Unraveling cocaine metabolism in patients with cocaine use disorder for the purpose of potentially improving bioanalytical tests for cocaine use

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Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON56992

Source
ToetsingOnline

Brief title
Unraveling cocaine metabolism in patients with CUD

Condition

- Other condition
- Psychiatric disorders NEC

Synonym
cocaine addiction, Cocaine use disorder

Health condition

Stoornis in het gebruik van cocaïne

Research involving

Human

Sponsors and support

Primary sponsor: Indigo i-psy PsyQ Brijder B.V.
Source(s) of monetary or material Support: Bedrijf: Di-AcetylM B.V. ,Di-AcetylM B.V.

Intervention

Keyword: bioanalysis, Cocaine metabolism, cocaine use disorder, HPLC-MS/MS

Outcome measures

Primary outcome

To observe the metabolic profile of cocaine in urine, saliva and blood of volunteers with cocaine use disorder participating in heroin-assisted treatment.

Secondary outcome

To explore whether the bioanalytical method for determining cocaine use in patients with cocaine use disorder could be improved by quantitative measurement, measurement of a metabolite other than benzoylecgonine, or measurement in a different biomatrix (saliva).

Study description

Background summary

Cocaine is rapidly converted into many different metabolites after entering the circulation (see Figure 1 in the study protocol). Benzoylecgonine is the most abundant metabolite of cocaine and the longest detectable metabolite in the body following cocaine use. [1] The cut-off value for a positive benzoylecgonine test in urine is 300 ng/ml. If cocaine is used recreationally, benzoylecgonine is detectable in urine up to 3 days after cocaine use.[2] However, benzoylecgonine can still be detected in urine for up to 7-16 days in patients with CUD.[3] This is partly due to the high cocaine concentrations relative to the cut-off value in urine of patients with CUD. The median

concentration is 22,562 ng/ml, and at concentrations around 300,000 ng/ml, no acute toxicity is observed.[1] In addition, the long detectability of benzoylecgonine in the urine of patients with CUD seems to be caused by tissue accumulation of benzoylecgonine.[4-6] With repeated exposure to cocaine, benzoylecgonine is accumulated in tissues. Following cessation of use, the cocaine is gradually released back into the bloodstream and subsequently into the urine.[4-6] Due to these mechanisms, cocaine analyses based on benzoylecgonine can give false-positive results and thereby overestimate cocaine use. Consequently, benzoylecgonine is not an ideal biomarker for the detection of cocaine use reduction in patients with CUD.

To date, no suitable method has been developed for measuring or interpreting cocaine use specifically for patients with CUD. Consequently, within RCTs, the effect of the drug on cocaine use may be underestimated. To prevent this within the planned REDUCE trial, we aim to investigate whether we can develop a bioanalytical method for the determination of cocaine use specifically for patients with CUD. To develop this bioanalytical method, it is necessary to conduct a preliminary study within a population similar to that of the study participants within the REDUCE trial.

The references can be found on pages 28-31 of the study protocol.

Study objective

To unravel cocaine metabolism in patients with cocaine use disorder for the purpose of potentially improving bioanalytical tests for cocaine use

Study design

Observational study

Study burden and risks

Participants do not directly benefit personally from participating in the study. The burden of this study includes eight visits to the treatment site. During all of these visits, subjects have to collect and submit urine and saliva eight times and undergo an interview in which there is asked about their recent drug use. In addition, blood will be drawn once during the first study visit. Sample collection, especially the single blood sample, can be perceived as burdensome. As this is an observational study where participants are not exposed to any intervention, the risk of participating in this study is limited to potential complications of venipuncture.

The study may lead to a bioanalytical method of measuring cocaine use in patients with CUD that is specific to this patient population, which may allow better assessment of drug efficacy in RCTs for the treatment of CUD.

Ultimately, this may contribute to an RCT that could lead to an effective drug treatment for CUD.

We believe that the benefits of the research are proportionate to the burden on participants.

Contacts

Public
Indigo i-psy PsyQ Brijder B.V.

Monsterseweg 93
s Gravenhage 2553 RJ
NL
Scientific
Indigo i-psy PsyQ Brijder B.V.

Monsterseweg 93
s Gravenhage 2553 RJ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

1. Age between 18 and 65 years of age;
2. Moderate or severe cocaine use disorder according to DSM-5 (>=4 criteria);
3. Active participation in heroine-assisted treatment;

4. Snorting, inhaling or injecting cocaine use as primary route of administration;
5. Able and willing to provide one blood sample;
6. Able and willing to provide urine- and saliva-samples and to be interviewed about recent drug use for 2 times per week during 4 consecutive weeks;
7. Understanding and speaking Dutch;
8. Able and willing to give written informed consent.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

1. Does not have a sufficiently good understanding of Dutch for informed consent.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	12-11-2024
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	06-09-2024
Application type:	First submission

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
CCMO	NL86849.058.24