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Improving treatment for women with co-morbid post-traumatic stress disorder (PTSD) and alcoholism: a randomized placebo-controlled study of the FAAH inhibitor PF-04457845 in trauma-focused cognitive and behavioral therapy with exposure.

Submission date
29/07/2014

Recruitment status
Stopped

Registration date
13/08/2014

Overall study status
Stopped

Last Edited
23/10/2018

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims

Post-traumatic stress disorder (PTSD) is an anxiety disorder caused by the sufferer experiencing a frightening, very stressful or distressing event. Such events include being in an accident, being attacked, witnessing a violent death or being involved in a natural disaster. The condition can develop immediately after the event or weeks, months or even years later. Symptoms include reliving the experience though nightmares and flashbacks, feeling hyper alert and on edge and avoiding people or places that remind them of the event. Nearly twice as many woman than men will suffer from PTSD then men during their lifetime. Many people with PTSD turn to alcohol or illegal drugs as a way of coping with the condition. There is a strong link between PTSD and alcohol abuse disorder (a term used to describe people who abuse alcohol or are alcoholics). PTSD is much more common among people who suffer from an alcohol use disorder (AD) and tends to be more severe. PTSD sufferers are more likely to also suffer a relapse in their AD. This strong link between the two disorders suggests there may be underlying disturbances in the brain that are common to both. A treatment called cognitive behavioural therapy (CBT) with exposure has proved to be a successful in helping people with PTSD . It involves exposing the patient to the traumatic event they suffered in a safe way and enables them to cope with their feelings about it. CBT with exposure has also been recently combined with techniques to prevent relapses of drug abuse and AD to treat people with PTSDs and such substance abuse disorders (Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure (COPE)). Drugs to treat PTSDs have not proved to be very successful. However, using drugs to enhance the effects of psychological treatment may be an option. One biological system in the brain, called the endo-cannabinoid system, may be a particularly useful target for such drug treatment, as it controls feelings of pain, reward and memory. Here, we are testing out a new drug, PF-04457845 (a FAAH-inhibitor), that may be able to influence the signaling in

the endo- cannabinoid system to treat women patients with PTSD and AD. The drug has been recently tested on patients with joint pain with no major side effects reported.

Who can participate?
Women aged at least 18 and diagnosed with PTSD and AD.

What does the study involve?
Participants are randomly allocated into one of two groups. They all receive 12 weekly sessions of COPE treatment. Those in group 1, however, are also treated with the drug PF-04457845 during the first 4 weeks of COPE therapy. Those in group 2 receive a placebo. The alcohol intake for all participants (in both groups) is monitored weekly though urine samples. Blood samples are also analyzed just before the treatment starts and then after 2, 4, 8 and 12 weeks of treatment. Stress levels for all participants are measured though analyzing the amount of cortisol (a hormone that is produced in response to stress) in hair samples just before and then after the treatment is complete. Participants also attend a follow up appointment 3 months after treatment.

What are the possible benefits and risks of participating?
Participants are paid the equivalent of about 5 euro after each session and about 30 euro after the 3 months follow-up. It is also hoped that the treatment with improve PTSD symptoms will reduce heavy alcohol use. No risks are reported.

Where is the study run from?
1. Akademiska Hospital in Uppsala (Sweden)
2. Capio Maria (health care provider) (Sweden)
3. The Stockholm Centre for Dependency Disorders in Stockholm County (Sweden)

When is the study starting and how long is it expected to run for?
October 2014 to October 2017

Who is funding the study?
1. Stockholm and Uppsala county (Sweden)
2. Capio Maria (health care provider) (Sweden)
3. Systembolaget's Alcohol Research Council (Systembolagets råd för alkoholforskning - SRA) (Sweden)
4. Söderström Königska foundation (Söderström-Königska Stiftelsen) (Sweden)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Clinical Trials Information System (CTIS)
2014-002456-90

Protocol serial number
14060802, version 3

Study information

Scientific Title
Integrated exposure-based therapy for co-occurring post-traumatic stress disorder and alcohol dependence: effects of the FAAH inhibitor PF-04457845 on extinction. A randomized controlled trial.

Study objectives
This study will evaluate the ability of the Fatty Acid Amide Hydrolase (FAAH) inhibitor PF-04457845 to potentiate extinction of trauma memories in women with co-morbid PTSD and alcohol dependence (AD). Two hypotheses will be evaluated: That FAAH inhibition will reduce PTSD symptom severity; and that reduction in PTSD symptom severity will be associated with reduction in heavy drinking.

Ethics approval required
Old ethics approval format

Ethics approval(s)
EPN, 06/08/2014, ref: Dnr 2014/119-30

Primary study design
Interventional

Study design
Double-blind randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Post traumatic stress disorder (PTSD) and alcohol dependence (AD).

Interventions
Following a screening phase (4 visits), all participants (n=120) will receive 12 weekly sessions of COPE as behavioral treatment. Participants will be randomized 1:1 to receive add-on treatment with PF-04457845 (4 mg q.d.) or placebo during the first four weeks of imaginal exposure, i.e. weeks 3 through 6 of the behavioral therapy; they will all receive placebo at other times during the behavioral treatment. Subjects receive 12 weekly 90 - minutes sessions of manual based behavioral therapy by trained therapists monitored for fidelity. Prior to each session, they complete assessments of PTSD symptoms and alcohol consumption, as well as alcohol craving and mood. Weekly urine samples are analyzed for biomarkers of alcohol use (ethylglucuronide) and illicit drugs. Before treatment start, after 2, 4, 8, 12 weeks of treatment and on three month follow-up, blood samples are analyzed for alcohol markers (GGT, CDT, PEth). A biomarker of stress-axis activity (cortisol) is analyzed in hair taken at baseline and on completion, after 12 weeks and after 3 months. Blood samples are obtained for analysis of genetic variation. Post-treatment follow up, obtained at a visit appr. 3 months following completions.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
The co-primary outcomes will be:
1. Change from baseline in PTSD symptom severity (Clinician-Administered PTSD Scale; CAPS-DX), measured after COPE session 12 and three months post treatment;
2. Change from baseline in alcohol consumption per week (grams per week) and heavy drinking days (HDD) derived from Timeline Follow back (TLFB), after COPE session 12 and three months post treatment.

Key secondary outcome(s)
1. PF-04457845 will decrease biomarkers of alcohol consumption (gamma glutamyltransferase (GGT), mean corpuscular volume (MCV), phosphatidylethanol (PEth), carbohydrate deficient transferrin (CDT), and ethylglucuronide (EtG))
2. PF-04457845 will decrease measures of stress, indexed as cortisol in hair.
3. Patient baseline characteristics, incl. genotype at loci within genes encoding elements of the EC system, interact with FAAH blockade to influence treatment outcomes.

Blood samples will be obtained during the screening period, before treatment, for analysis of genetic variation (CNRI,FAAH). Blood samples will be obtained for analysis of alcohol biomarkers (GGT, CDT, PEth) on baseline, after 2, 4, 8, 12 weeks of COPE treatment, and on three month follow-up. Hair samples will be obtained for analysis of cortisol, a biomarker of stress-axis activity, on baseline, on completion of COPE treatment, and on 3 month follow-up.

Completion date
15/10/2017

Reason abandoned (if study stopped)
Study stopped following serious adverse effects in a phase I trial of Bial's FAAH inhibitor BIA 10-2474.

Eligibility

Key inclusion criteria
1. Female
2. Age >18 years
3. Diagnosed with current PTSD and current alcohol dependence according to the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) (DSM-IV), as determined by The Structured Clinical Interview for DSM IV Disorders (35) and clinical examination by a psychiatrist.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Female

Key exclusion criteria
1. Current DSM-IV substance dependence other than nicotine, as determined by the SCID and clinical examination by a psychiatrist and negative urine screen for illicit drugs.
2. Current DSM-IV psychotic, as determined by the SCID, and clinical examination by a psychiatrist.
3. Clinically significant suicidal or homicidal ideation on clinical assessment with the relevant section of The Mini International Neuropsychiatric Interview (MINI; (36)) and clinical examination by a psychiatrist.
4. Any current medication or medical condition that in the judgment of the investigator could interfere with treatment.
5. Pregnancy or nursing. To be eligible, women of childbearing potential must have a negative serum or urine pregnancy test prior to the start of study drug, and agree to using a method of contraception that is adequate in the judgment of the investigator for the duration of the study.
6. Insufficient memory of the trauma (for prolonged exposure to be effective).
7. Dissociative disorder which is more severe or affects the subject more than her PTSD.

Date of first enrolment
15/10/2014

Date of final enrolment
15/10/2017

Locations

Countries of recruitment
Sweden

Study participating centre
Stockholm Centre for Dependency Disorders
Stockholm
Sweden
118 69

Sponsor information

Organisation
Stockholm Centre for Dependency Disorders (Sweden)

ROR
https://ror.org/02zrae794

Funder(s)

Funder type
Other

Funder Name
Stockholm and Uppsala county (Sweden)

Funder Name
Capio Maria (health care provider) (Sweden)

Funder Name
Systembolaget's Alcohol Research Council (Systembolagets råd för alkoholforskning - SRA) (Sweden)

Funder Name
Söderström Königska foundation (Söderström-Königska Stiftelsen) (Sweden)

Funder Name
Funding have also been applied for from the Swedish Research Council for Health, working life and welfare (FORTE) and from The Swedish Research Council.

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration