The effectiveness of Paroxetine vs Trauma Focused Cognitive Behavioural Therapy (TF-CBT) in the treatment of Posttraumatic Stress Disorder (PTSD).

Published: 08-03-2010
Last updated: 05-05-2024

Primary Objective: The main objective is to compare the effectiveness and cost-effectiveness of Cognitive Behavioural Therapy (CBT) to psychopharmacological treatment with paroxetine in patients with Posttraumatic stress disorder (PTSD) in a...

Ethical review	Approved WMO
Status	Pending
Health condition type	Psychiatric disorders
Study type	Interventional

Summary

ID

NL-OMON33037

Source
ToetsingOnline

Brief title
Paroxetine versus TF-CBT

Condition

- Psychiatric disorders

Synonym
PTSD en stress disorder

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: costeffectiveness, psychotherapy, PTSD, SSRI

Outcome measures

Primary outcome

The change in PTSD symptoms before and after treatment (at week 1, 3, 6 months, 12 and 18 months after treatment), measured by the CAPS and determination of the cost-effectiveness. The primary cost-effectiveness analysis will be one that evaluates costs associated with an improved PTSD outcome in terms of CAPS scores.

Secondary outcome

At 1 week, and 3, 6, 12 and 18 months post-intervention the following secondary outcomes will be assessed as well: response rate (criteria for response are a 30% or more change compared to baseline on CAPS and a CGI score from 1 or two ("much improved" or "very much improved"), possible other psychopathology, quality of life, anxiety and depression and costs, as well as neuroendocrine and neuro-immune measures, neurocognitive functioning and genetic measures.

Study description

Background summary

It is widely recognized that PTSD has an excessive health and economic burden on patients, their relatives and society as a whole. Individuals suffering from PTSD should therefore be provided the most effective treatments in terms of patient recovery and cost-effectiveness. Of the psychological interventions for PTSD, *trauma-focused* treatments such as Cognitive Behavioural Therapy (CBT) have been found most effective. CBT is the most widely researched treatment and

consists of a broad array of techniques, with exposure to the traumatic memory and cognitive restructuring as prominent elements. Of the pharmacological interventions, selective serotonin reuptake inhibitors (SSRIs) have been found effective in PTSD. Especially paroxetine is a well-tolerated and effective drug in reducing symptoms of PTSD in both male and female patients. The majority of PTSD patients (i.e., 80%) is treated with pharmacotherapy in clinical practice. National and international guidelines, however, recommend trauma focused psychological therapies as first-choice treatment for PTSD. This recommendation is not supported by evidence from randomized controlled trials (RCTs) comparing the efficacy of psychotherapy to pharmacotherapy. Up till now, two RCTs have been conducted to directly compare trauma-focused therapy with pharmacotherapy. Findings of one trial (N = 21) show a slightly stronger decrease of PTSD symptoms at 6 months follow-up in the CBT group than in the paroxetine group and another trial (N = 88) indicates that PTSD symptom reduction is stronger in the trauma focused psychological therapy group than in the SSRI group. These studies are, however, rather small and lack follow-up to examine whether improvements sustain after cessation of the treatment. A meta-analysis comparing effect sizes of both psychotherapeutic and pharmacological treatments for PTSD, showed a slight advantage of CBT compared to other treatments on observer-related total PTSD symptoms. Caution is, however, required when comparing effect sizes of pharmacological to psychotherapy trials as in pharmacological trials control for non-specific attentional effects when a placebo is used is greater than in psychological therapy trials with waiting list controls. Although medication treatment has been shown to be effective in the treatment of PTSD findings of long-term consolidation of this effectiveness have not been reported. Moreover, increased relapse rates in trials of SSRIs support the notion that a short-term course of treatment with SSRIs may be inadequate and that at least twelve months of medication treatment might be needed to prevent relapse in the treatment of chronic PTSD.

Study objective

Primary Objective: The main objective is to compare the effectiveness and cost-effectiveness of Cognitive Behavioural Therapy (CBT) to psychopharmacological treatment with paroxetine in patients with Posttraumatic stress disorder (PTSD) in a randomized controlled trial in terms of PTSD symptom reduction.
Secondary Objective(s): The secondary objective is to compare the effectiveness of both treatments in terms of costs associated with PTSD symptom reduction, comorbid anxiety and depression and health-related quality-of-life. Hypotheses generating subgroup analyses will be performed to evaluate treatment responses by gender, age, and socioeconomic status (incl. ethnic and cultural background).
Tertiary objectives:
In sub-study I, effects of treatment of PTSD with trauma-focussed cognitive behavioural therapy (TF-CBT) and with pharmacotherapy (SSRI) on interrelated neuroimmune and neuroendocriene measures, i.e, cortisol and cytokine changes

are explored based on potential effects of both treatments on such parameters.
In sub-study II, effects of both treatments, trauma-focussed cognitive behavioural therapy (TF-CBT) and pharmacotherapy (SSRI, paroxetine), on neurocognitive functioning, primarily verbal and executive functioning, will be examined.
In sub-study III, the relation between GR and 5-HTT polymorphisms in PTSD and their possible relation with in particular HPA-axis activity will be examined.

Study design

The patients will randomized be allocated to either the trauma-focused cognitive behavioural therapy (TF-CBT) or the pharmacotherapy (paroxetine). Several measurements will be done after the intervention, after 1 week, 3 months, 6 months, 12 months and 18 months, which will include assessments standardized diagnostic interviews, questionnaires, neurocognitive tests and neuro-endocriene and neuro-immune measures. Also laboratory analysis will be done (patients which will receive a Paroxetine treatment (of 24 weeks) will have several more measurements, at weeks 2, 12 and 20 and patients receiving TF-CBT (of 12 weeks) at weeks 2, 6 and 10).

Intervention

Patients participating in this study, will be randomly allocated to one of two interventions: either paroxetine or TF-CBT.

Paroxetine treatment will have a duration of 24 weeks. The dosage will start at 20 mg and can be increased with increments of 10mg/daily each four weeks up to a maximum of 60 mg/daily if according to the judgement of the study psychiatrist, the patient does not respond to lower dosages and if clinically tolerated (see for details page 18 of the protocol).

The TF-CBT treatment consists of 12 weekly sessions of 45 * 60 minutes. Every session, subjects will be seen by the same therapist (see for details page 18 of the protocol).

Study burden and risks

The burden and risks associated with participation in this study is very limited, due to the naturalistic design of the study. The visits in the context of the interventions, pre-intervention blood samples and physical examinations and diagnostic questionnaires are all part of the usual care at the Zorglijn Angststoornissen, AMC Psychiatrie. Additional and only in the context of the study are: laboratory assessments (blood samples) during the course of the treatments (at 2, 12 and 20 weeks), and at 1 week, 3, 6, 12, and 18 months post-intervention. Additional are also saliva sampling, a dexamethasone suppression-test and assessment of neurocognitive functioning and some extra

questionnaire on costs and secondary study parameters (e.g., quality of life) at pre- and post-intervention assessments.

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

CAPS score of * 50
Male and female, aged 18 years and above
Written informed consent
Eligible for exposure therapy

Exclusion criteria

Suicidal risk
Presence of a psychotic disorder, a bipolar disorder, depression with psychotic features, or excessive substance related disorder over the past 6 months.
Primary diagnosis of severe depressive disorder
An organic disorder
Intolerance to paroxetine or any other SSRI, taking psychotropic medications
Pregnancy

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2009
Enrollment:	234
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Paxil
Generic name:	Paroxetine
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Application type:	First submission
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	EUCTR2009-010223-81-NL
CCMO	NL26766.018.09