentioned patients and they had no cardiac arrhythmias.

In another study, a 54-year-old woman was described with a history of diabetes mellitus who used metformin on a daily basis and 144 mg loperamide for about two years. She was referred to the emergency ward because of frequent syncope. The patient had dangerous ventricular arrhythmias leading to pacemaker placement.<sup>1</sup> In another case report, a 34-year-old woman was

described with gastrointestinal symptoms secondary to anxiety. She had used 16 mg loperamide daily for ten years and treated with diazepam. Her diarrhea and anxiety were gradually treated; but she became dependent to benzodiazepines. The patient was then admitted and symptoms of diarrhea and anxiety gradually subsided. She did not have any cardiac arrhythmias.<sup>10</sup>

In a recent case series, five patients aged 30-43 years with a history of loperamide abuse and subsequent cardiac complications were reported. In three patients, the arrhythmias were life-threatening. In these patients, loperamide was abused as follows: up to 400 mg of loperamide daily for several weeks, 2 mg loperamide daily for 144 days, escalating use of 792 mg loperamide daily, 120-200 mg loperamide over the 6 hours, and 70 mg loperamide daily for months.<sup>5</sup>

In the reported patients with anxiety, either the amount of loperamide abuse has not been mentioned or dosages of 6 mg (in stressful situations) to 16 mg (from 10 years prior to referral) have been reported. No arrhythmias have been reported in patients with anxiety.

## Conclusion

In conclusion, although reports of patients referring to emergency wards indicate that the use of 2 mg loperamide during several weeks leads to cardiac arrhythmias, our case showed that the abuse of 200 mg loperamide daily can be tolerated by a healthy person. This would increase the risk of overdose and considering the high risk of cardiac arrhythmia, some unknown sudden deaths in addicted individuals could be related to this fact.

## Conflict of Interests

The Authors have no conflict of interest.

## Acknowledgements

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## سوء مصرف قرص لوپرامید: گزارش مورد

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### گزارش مورد

#### چکیده

**مقدمه:** لوپرامید که به عنوان داروی ضد اسهال به صورت بدون نسخه در دسترس می‌باشد، قادر به عبور از سد خونی- مغزی نیست و طبق گزارش‌های متعدد، پتانسیل سوء مصرف چندانی ندارد. این دارو ممکن است منجر به آریتمی‌های خطرناک قلبی شود.

**گزارش مورد:** بیمار آقای ۳۵ ساله‌ای با سابقه اعتیاد به مواد اپیوئیدی به مدت ۱۳ سال بود و طی این مدت ۴ بار اقدام به سم‌زدایی کرده بود و به علت مصرف روزانه ۲۰۰ میلی‌گرم لوپرامید با کمک داروهای آنتی‌کولینرژیک (دی‌سیکلومین، تری‌هگزری فنیدیل و آتروپین) و کلونیدین و مسکن‌های غیر استروئیدی و دیازپام، سم‌زدایی شد. در این بیمار شواهدی از آریتمی قلبی وجود نداشت.

**نتیجه‌گیری:** با وجود عبور ناچیز داروی لوپرامید از سد خونی- مغزی، این دارو پتانسیل سوء مصرف بدون تظاهرات قلبی- تنفسی با دوزهای بالایی همچون ۲۰۰ میلی‌گرم در روز را دارد. تحمل دوز بالای لوپرامید می‌تواند خطر افزودن دوز مصرفی و احتمال بروز آریتمی‌های خطرناک قلبی را به دنبال داشته باشد.

**واژگان کلیدی:** لوپرامید، اعتیاد، آریتمی قلبی

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