# Life-threatening complications of ibogaine: three case reports

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#### ABSTRACT

Ibogaine is a naturally occurring psychoactive alkaloid extracted from the roots of the Tabernanthe iboga plant, which in alternative medicine is used to treat drug dependency. However, this upcoming, online advocated therapy can be dangerous due to its potentially lethal adverse effects. We present three cases in which toxic side effects were noted. We used the Naranjo scale to estimate the probability of a causal relationship between these effects and ibogaine. Findings in these three cases are suggestive of a causal relationship between the use of ibogaine and serious respiratory and cardiac problems (including lengthening of the QT interval). In our opinion it is of great importance that clinicians are aware of these potentially serious side effects and realise that widespread online marketing practices will give many more people access to ibogaine.

# KEYWORDS

Iboga, ibogaine, long QT interval, tachyarrhythmia

## INTRODUCTION

Ibogaine is a naturally occurring psychoactive alkaloid which is extracted from the roots of the *Tabernanthe iboga* plant. The plant is mainly found in West and Central Africa and has long been used in rituals and to fight fatigue, hunger and thirst. In the last decades it drew the attention of the Western world for its potential to inhibit withdrawal symptoms associated with weaning from drugs.<sup>1,2</sup>

Anecdotal evidence and results of small open-label studies investigating the effects of ibogaine have been promising.<sup>2-3</sup>

# What was known about this topic?

Ibogaine is a naturally occurring psychoactive alkaloid which in the last decades drew the attention of the Western world for its potential to inhibit withdrawal symptoms associated with weaning from drugs. <sup>1,2</sup> Even though small open-label studies investigating the effects of ibogaine have been promising, <sup>2,3</sup> controlled clinical trials were never carried out because research showed possible serious side effects and one fatality in Alper's open-label study.<sup>3,4</sup>

### What do these cases add?

The non-medical use of ibogaine in the treatment of opioid addiction is increasing; it is important for health professionals to be aware of the risks and take a clear stand on this practice. The limited available evidence will be discussed here and complemented with new cases of probable ibogaine intoxications.

However, controlled clinical trials were never carried out because both laboratory studies pointed to the risk of serious side effects and one fatality in Alper's open-label study.<sup>3,4</sup> Nevertheless, the non-medical use of ibogaine in the treatment of opioid addiction is increasing; it is important for health professionals to be aware of the risks and take a clear stand on this practice.

The limited available evidence will be discussed here and complemented with new cases of probable ibogaine intoxications. One case was previously published by Hoelen *et al.* in 2009.<sup>5</sup> We applied the Naranjo scale to estimate the probability of a causal relationship.<sup>6</sup>

## CASE 1

A 49-year-old Scottish male with a history of heroin addiction presented to the emergency department with collapse. He had received his first anti-addictive dose of ibogaine one or two days earlier. History taking was complicated due to intermittent unresponsiveness, but the patient stated he had no specific complaints. Apart from hypothyroidism and asthmatic symptoms, his medical history was unremarkable.

Electrocardiography (ECG) of this patient showed intermittent ventricular tachyarrhythmias, known as torsade de pointes, with underlying sinus rhythm and a QT interval of >700 ms. Laboratory testing showed mild hypophosphataemia (0.76 mmol/l [reference 0.8-1.50]), and mild hypokalaemia (3.5 mmol/l [reference 3.5-5.0]) but no other deviations (calcium 2.23 mmol/l [reference 2.1-2.6]). A computed tomography (CT) scan of the brain showed no abnormalities. Urine screening showed traces of opioids. The patient was admitted to the intensive care unit (ICU), where he was defibrillated twice for tachyarrhythmias. Over the following days he recovered quickly; his QT interval, however, remained prolonged during the entire stay in our hospital. He was discharged after being free of ventricular tachyarrhythmias for ten days, with a QT interval of 475 ms.

# CASE 2

A 31-year-old American woman with a history of persistent alcohol addiction presented to the emergency room with a seizure-like attack after taking a first dose of 3.5 g of ibogaine. She had started on ibogaine as an alternative therapy for her treatment-resistant alcohol dependence. Apart from this single dose of 3.5 g ibogaine 15% (usual dose, 2 to 6 g) she had not taken any other medication or drugs, and her family history was unremarkable. She only complained of nausea. ECG revealed a strikingly prolonged QT interval (corrected 616 ms) and torsade de pointes. Laboratory testing showed mild electrolyte deviations (magnesium 0.49 mmol/l [reference 0.65-1.05], potassium 3.2 mmol/l [reference 3.5-5.0]), which were rapidly corrected, however without any effect on the QT interval.

The patient was admitted to the ICU, where after 42 hours of monitoring her QT interval normalised. During her stay in the ICU no new seizures occurred and no further intervention was needed. She was discharged home in good condition.

# CASE 3

A 43-year-old Italian woman, also being treated with ibogaine for heroin and benzodiazepines addiction, was admitted to the emergency room in an unresponsive state,

which had lasted longer since she had been found earlier that morning. She had vomited and possibly had shown some contractions around her mouth.

Physical examination showed a non-responsive, tachypnoeic and subfebrile woman, who moved her arms and legs symmetrically. Blood testing showed only leukocytosis (12.7 [reference 4.0-10.0]), slightly elevated erythrocyte sedimentation rate of 38 mm/h [reference 2-12] and mild hypokalaemia (3.1 mmol/l). A CT scan of the brain, chest X-ray and ECG (QTc around 480 ms) were performed but showed no abnormalities. Because urine screening tested positive for opioids, she was injected with flumazenil (Anexate) and naloxone upon which she developed mild withdrawal symptoms, but no improvement in consciousness. Electroencephalography showed encephalopathy of unknown origin, possibly related to earlier hypoxia. No epileptic activity was seen. She was admitted to the ICU, where she was intubated on day 2, due to respiratory insufficiency. She remained unstable for several days, but was extubated after 24 hours. No cardiac arrhythmias were observed, but she did develop urine retention and aspiration pneumonia during the ICU stay. Later, blood samples showed potentially lethal ibogaine levels (0.37 mg/ml).7 The patient was discharged home in good condition after seven days.

# DISCUSSION

The three cases presented here concerned patients who used ibogaine shortly before experiencing cardiac or respiratory instability. Unexplained death or adverse events after the use of ibogaine have been described before incidentally; they have rarely been related with ibogaine blood levels.<sup>8</sup>

First, we would like to discuss the likelihood of whether the adverse reactions in these cases were actually due to ibogaine rather than the result of other factors. We applied the Naranjo scale to assess the probability of a causal relationship. Probability is assigned via a score termed definite, probable, possible or doubtful (table 1).6 In cases 1 and 3 traces of opioids were found in serum and/or urine. The patient in case I claimed not to have used drugs recently before presentation, but in case 3 the patient was on a methadone regime. Thus, in case 3, a combination of ibogaine and opioid intoxication could be considered, especially in view of the dominant respiratory problems. In this context, it is of interest that ibogaine is thought to potentiate opioids and their toxic effects.8 Applying the score to patient 1 and 3, they score 6 to 8 points, thus a causal relationship is probable. In case 2 there appeared to be no other explanation for the symptoms, adding up to 8 points and a probable causal relationship. Electrolyte deviations in all three patients were too minimal to expect to produce the symptoms as presented here.

**Table 1.** Scale of Naranjo. Causal relationship is certain  $(\geq 9)$ , probable (5-8), possible (1-4), doubtful  $(0)^6$ 

| Yes<br>I<br>2 | 0                 | Unknown                      |
|---------------|-------------------|------------------------------|
| -             | -                 | 0                            |
| 2             |                   |                              |
|               | -I                | 0                            |
| I             | 0                 | 0                            |
| 2             | <b>-</b> I        | 0                            |
| -I            | 2                 | 0                            |
| -I            | I                 | 0                            |
| I             | 0                 | 0                            |
| I             | 0                 | 0                            |
| I             | 0                 | 0                            |
| I             | 0                 | 0                            |
|               | -I 2 -I I I I I I | I O 2 -I -I 2 -I I O I O I O |

Apart from the presented cases, there is only one previous report in the literature describing ventricular tachyarrhythmia and long QT interval in relation to recent ibogaine ingestion.9 The similarity of this case report with cases I and 2 described here is striking and contributes to our view that ibogaine can cause serious cardiac problems. In conclusion, findings in these three cases are suggestive of a causal relationship between the use of ibogaine and serious respiratory and cardiac problems (including prolonged QT interval). One other publication supports these findings.9 Considering more and more people have access to ibogaine through widespread online availability, we would suggest professionals to get in line and explicitly issue a clear negative advice against the use of ibogaine. Furthermore, in our opinion ibogaine should be added to the list of drugs causing long QT interval.

#### ACKNOWLEDGEMENTS

Dr. D.W. Hoelen, PhD, University Medical Centre, Utrecht, the Netherlands. No conflict of interest or funding was reported.

Presented as an oral presentation at the Annual Meeting of the Netherlands Association of Internal Medicine, 25-27 April 2012, Maastricht, the Netherlands.

#### REFERENCES

- Werneke U, Turner T, Priebe S. Complementary medicines in psychiatry: review of effectiveness and safety. Br J Psychiatry. 2006;188:109-21.
- Mash DC, Kovera CA, Pablo J, et al. Ibogaine: complex pharmacokinetics, concerns for safety, and preliminary efficacy measures. Ann N Y Acad Sci. 2000;914:394-401.
- Alper KR, Lotsof HS, Frenken GM, Luciano DJ, Bastiaans J. Ibogaine in acute opioid withdrawal. An open label case series. Ann N Y Acad Sci. 2000;909:257-9.
- O'Hearn E, Molliver ME. The olivocerebellar projection mediates ibogaine-induced degeneration of Purkinje cells: a model of indirect, trans-synaptic excitotoxicity. J Neurosci. 1997;17:8828-41.
- Hoelen DW, Spiering W, Valk GD. Long-QT syndrome induced by the antiaddiction drug ibogaine. N Engl J Med. 2009;360:308-9.
- Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30:239-45.
- Molina D. Handbook of Forensic Toxicology for Medical Examiners. Taylor and Francis Inc; 2009.
- 8. Alper KR, Stajic M, Gill JR. Fatalities Temporally Associated with the Ingestion of Ibogaine. J Forensic Sci. 2012;57:398-412.
- Pleskovic A, Gorjup V, Brvar M, Kozelj G. Ibogaine-associated ventricular tachyarrhythmias. Clinical toxicology (Philadelphia, Pa.) 2012;50(2):157.