# The Efficacy of Ibogaine in the Treatment of Addiction; an open label, single fixed dose pilot-study of the efficacy of ibogaine in opiod-dependent subjects

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1. To investigate, in patients with opioid dependence, the short and long term effects of a single administration of ibogaine on craving and substance use during a six month follow up period.2. To investigate what effect ibogaine causes on Event...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Impulse control disorders NEC |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON40645

**Source**
ToetsingOnline

**Brief title**
Ibogaine in opioid addiction

### Condition

- Impulse control disorders NEC

**Synonym**
opioid addiction, opioid dependence

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum Sint Radboud

**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** addiciton, ibogaine, opioid, treatment

## Outcome measures

### Primary outcome

The main study parameters are number of relapse, experienced subjective craving

after detoxification,

### Secondary outcome

Secundary outcome measures will consist in changes in brain activity as

measured by Event Related Potentials (ERPs) (as measured on EEG) related to

cue-responsivity.

# Study description

### Background summary

Addiction is one of the most challenging consequences of chronic substance use. Considered together, tobacco, alcohol and illicit drug use are implicated in over 12% of mortality worldwide. Addiction treatment methods remain limited in number and long-term success rates are poor. This applies in particular to addiction to opioids. There is a great need for more effective treatment modalities.

In animal studies and case reports, ibogaine appears to attenuate the physiological symptoms associated with opiate withdrawal and prevents relapse that most often occurs following acute detoxification by reducing craving and thus enhancing the possible effectiveness of post-detoxification-treatment .

The main hypotheses of this investigation are:
• A single administration of ibogaine is effective in interrupting the opioid dependence syndrome, as measured by craving and drug use.
• Detoxification by means of Ibogaine reduces craving during several months which gives a window of opportunity in which treatment as usual can take place with less dropout and better results.

• The adverse short and long term somatic and psychological effects of Ibogaine are relatively mild and transient in nature.

**Study objective**

1. To investigate, in patients with opioid dependence, the short and long term effects of a single administration of ibogaine on craving and substance use during a six month follow up period.
2. To investigate what effect ibogaine causes on Event Related Potentials (ERP), and functional MRI neuroimaging, as a measure of cognitive processes linked to craving.
3. To investigate the decrease in numbers of drop-out during treatment after detoxification.
4. To investigate the safety of ibogaine during acute in-hospital opioid withdrawal and during a 6 month post treatment evaluation.
5. Secondary objectives concern the exploration of possible predictive factors for response on ibogaine (demographics, pretreatment ERP*s).

**Study design**

This is an exploratory, open label study without control condition.

**Intervention**

The pilot is divided into an in-patient and an out-patient phase:

1. The first phase, the in-patient phase, consists of (minimal) 10 days of hospitalization. During a short in-patient stabilization period including comprehensive medical and psychiatric assessment, patients will receive short acting oral morphine sulphate as opioid substitution therapy instead of methadone. This is to prevent the presence of opioids in the body after treatment with ibogaine. In this pre-treament phase patiente are in the clinic of Iriszorg.
Thereafter a single dose of ibogaine will be administered orally (10 mg/kg body weight). During and directly after the administration of the ibogaine patients will be monitored intensively, with respect to somatic and mental signs, including cardiovascular monitoring. During an directly after ibogaine administration patients will stay at the department of psychiatry of the Radboud UMC.

2. Next patients will return to the clinic of Iriszorg for minimally one week and will be prepared for the out-patient follow-up trajectory. During this week patient and therapist will be develop an individual treatment plan consisting in a proposal how to handle changes in life after stopping methadone and how to anticipate periods with recurring craving. Upon hospital discharge at at least at 2, 4, 8,12 and 24 weeks follow-up visits will be scheduled in order to

provide the therapy and to evaluate the long term effects of the intervention. During this phase, conventional *treatment as usual* will be provided based on Community Reinforcement Approach (CRA), including Cognitive Behavioral Therapy.

**Study burden and risks**

Burden associated with participation:
During the screening a physical exam will be performed as well as an ECG and blood sampling for a routine blood testing. There will be a psychiatric exam including Mini International Neuropsychiatric Interview (MINI), and Addiction Severity Index (ASI). Patients will be hospitalized for at least 10 days. This burden is comparable to the burden of a standard opioid detox. On top of this an EEG (1 hour) and a fMRI investigation will performed during the first days of hospitalization.
During the detox phase patients may suffer from nausea. This will be addressed with the anti-emetic medication metoclopramide prior to the ingestion of ibogaine. Although patients who undergo a opioid detox often experience nausea (which is also addressed with a standard prescription of anti-emetics), ibogaine may have an extra nauseating effect.
During the detox phase patients may experience ataxia during several hours. They might experience intense dreamlike images which might get emotional value and meaning during and after the detox. This will be addressed by letting people lie on a bed in a darkened room with medical, psychiatric and nursing care at site.
During the detox people are ECG monitored every 30.

Risks:
The dominant risk during the detox phase with ibogaine is the possibility of heart rhythm disturbances (bradycardia and/or QT-prolongation). Extreme bradycardia or QT-prolongation (which may lead to Torsade des Pointes) may involve the risk of a cardiac arrest.
This risk has never been assessed in a study. During detoxification of 400 patients in hospital conditions severe side effects were not observed (Mash 2005). The suspicion of these risks is based on case-histories in which cardiac fatalities occurred in a period after the ibogaine ingestion.
These risks are addressed by a thorough medical screening so all patients with (possible) factors that might enhance the effect of ibogaine on the heart rhythm are excluded from treatment. Hospitalization during 10 days, change of long acting to short acting substitution opioids and urine-monitoring of illegal drug-use. This will guarantee a maximum stability.
During treatment participants will be monitored on cardiac activity by use of ECG. This will be supervised by an internist/cardiologist who also will perform medical treatment in case of a cardiac emergency.

# Contacts

**Public**
Universitair Medisch Centrum Sint Radboud

Reinier Postlaan 6
Nijmegen 6525 GC
NL
**Scientific**
Universitair Medisch Centrum Sint Radboud

Reinier Postlaan 6
Nijmegen 6525 GC
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

• Males or females 23 to 60 years of age, currently dependent on opiate narcotics, as assessed by DSM-IV (304.00) criteria.
• Wish for detoxification of the opioids used and wish for lasting abstinence.
• Did not succeed in intensive treatment as usual.
• Subjects must be willing and properly motivated to participate in the study in accordance with the study requirements as evidenced by signing a written informed consent, willing to cooperate with the investigators and willing to participate in all the evaluations.

## Exclusion criteria

• Patients with cardiac illness: Ventricle fibrillation in history, Long QT syndrome, history of

syncope, QTc >500 ms on ECG at screening.
• Patients who are diagnosed with schizophrenia, patients with a history of psychotic symptoms. Severe major depressive disorder.
• Patients who are homeless.
• Pregnancy.
• Patients who are actively suicidal.
• Has any clinical significant chronic or acute cardiac, renal or medical condition or has any unstable medical condition.
• Has a disorder that would interfere with the absorption, distribution, metabolism or excretion of Ibogaine (patients with major gastrointestinal problems including ulcers, regional enteritis, or gastrointestinal bleeding; patients with liver enzymes higher than four times normal range).
• Patients who don*t have opiates and/or methadone in urine test at screening
• Patient requiring concomitant medications that may severely interfere with use of ibogaine (i.e., anti-epileptic drugs, neuroleptics, antidepressants): especially those medications which have a QT-prolonging effect and those who are significantly interfering with the CYP2D6 enzyme system.
• Patient who has received any drug known to have a well defined potential for toxicity to a major organ system within one month prior to entering the study or have previously received any investigational new drug within the previous six months.

# Study design

## Design

**Study type:** Interventional

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

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| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 05-10-2015 |
| Enrollment: | 12 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |

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|---|---|
| Brand name: | ibogaine HCl |
| Generic name: | ibogaine HCl |

## Ethics review

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| Approved WMO Date: | 10-11-2014 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 30-04-2021 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2014-000354-11-NL |
| CCMO | NL47613.091.14 |