ICEERS INTERNATIONAL CENTER FOR ETHNOBOTANICAL EDUCATION RESEARCH & SERVICE

Iboga

Scientific information

Ibogaine is a naturally occurring alkaloid obtained from the root bark of the African plant Tabernanthe iboga. Animal studies and accumulated anecdotal evidence suggest that ibogaine eliminates withdrawal, reverses tolerance, suppresses drug craving and reduces relapse into drug use in humans. But what is the real evidence of efficacy in addiction treatment? Do we know its mechanisms of action? What are the risk factors? And what are its psychological effects?

Evidence of Efficacy

Ibogaine shows promise as a tool in treating drug craving and opioid withdrawal syndrome. There are currently no efficient treatments to combat drug craving. Additionally, other than opioid substitution therapies, there is a lack of pharmaceuticals that can eliminate the opioid withdrawal syndrome and help opioid-dependent patients to give up the use of opiates such as morphine, heroin, methadone and oxycontin. Furthermore, standard pharmacological and psychological approaches used in the treatment of addiction have very limited success. It seems necessary to investigate new and potentially more efficient tools for this growing individual and social problem.

Animal studies have found consistent decreases in drug self-administration after treatment with this alkaloid. Preclinical studies show that iboga alkaloids produce significant attenuation of opioid withdrawal signs in different animal species, and reduce self-administration of cocaine, amphetamine, methamphetamine, alcohol, and nicotine (1).

In humans, one paper describing 33 treatments for opioid dependence showed complete resolution of withdrawal signs in 29 (88%) (2). An open label prospective study showed resolution of withdrawal signs and symptoms at 24 hours (3). No controlled clinical trials have been conducted to assess clinical efficacy.

Anecdotal evidence suggests that a single administration of ibogaine is capable of alleviating drug craving and relapse of drug use for a period of time of weeks to months. The only follow-up study done until now showed that 67% of the 21 participants ended the use of either all or the primary and secondary drugs of abuse after ibogaine treatment. Thirty-three percent of them did not end the use of their primary or secondary drugs of abuse, but decreased the amount of drug use. The overall average drug free period (from primary and secondary drugs of abuse) of all participants was 21.8 months. The median was, however, lower - 6 months. (4).

Informal addiction treatments with ibogaine have spread throughout the world during the last three decades. These are typically performed in private clinics with medical backup and underground settings (such as private houses, apartments or even hotel rooms) outside of medical facilities by providers that often lack medical training. Until 2006 a total of 3414 reported ibogaine treatments had taken place all over the world, a fourfold increase relative to 5 years earlier. Sixty-eight percent of these users took ibogaine with the intention of treating a substance-related disorder, mainly opioid withdrawal (5). This fast increase in ibogaine's popularity in unofficial contexts, mostly spread by word of mouth, suggests efficacy as an addiction treatment tool.

Mechanisms of Action

Ibogaine (12-methoxyibogamine) is the main alkaloid of at least 12 alkaloids found in the Tabernanthe iboga plant. After ingestion, ibogaine is metabolized by the cytochrome P450 2D6 (CYP2D6) into also active metabolite noribogaine (12-hydroxyibogamine) (6). Since it has been shown that noribogaine persists in plasma for at least 24 hours after oral ibogaine administration, it has been speculated that noribogaine may selectively mediate putative anti-addictive effects that persist for prolonged periods of time.

Ibogaine and noribogaine interact with several different neurotransmitter systems, each with its own infinitely complex realm of metabolism, pharmacokinetics and affinity. Furthermore, although ibogaine and noribogaine share some mechanisms of action, their pharmacological profiles are different. In that way, the mechanisms of the anti-addictive properties of ibogaine are not unequivocally defined.

Ibogaine interacts with multiple binding sites within the central nervous system (CNS), including N-methyl-D-aspartate (NMDA), receptor coupled ion channels, κ-opioid (κ1 and κ2), μ-opioid and σ2, serotonin (5-HT2 and 5-HT3), muscarinic (M1 and M2) receptors and monoamine uptake sites as well as inhibition of monoamine oxidase, and nicotinic acetylcholine receptors (1). This prolific mechanism of action of ibogaine may be the reason why it may be effective in the treatment of such different pharmacological classes of drugs.

A recent mechanism of action of ibogaine has been discovered that may help to explain its anti-addictive properties. Ibogaine seems to activate the glial cell line–derived neurotrophic factor (GDNF) pathway in the ventral segmental area of the brain. Short term ibogaine exposure results in a sustained increase in GDNF expression, caused by an increase in GDNF mRNA leading to protein synthesis and resulting in the corresponding activation of the GDNF signaling pathway (1). Accumulating evidence suggests that GDNF plays a unique role in opposing the negative actions of drugs of abuse and raises the survival of adult dopaminergic neurons. These changes mediated by GDNF could lead to synaptic remodeling and change the responsiveness of the mesolimbic dopaminergic system and by doing so, counter the incentive and/or rewarding value of, and the neuroadaptations induced by, drugs of abuse (7).

Furthermore, Ibogaine triggers remodeling of the basic cellular metabolism. Under the initial energy cost this results in increased efficacy of physiological anti-oxidative systems, which reduce oxidative damage and lowers basal metabolic needs. Together with induced catabolic enzymes they set a new metabolic equilibrium that saves energy and makes it easily available in case of extra needs. While healthy organism profits from improved fitness and mental performance and can withstand higher stress without risking a disease, due to the same principle ibogaine provides beneficial support at the recovery after diseases including addiction syndrome (8).

Finally, differently from most drug of abuse, ibogaine does not increase dopamine levels in the nucleus accumbens, so there is no 'reward' effect, indicating Ibogaine has a low potential for abuse, even though it is currently schedule 1 drug in the US which is the schedule for drugs that have 'a high potential for abuse and no medical use'.

Psychology

The ibogaine experience has been described to consist of three different phases (4) (9).

In the first phase (0-1 hours) the onset of the effects progress gradually and changes of visual, auditory and body perception appear. Also physical symptoms such as dry mouth and difficulties in coordination may appear.

The second phase of the ibogaine experience (1-10 hours) is often called 'waking dream' or oneiric state. Patients typically lie down and experience the visual and cognitive effects of ibogaine: eyes closed visuals, a buzzing sound, changes in perception of their own body, time and space. Patients feel physically heavy, have ataxia and movement induces nausea. The form of the material experienced during this ibogaine visualization period can be as varied as the scope of material seen in ordinary dreaming, in that it may be realistic or symbolic, in black and white or color, and diverse in subject matter. Scenes of exotic cultures, objects, deceased people, memories from childhood or traveling

through the own brain and DNA may be experienced (some hear, some more feel...). The visual content has often a limited emotional charge, but this is not always the case. The visualization will be interrupted if people open their eyes. It should also be noted that this dreamlike phase tends to end abruptly.

The third phase (10-36 hours) is often called “the cognitive phase of deep introspection”. The material reviewed and reported by patients during the cognitive evaluation phase may consist of material from the dreamlike experience, or of other memories, and often concerns traumatic or emotional experiences, personal relationships, and important decisions that the patient has made. There is an intellectual evaluation of earlier experiences in life and choices made along one’s personal growth process. Subjects may discover that there were other alternatives to these choices. This may result in a more responsible attitude towards future choices and forgiveness towards oneself or his/her relatives for past mistakes, pain caused, etc.

Even though there is a lack of ritual setting in most Western ibogaine therapy contexts, the experience is often described as a transformative rite of passage. Apart from the clinical use of ibogaine in contemporary society, also religious contexts are found, in the form of officially established churches or unofficial religious groups.

Safety

Although ibogaine seems a promising drug for treating drug addiction, adverse events have also been reported, mostly in uncontrolled non-medical settings. Seemingly, ibogaine can induce autonomic responses (10) and a prolonged QT interval (11), so its medical use may be limited in people suffering from premorbid cardiovascular diseases or in the presence of other medications.

In fact, from 1990 through 2008, at least 15 individuals are known to have died within 1.5–76 h of taking ibogaine, although in most of them advanced comorbidities and contributing conditions including preexisting medical issues, particularly cardiovascular disease, and drug use around the time of treatment seemed to be the cause (12). Therefore people with a history of heart attack, heart murmurs, arrhythmia, heart operation or severe obesity should not take ibogaine. Before taking ibogaine the individual should not use his drug of choice for the time period the drug needs to be sufficiently eliminated. This depends on the drug’s half life and is different for each substance and differs between subjects. One should be in good condition; abstinence syndrome causes dehydration, electrolyte disbalance, energy exhaustion etc. Previous detox is recommendable, if possible, and ideally, obligatory. Also substances or foods that are broken down by the CYP 450 2D6 should be avoided, as they could interact with ibogaine potentiating its effect of bradycardia and QT prolongation.

Another risk factor is history of pulmonary embolism, especially after a physical injury caused by an accident or long immobility during airplane travels to the treatment center. People with bleeding problems, chronic blood clots or people who got into a recent accident which could have caused bruises and bleedings should be excluded from this treatment.

Also asthma, Cancer, Cerebellar dysfunction (Meneire’s disease, balance problems), Chronic fainting, Diabetes, Emphysema, Epilepsy, Gastrointestinal tract diseases (Crohn’s, Inflammatory Bowel Disease), Gynecological problems, HIV, AIDS, Hepatitis C (if active and with liver enzymes 200% above normal), Kidney problems/Renal Disease, Liver disease, Respiratory Disease, Palsy, Pregnancy, Seizures, Stroke, Thyroid problems, Tremors, Tuberculosis and Ulcers are often contraindications in treatment centers, depending on the severity.

The most frequent side effects observed after a single dose of ibogaine were nausea, mild tremor and ataxia at early time points after drug administration. Respiration rate, systolic and diastolic blood pressures, and pulse do not seem to changes across time. However, a hypotensive response to ibogaine may occur in cocaine-dependent subjects (13).
The settings in which ibogaine is being taken or given vary greatly, from full medical backup conditions with prior medical and psychological examinations (including ECG, stress EGG or Holter monitor, blood tests, liver panel, etc.) to conditions lacking any preselection or medical backup. Taking this into account, a comparative of the safety perspectives between ibogaine and Methadone indicates ibogaine has an acceptable risk-benefit ratio;

Between 1989 and 2006: 11 fatalities (at least 3 in which anatomically verified, preexisting medical conditions were identified as the cause of death by the medical examiner with no mention of ibogaine) occurred of all 3,414 reported Treatment Episodes (TEs). This is 1 ibogaine-related death on 427 TEs (2).

In Australia between 2000 and 2003 there were 282 fatalities that met author’s criteria for methadone-related death occurred on 102.615 TEs, which is 1 methadone-related death on 364 TEs (14) (15).

In 2004 110 fatalities in which the medical examiner mentioned methadone as a cause of death occurred in Utah on 52,350 methadone prescriptions, which is 1 methadone-related death on 476 methadone prescriptions (16).

In case ibogaine would be available in medically controlled settings with thorough preparation and follow up program, adverse events would probably be greatly reduced.

References

1. Maciulaitis R, Kontrimaviciute V, Bressolle FM, Briedis V. Ibogaine, an anti-addictive drug: pharmacology and time to go further in development. A narrative review. Hum Exp Toxicol. 2008; 27(3):181-94.

2. Alper KR, Lotsof HS, Frenken GM, Luciano DJ, Bastiaans J. Treatment of acute opioid withdrawal with ibogaine. Am J Addict. 1999; 8(3):234-42.

3. Mash DC, Kovera CA, Pablo J, Tyndale RF, Ervin FD, Williams IC, Singleton EG, Mayor M. Ibogaine: complex pharmacokinetics, concerns for safety, and preliminary efficacy measures. Ann N Y Acad Sci. 2000; 914:394-401.

4. Bastiaans E. Life after Ibogaine. An exploratory study of the long-term effects of ibogaine treatment on drug addicts. Science Internship Report, Vrije Universiteit Amsterdam. http://www.ibogaine.desk.nl/ibogaine_udi_bastiaans.pdf

5. Alper KR, Lotsof Alper KR, Lotsof HS, Kaplan ChD. The ibogaine medical subculture. J. Ethnopharmacol. 2008; 115: 9–24.

6. Alper K. Ibogaine: A review. In Alpert KR, Glick SD, Cordell GA (Eds.) Ibogaine: Proceedings of the First International Conference (Also published as Volume 56 of The Alkaloids Chemistry and Biology). San Diego: Academic Press, pp 1-38., 2001.

7. Carnicella S, Ron D. GDNF--a potential target to treat addiction. Pharmacol Ther. 2009;122(1):9-18

8. Paškulin R, Jamnik P, Danevčič T, Koželj G, Krašovec R, Krstić-Milošević D, Blagojević D, Štrukelj B. Metabolic plasticity and the energy economizing effect of ibogaine, the principal alkaloid of Tabernanthe iboga. Journal of Ethnopharmacology 2012; 143 (2012) 319–324.

9. Lotsof HS, Alexander NE. Case studies of ibogaine treatment: Implications for patient management strategies. Alkaloids Chem Biol. 2001; 56:293-313.

10. Maas U, Strubelt S. Fatalities after taking ibogaine in addiction treatment could be related to sudden cardiac death caused by autonomic dysfunction. Med Hypotheses. 2006; 67(4):960-4.

11. Hoelen DW, Spiering W, Valk GD. Long-QT syndrome induced by the antiaddiction drug ibogaine. N Engl J Med. 2009; 360(3):308-9.

12. Alper KR, Stajić M, Gill JR. Fatalities temporally associated with the ingestion of ibogaine. J Forensic Sci. 2012 Mar;57(2):398-412.

13. Mash DC, Kovera CA, Pablo J, Tyndale R, Ervin FR, Kamlet JD, Hearn WL. Ibogaine in the treatment of heroin withdrawal. Alkaloids Chem Biol. 2001;56:155-71.

14. Gibson, A.E. and Degenhardt, L.J., (2007). Mortality related to pharmacotherapies for opioid dependence: a comparative analysis of coronial records. Drug and Alcohol Review 26, 405-410.

15. Gibson, A. and Degenhardt, L.,(2005). Mortality related to naltrexone in the treatment of opioid dependence: A comparative analysis. NDARC Technical Report No. 229. National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia 92 pp.

16. Sims SA, Snow LA, Porucznik CA (2007): Surveillance of methadone-related adverse drug events using multiple public health data sources. Journal of Biomedical Informatics 40:382-389.

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