Ibogaine in Acute Opioid Withdrawal
An Open Label Case Series
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INTRODUCTION
Ibogaine is an indole alkaloid derived from the bark of the African shrub Tabernanthe iboga. It has a history of use as a medicinal and ceremonial agent in West Central Africa, and has also been alleged to be effective in the treatment of drug abuse. The National Institute on Drug Abuse (NIDA) has given significant support to animal research, and the US Food and Drug Administration (FDA) has approved phase 1 studies in humans. Evidence for ibogaine’s effectiveness includes a substantial pre-clinical literature on reduced drug self-administration and withdrawal in animals, and case reports in humans.

From a pharmacologic standpoint, ibogaine is interesting because it appears to have a novel mechanism of action distinct from other existing pharmacotherapeutic approaches to addiction. Ibogaine is not a substitution therapy, such as methadone. Ibogaine has activity at a variety of different receptors in the brain, and its effects may involve complex interactions between multiple neurotransmitter systems and persistent changes in second messenger signal transduction. There is evidence to suggest that ibogaine treatment might result in the “resetting” or “normalization” of neural adaptations related to sensitization or tolerance.

The lack of official approval of ibogaine led to the advent of a distinctive informal treatment network involving lay “treatment guides.” Over the past several years this network has been increasingly active, particularly in Europe. Opioid dependence is the indication for which addicts have most commonly sought ibogaine treatment, and the focus of a large proportion of published research on evidence of efficacy

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in animals. In this present study we report on series of cases of treatments for the indication of opioid detoxification performed under open label conditions in nonmedical settings.

METHODS

The cases presented in this paper are a set of 33 cases of patients treated with ibogaine between 1962 and 1993 which were presented at the Ibogaine Review Meeting held by MDD-NIDA in Rockville on March 8, 1995. The subjects in this study were 22 males and 11 females who reported an average daily use of heroin of 64 ± 50 grams, primarily by the intravenous route (26 intravenous, 4 intranasal, 3 smoking). Eight subjects reported concurrent methadone use of an average of 48 ± 30 milligrams per day, and 8 subjects also used cocaine, averaging 1.4 ± 2.3 grams per day. The subjects in this series of cases received an average dose of ibogaine of 19.3 ± 6.9 mg/kg (range of 6 to 29 mg/kg). These cases met the following criteria:

1. Heroin dependence, with or without other comorbid substance use disorders, as an indication for treatment with ibogaine (all 8 of the subjects who were receiving methadone at the time of their treatment also reported concurrent use of heroin). All patients in this study retrospectively met the DSM IV criteria for Opioid Dependence with Physiological Dependence at the time of their treatment;

2. Having been directly observed by either or both co-authors H.S.L. and/or G.M.N.F., continuously at the scene for at least 48 hours following treatment with ibogaine.

Observers well known to the above co-authors were additionally present when the co-authors slept and immediately notified the co-authors of withdrawal signs or symptoms, or drug seeking behavior. Patient behaviors between 48 and 72 hours were monitored by H.S.L. or G.M.N.F., or their observers. Eighteen of the 33 patients in this study were under the care of Dr. Ian Bastiaans, who saw the patients before and after their treatments, and was typically present for the first 4 to 8 hours, and returning 24 hours post ibogaine administration.

RESULTS

Resolution of the signs of opioid withdrawal without further drug-seeking behavior was observed within 24 hours in 25 patients, and was maintained throughout the 72 hour period of post-treatment observation. Other outcomes included drug-seeking behavior without withdrawal signs (4 patients), drug abstinence without attenuated withdrawal signs (2 patients), drug-seeking behavior with continued withdrawal signs (1 patient), and one fatality possibly involving self-injection herion use.

DISCUSSION

The major finding which is emphasized in this series of open label case studies is the reported evidence of apparent efficacy of ibogaine in the acute opioid withdrawal syndrome. While the lack of formal clinical methodology such as a structured instrument rating withdrawal is unfortunate, the apparent validity of the findings rests largely on the ability of the two co-authors H.S.L. and G.M.N.F. to reliably recognize the symptoms of the acute opiate withdrawal syndrome. Both of the above co-authors have extensive experience in observing the clinical feature of opioid dependence, and recorded their observations on withdrawal signs and symptoms. The correspondence of Dr. Bastiaans on over half the cases provided some additional assurance regarding the accurate assessment of the features of opioid withdrawal.

There are significant safety concerns that will need to be addressed by careful investigation in clinical research settings if ibogaine is to be considered as a clinical option for opioid detoxification. Despite ibogaine treatments having taken place under conditions of relatively "low tech" improvisation, the need for supervisory personnel to serve the functions that are presently served by volunteer participants in the existing informal treatment network would need to be included in calculating the cost of ibogaine treatment in a conventional medical setting. Although it has been suggested that the material recalled under the influence of ibogaine might have potential psychotherapeutic significance, the significant subjective psychoactive state produced by ibogaine might not be widely desired or tolerated. It remains to be seen whether a modification of ibogaine can provide the option of resolving the psychoactive effects of the drug from its putative anti-addictive qualities. An ibogaine congenor, 18-methoxycoronaridine reportedly produces effects similar to ibogaine on morphine and cocaine administration in rats but might produce less of ibogaine's psychoactive effects.

Despite the methodologic disadvantages of the informal treatment context, the case series presented here appears to provide some support for the efficacy of ibogaine in the treatment of acute opioid withdrawal. Whether or not ibogaine emerges as a viable conventional treatment option, the question of its clinical efficacy is interesting because it appears that ibogaine may represent a novel pharmacologic mechanism that is not currently being utilized in the treatment of drug dependence. If it is indeed effective, ibogaine could eventually prove to be a productive paradigm for the study of the neurobiology and development of new approaches to addiction. The reported effectiveness of ibogaine in this series suggests the need for systematic investigation in a conventional clinical research setting.
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18-Methoxycoronaridine Differentially Alters the Sensitized Behavioral and Dopaminergic Responses to Repeated Cocaine and Morphine Administration

Implications for Sensitization in the Mediation of Drug Addiction

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The repeated, intermittent administration of a variety of drugs of abuse can induce a progressive increase in certain drug effects. Terminated sensitization, this phenomenon has been implicated in the development of a variety of neuropsychiatric disorders, most recently, drug addiction. In particular, it has been theorized that the sensitization of neurotransmission in the mesolimbic dopamine (DA) system underlies the development of craving, which often leads to relapse in drug addiction. The sensitization of DA transmission in the NAC also appears to be critical for the sensitization of the psychomotor-activating effects of addictive drugs (e.g., refs. 5 and 6) and as such, has been implicated in the development of drug-induced psychosis. Given the putative role for sensitization in the development of drug addiction, it was postulated that the anti-addictive efficacies of iboga agents (e.g., 7 and 8) might be related to an ability to modulate the expression of drug-induced sensitization in drug-experienced animals. To that end, a series of experiments were conducted which assessed the effects of pretreatment with the potential anti-addictive drug, 18-methoxycoronaridine (18-MC), on the expression of neurochemical and behavioral sensitization in rats with previous MOR and COC experience.

The methods used in this study are summarized in Table 1, and Table 2 summarizes the results.

Several results of this study are worthy of discussion as they

1. challenge our current understanding of the role for DA in the NAC in mediating the psychomotor-activating effects of stimulant and opioid drugs and
2. relate to the theory that DA sensitization is the critical neuroadaptation underlying the development of drug addiction.2,3

1 and 2 should be equal to each other