High-dose baclofen for the treatment of alcohol addiction * A double-blind, randomized, placebo-controlled study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON41310

Source
ToetsingOnline

Brief title
High-dose baclofen for the treatment of alcohol addiction

Condition

- Other condition

Synonym
addiction

Health condition

verslaving

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Amsterdams fonds voor verslavingsonderzoek

Intervention

Keyword: alcohol dependence, Baclofen, high dose

Outcome measures

Primary outcome

The primary outcome measure is the time to the first relapse. Lapse is defined as the first occurrence of alcohol intake of more than four standard drinks on one occasion for females and five standard drinks on one occasion for males. Relapse will be defined as the second occurrence of alcohol intake of more than four standard drinks per occasion for females and five standard drinks per occasion for males.

Secondary outcome

Key secondary substance related outcome measures 16 weeks are:

- cumulative abstinence duration percentage (CADP). CADP is an estimate of the proportion of abstinent days over 16 weeks
- number of drinks (total alcohol consumption (TAC) during 16 weeks)
- number of heavy drinking days

Other secondary outcome measures after 4 weeks and 16 weeks are:

- number of drinks
- the level of craving
- the presence of alcohol dependence according to DSM-IV

- cognitive biases

- level of anxiety

- sleep pattern

- compliance with therapy (pill counts and attendance at outpatient therapy sessions)

- biological markers of heavy alcohol consumption (carbohydrate deficient transferring, CDT)

- the use of other drugs

- the general quality of life

- adverse events

Study description

Background summary

First animal studies showed a reduction of alcohol drinking behavior and a decrease of the intensity of withdrawal signs in alcohol-preferring rats caused by the administration of baclofen (Colombo et al., 2000; 2003; Stromberg, 2004; Liang et al., 2006). Consistent with animal research, two open label studies showed that the administration of 30 mg/day of baclofen for 27 days or 12 weeks increased abstinence and reduced alcohol intake and craving for alcohol in alcohol-dependent patients (Addolorato et al., 2000; Flannery et al., 2004). The efficacy of baclofen was further evaluated in two double-blind randomized controlled studies, in which the positive effects of 30 mg/day baclofen could be replicated (Addolorato et al., 2002; Addolorato et al., 2006). In summary, although one recent double blind randomized controlled study failed to find any evidence for the efficacy of low dose baclofen (Garbutt et al., 2010), overall, literature supports the potential value of baclofen in the treatment of AD.

Although, the efficacy of low doses of baclofen has been studied, randomized controlled studies examining higher doses of baclofen are lacking. Two case studies demonstrated that the administration of higher doses (up to 270 mg) of baclofen can completely suppress alcohol craving (Ameisen, 2005; Bucknam, 2007). These studies suggest the use of higher doses of baclofen in the treatment of alcohol dependence. To date, no randomized controlled studies have

been done comparing high-dose baclofen with placebo treatment. Furthermore, studies aiming to examine of possible other factors, which could play a role in the effectiveness of baclofen are missing. Based on earlier literature, potential predictors of treatment response could be the individual*s anxiety level, motives to drink, role of family history, genetic endowments or personality (Garbutt et al., 2010; Addolorato et al., 2002; 2006; Flannery et al., 2004; Cooper et al., 1995; Lesch & Walter, 1996; Monterosso et al., 2001; Rohsenow et al., 2007; Oslin et al., 2003; Anton et al., 2008).

Study objective

The primary goal of the present study is to examine the efficacy of high dose baclofen for the treatment of patients with AD in a double-blind, randomized, placebo controlled study. Therefore high dose baclofen will be compared with placebo.

Furthermore, as a secondary study objective, factors, which may predict the treatment response of baclofen are investigated. In order to assess which patients benefit the most of the treatment with baclofen, it is proposed to examine the role of:
- anxiety
- motives to drink
- personality
- family history and age of onset of AD
- genetic endowments

Additionally, as a third goal, the effect of baclofen on cognitive biases concerning alcohol will be assessed. The following cognitive biases will be examined:
- attentional bias
- approach/ avoidance bias
- affective associations

Study design

In order to test the efficiency of baclofen a double blind, randomized, placebo controlled study will be conducted. There will be an intervention.
It is planned to recruit 130 patients. 65 patients will receive treatment with a high dose of baclofen (150 mg, 120 mg or 90 mg) and 65 participants will receive placebo.
The study is conducted in six clinics: SolutionS Center, Ready for Change, U-Center, The Home Clinic and the Stichting voor Alcoholverslavingszorg, Clear Mind Amsterdam. Furthermore, patients who followed a treatment at SolutionS without success get the possibility to get a ambulant treatment with baclofen at SolutionS Center.

Intervention

Baclofen or placebo will be administered for the duration of 16 weeks. Thereafter the medication will be decreased. All participants receiving baclofen will start with a dose of 30 mg/day. In the high dose group, the dosage will be increased up to a maximum of 150 mg within six weeks. From the start of the second week, the dosage will be increased with 30 mg every seven days. In order to ensure a slow habituation the dosage is increased with 10 mg every other day. Every seven days possible side effects are assessed by means of a questionnaire. In case of prolonged side effects, the dosage will be decreased to the former 30 mg step and will be slowly increased again. If no side effects occur, the dosage will be increased to the following 30 mg step. If side effects occur during the six days, a physician from the clinic can decide not to administer the additional tablets for increasing the dosage. After six weeks the final dosage is reached and patients are stabilized on this dose. In the high dose group it is possible to reach 90 mg, 120 mg or 150 mg. In the placebo group the dosage will be increased with placebo pills. Patients continue taking one of these dosages until week 16, thereafter the dosage will be slowly decreased.

Baclofen is administered in 10 mg pills. All tablets will be identical in appearance. Participants in all groups will start with three tablets per day and can end up taking a maximum of 15 tablets, depending on the occurrence of side effects. Pills are taken orally three times a day.

Study burden and risks

Paticipants are tested three times. The first testing session is scheduled after detoxification. Testing will take place at SolutionS, Ready for Change, U-Center, at home (via The Home Clinic), in the office of the Stichting voor Alcoholveslavingszorg, Clear Mind Amsterdam or in the office of Terwille. After signing the informed consent, participants are asked to fill in questionnaires in order to collect information about about alcohol use, alcohol drinking history, family history, use of other drugs, psychological problems and personality. Participants are asked to conduct three behavioral tasks on a computer. Each task will take about 12 minutes.The first testing session will take about 60 - 90 minutes.
After 4 and 16 weeks participants are asked to repeat the same procedure. Each session will take about 60 to 90 minutes. After 6 month, participants are contacted by phone in order to ask questions about alcohol use, craving and wellbeing. This phone calls will take about 10 minutes each.
Participants are asked to give twice a blood sample of 30 ml in order to determine biological markers of alcohol consumption.
Furthermore, in order to test for alcohol use, breath alcohol concentration will be measured prior to the screening session and prior to therapy sessions during the out-patient period. DNA will be collected through saliva samples.

Risks:
- The negative mood induction and the fear inducing pictures may evoke negative thoughts in participants. In order to diminish possible negative affect, a positive mood is induced at the end of each session. Additionally, participants get the possibility to talk to a psychiatrist, if desired.
- The use of baclofen can cause various side-effects, although side effects do not occur in all users and many users have no, or minor, side effects. Very frequently (>10%) occurring side effects include sedation, drowsiness, and nausea. Frequently (1-10%) occurring side effects include decrease in cardiac output, dizziness, headache, ataxia, tremor, nystagmus, coordination disorder, reduction in acuity, breath depression, hypotension, vomiting, weakness, dry mouth, constipation, diarrhea, hyperhidrosis, skin rash, pollakisuria, enuresis, dysuria, fatigue, confusion, euphoria, depression, hallucination, muscle weakness, and myalgia. Rarely (0.01-0.1%) occurring side effects include paresthesia, dysartria, urinary retention, erectile dysfunction, dysgeusia, and abdominal pain. Very rarely (< 0.01%) occurring side effects include hypothermia.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Male and Female patients, aged between 18-70 years
- Participants have a current DSM-IV diagnosis of alcohol dependence
- Participants sign a witnessed informed consent
- Participants have a breath alcohol concentration lower than 0.05 at the screening visit
- Participants must have been drinking * 14 drinks (female) or * 21 drinks (males) on average per week over a consecutive 30-day period in the 90-day period prior to the start of the study and have two or more days of heavy drinking (5 drinks for females, 6 drinks for males) in the 90-day period prior to the start of the study
- Participants must have had a minimum of 96 hours of abstinence prior to the start of the medication
- Participants can be abstinent for a maximum of 21 days prior to the start of the study
- Participants must be able to speak and understand dutch
- Participants provide an identified locator person that can be contacted during the study in the event of loss of contact

Exclusion criteria

- Participants with severe psychiatric disorders (schizophrenia, schizoaffective disorder, bulimia/anorexia, dementia, or ADHD requiring medication) except for depression, bipolar disorder and anxiety
- Participants with serious medical illnesses (Parkinson*s disease, gastric ulcer, duodenal ulcer, cerebrovascular disease, respiratory insufficiency, hepatic or renal insufficiency, and epilepsy)
*- Patients who are treated with anti-hypertensiva
- Participants who are at risk of suicide evaluated by the suicidality module of M.I.N.I.
- Participants who have a cognitive impairment which is likely to interfere with the understanding of the study and its procedures
- Participants with a diagnosis of dependence on any drugs except for nicotine, cannabis, alcohol and caffeine, if alcohol dependence doesn*t represent the main addiction
- Participants who are/or could be pregnant or nursing infants.
- Participants who intend to engage in additional treatment for alcohol-related problems (except for self-help treatments which are not considered as formal treatment).
- Participants with current or recent (3 month prior to the start of the study) treatment with anti-craving medication (acamprosate, naltrexone, disulfiram, or topiramate)
- Participants who have had more than seven days of inpatient treatment for substance use disorder in the 30 days prior to the start of the study.

- Participants who have used baclofen in the last 30 days

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-12-2012
Enrollment:	130
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	baclofen, Lioresal
Generic name:	baclofen
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	24-02-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	09-10-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-01-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-01-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	14-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-08-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2011-004142-17-NL
CCMO	NL37378.018.11