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Remission of severe opioid use disorder with ibogaine: a case report

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Abstract

Background—Opioid Use Disorders (OUD) translate into major health, social, and economic consequences. Opioid agonist medications, which generally require long-term administration, are the mainstay pharmacological treatment of OUD. However, a large proportion of individuals with OUD either refuse or fail to respond to these therapies. Ibogaine, a naturally occurring substance found in the *Tabernanthe iboga* plant, has shown potential to bring about transformative or spiritual experiences that have reportedly been associated with long-term abstinence. Although research on ibogaine is limited, an ibogaine subculture persists offering unregulated ibogaine preparations for the treatment of addiction.

Case presentation—We describe the case of a 37-year-old female with a 19-year history of severe OUD achieving an ongoing 18-month period of abstinence following a four-day ibogaine treatment. Her previous longest period of continuous abstinence from opioids was 2 months while on methadone. No safety issues associated with ibogaine were observed.

Conclusions—A four-day treatment with ibogaine was successful in achieving long-term remission of a previously treatment-refractory patient with severe OUD. While rigorous trials are required to establish safety and efficacy, future studies should seek to delineate the potential role of ibogaine or other molecules that may produce transformative experiences for individuals with substance use disorder.

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Keywords

ibogaine; opioid use disorders; opioid agonist treatment; methadone; methadone maintenance therapy

In North America, an estimated 1 million individuals are affected by Opioid Use Disorders (OUD) (Vashishtha 2008). Although this prevalence is relatively low, these figures translate into major health and societal costs. Overdose, suicide, end-stage liver disease, psychiatric illnesses, as well as increased risk of Hepatitis C (HCV) and HIV infection are frequent health consequences of untreated OUD (Fischer et al. 2005). The economic burden of OUD is also large, including health care costs, loss in productivity and criminal justice expenditures (National Drug Intelligence Center 2011).

At present, Opioid Agonist Treatment (OAT, e.g. methadone, buprenorphine) is considered the gold standard treatment for OUD. Methadone Maintenance Therapy (MMT) has been shown to effectively reduce heroin use (Mattick et al. 2014), as well as improve the physical and mental health status of those who are retained in treatment (Ward, Hall & Mattick 1999). However, many patients are unwilling to take daily OAT or do not respond to these treatments. For instance, some studies report that up to 40% of individuals with OUD have an unfavorable response to MMT (Mattick et al. 2014; Oviedo-Joekes et al. 2009). Furthermore, previous studies show that MMT programs fail to meet self-perceived needs and preferences of many opioid users, which might contribute to the high attrition rate observed in these programs (Fischer et al. 2005). The limited efficacy of OAT could be in part related to the need for long-term adherence to therapy. Thus, further research and development of new treatment programs for OUD is warranted to better meet the needs of individuals with OUD for whom available treatment options have failed or are unsuitable.

Ibogaine is an alkaloid found in the *Tabernanthe iboga* root bark, traditionally used in initiatory rituals in West Central Africa (Brown 2013; Koenig & Hilber 2015). Since the 1960s, anecdotal evidence has suggested its potential to treat addictions without the need for ongoing administration (Alper 2001; Brown 2013; Glick et al. 1991; Maisonneuve, Keller & Glick 1991). This initial evidence of ibogaine's anti-addictive properties has been subsequently supported by pre-clinical and observational studies (Brown 2013). However, ibogaine's toxicity profile, including fatalities temporally-associated with its ingestion, have likely hampered subsequent clinical research on ibogaine's anti-addictive properties (Brown 2013).

Although ibogaine is a Schedule I substance in the United States, it is unregulated in most countries, including Canada. Dozens of clinics worldwide are hence offering ibogaine for the treatment of addictions in both non-medical and medical settings (Koenig & Hilber 2015). For instance, as of February 2006, it was estimated that 3414 individuals had taken ibogaine (Alper, Lotsof & Kaplan 2008). Of those, 68% had used it for the treatment of a substance use disorder and most commonly for opioid detoxification (53%) (Alper, Lotsof & Kaplan 2008).

We present a case of a woman with long standing severe OUD and a history of multiple previous unsuccessful treatments. Eighteen months after a short treatment course with ibogaine, she remains abstinent from opioids.

CASE REPORT

A 37-year-old Caucasian woman was referred to the Addiction Outpatient Clinic at St-Paul's hospital in Vancouver for follow-up of her OUD remission subsequent to a 4-day treatment with ibogaine 18 months prior. She had been addicted to heroin since she was 18 years old. Apart from her substance use disorder, other medical comorbidities included stable angina, dyslipidemia, obesity, chronic HCV, peripheral vascular disease, and attention-deficit hyperactivity disorder. Before undergoing her ibogaine treatment, the patient repeatedly tried and exhausted most available addiction treatment options, including 12-step programs, detoxification centers, support groups, sponsors, recovery houses and MMT, all without sustained success. Her prior longest period of continuous abstinence was 2 months while on MMT.

As previously stated, 18 months prior to this consultation the patient was admitted to a residential ibogaine program in Vancouver to receive ibogaine therapy for her OUD. She had last used opioids (16 mg of hydromorphone) approximately 12 hours prior to admission to the centre. The center's protocol involved a series of ibogaine HCl (hydrochloride) test doses (up to 2.5 mg/kg) on the first day, followed by a series of larger doses (up to 20 mg/kg) on the second day, and booster doses on the last 2 days (5 mg/kg/day). Over the course of the four-day admission, she received a total of 2300 mg (32 mg/kg) of ibogaine HCl. The clinic's protocol also allowed for the use of oral hydromorphone to manage acute withdrawal. The patient required 32 mg of hydromorphone on the first day and 45 mg on the second day to manage her withdrawal symptoms which were already present on admission.

During the ibogaine treatment, the center provided food and a quiet place to rest, but there was no formal psychotherapy performed. In addition to continuous nursing monitoring with hourly heart rate and blood pressure, the clinic safety protocol included liver and cardiovascular screening prior to the initiation of the ibogaine treatment. Patient's baseline ECG was within normal parameters, including a normal QTc.

The patient maintained an overall stable blood pressure during the 4-day treatment, but developed mild bradycardia (average measured heart rate on day 1, 2, 3, 4 was 67 beats per minute [bpm], 57 bpm, 51 bpm, and 57 bpm respectively). In addition, she experienced mild and transitory side effects such as weakness, dizziness, and diaphoresis. Minor concentration deficits were reported during the first few weeks following therapy, but the patient did not suffer from any other overt persistent side effects. At the time of this consultation, the patient denied any opioid use since she left the ibogaine clinic 18 months ago. She attributed her sustained recovery more to a spiritual awakening induced by the ibogaine experience than to a painless withdrawal, as she had been able to go through physical withdrawals successfully on various occasions in the past without subsequent sustained abstinence. The patient described that the ibogaine experience allowed her to revisit various recent events of her life, including the loss of her partner to an opioid overdose, as well as other moments

where the patient herself suffered nearly fatal overdoses. This new insight into her OUD, became an eye-opening opportunity, giving her emotional strength to attempt and sustain abstinence.

DISCUSSION

We described the case of a 37-year old woman who as of the time of writing of this report denied any opioid use over an 18-month period subsequent to a 4-day treatment with ibogaine without any significant adverse events. This is noteworthy in the setting of a 19 year history of severe OUD and multiple failed attempts at abstinence following various widely accepted treatment modalities. A number of evidence-based pharmacotherapies for the treatment of OUD exist, including methadone and buprenorphine (Mattick et al. 2014). However, OAT requires long-term adherence, which can be challenging for many individuals. As such, novel therapies are needed for patients who fail to respond to OAT or are reluctant to engage in long-term OAT programs.

Ibogaine shows potential as an alternative treatment for OUD, particularly among cases refractory to OAT for a number of reasons. First, studies have suggested that ibogaine is effective in easing opioid withdrawal, as well as in reducing cravings (Brown 2013). Although the pharmacological bases of ibogaine's anti-addictive properties are not fully understood, ibogaine and noribogaine (ibogaine's main metabolite) simultaneous action on a diversity of neurotransmitter transporters and receptors provides a biological plausibility for its anti-addictive effects (Antonio et al. 2013; Koenig & Hilber 2015). Second, ibogaine is usually administered in a single session, not requiring ongoing administration (Brown 2013), which can be a substantial advantage for many individuals with OUD. Without the time and logistical constraints commonly associated with daily-witnessed injection of methadone, individuals could have an easier transition back to employment and other factors associated with recovery, which in turn could reduce direct and indirect societal costs. Third, it has been suggested that the mystical experiences associated with ibogaine and other traditional psychedelic drugs might result in the resetting of psychological processes or neuroadaptations underlying substance use disorders, which could contribute to long-term abstinence (Bogenschutz & Johnson 2016). Our patient herself volunteered that it was such transformative phenomenon that was the key to her success this time. Fourth, ibogaine has a low abuse potential, as indicated by animal models where ibogaine did not lead to either desire for the substance or aversion to it (Alper 2001; Brown 2013).

Despite these promising characteristics of ibogaine, clinical research on its potential for the treatment of substance use disorders has been hindered due in part to safety concerns. However, this research gap has resulted in a lack of evidence-base clinical and pharmaceutical standards of how to safely administer ibogaine, further exacerbating its potential risks. Twenty-two deaths temporally related to ibogaine use have been reported between 1991 and 2014, most of which were associated with pre-existing medical comorbidities (particularly cardiovascular disease), concurrent use of other substances, and electrolyte imbalances (i.e. hypokalemia) (Alper, Stajic & Gill 2012; Koenig & Hilber 2015). Clinical reports and studies in animal models suggest that cardiac arrhythmias, induced by ibogaine's propensity to prolong the QT interval, might have been responsible

for many of these deaths (Koenig & Hilber 2015). As such, ibogaine's safe administration would theoretically dictate, amongst other safety measures, the need for an electrolytes and ECG screening prior to treatment, abstinence from any other potentially QTc prolonging substances, as well as exclusion of patients with cardiovascular disease (Alper 2001; Brown 2013).

In summary, the case presented here illustrates the challenges associated with the treatment of refractory OUD, and underscores the urgent need for expanding options to treat these cases, as well as for other substances (e.g., cocaine) for which pharmacotherapies are currently unavailable. Although ibogaine is a promising compound, its use on individual patients must be based on a risk-benefit analysis (e.g., potential cardiotoxicity versus untreated substance use disorder), as well as on a careful selection of eligible candidates and ibogaine's administration in adequately safe settings (Koenig & Hilber 2015). With the growing number of ibogaine users in uncontrolled settings, further clinical research is warranted to clarify the potential role of ibogaine and related congeners (e.g., 18-methoxycoronaridine [18-MC]), as well as other molecules that may produce transformative experiences in the treatment of substance use disorders, as well as to help inform guidelines for their safer administration (Brown 2013; Tupper et al. 2015).

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