Δ9-THC (Namisol®) in chronic pancreatitis patients suffering from persistent abdominal pain: a randomized, double-blinded, placebo-controlled, parallel design

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Primary objective:- To investigate the analgesic efficacy of a stable dose treatment Namisol® in chronic pancreatitis patients suffering from abdominal pain. Analgesic efficacy is measured as mean difference in visual analogue scale (VAS) score (i.e...

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

Summary

ID

NL-OMON37765

Source
ToetsingOnline

Brief title
Δ9-THC in chronic pancreatitis

Condition

- Other condition
- Exocrine pancreas conditions

Synonym
chronic pancreatitis; chronic pancreas inflammation

Health condition

viscerale pijn

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: EU

Intervention

Keyword: Abdominal pain, Cannabis, Chronic pancreatitis, Tetrahydrocannabinol

Outcome measures

Primary outcome

• Pain intensity (diary)

o VAS average pain

Secondary outcome

• Pain intensity (diary)

o VAS minimal pain

o VAS maximal pain

• EEG

o ERPs to noxious electrical stimuli

o ERPs to auditory stimuli (oddball)

o FFT spontaneous EEG

• QST (visceral screenings protocol)

o Pressure pain thresholds

o Electric pain thresholds

o Electric wind-up response

o DNIC

• Questionnaires

o Izbicki

o PGIC

o PCS

o VASBond & Lader

o VASBowdle

o SF-36

o HADS

o PASS

• Pharmacodynamics

o Body Sway

• Functional

o Body weight

o Supplementary feeding

• Safety

o Laboratory

o ECG

o HF / BP

o Adverse events

• Pharmacokinetics

o THC, 11-OH-THC and THC-COOH concentrations

Study description

Background summary

Abdominal pain resulting from chronic pancreatitis (CP) is often recurrent, intense and long-lasting, and is extremely difficult to treat. Medical analgesic therapy is considered as first choice in pain management of CP, resulting in regularly prescription of opioids. The adverse consequences of prolonged opioid use, including addiction, tolerance and opioid induced hyperalgesia, call for an alternative medical treatment. Cannabis has been used to treat pain for many centuries. Delta-9-tetrahydrocannabinol (Δ9-THC), the psychoactive substance of the cannabis plant, has been shown in previous studies to be a promising analgesic. The development of Namisol®, a tablet containing purified Δ9-THC showing an improved pharmacokinetic profile, provides the opportunity to test the analgesic potential of Δ9-THC in favourable conditions.

Study objective

Primary objective:
- To investigate the analgesic efficacy of a stable dose treatment Namisol® in chronic pancreatitis patients suffering from abdominal pain.
Analgesic efficacy is measured as mean difference in visual analogue scale (VAS) score (i.e. VASpain) at day 50-52 minus baseline (pre-treatment, day 1), between placebo vs. Namisol®.

Secundary objectives:
- To investigate the efficacy of Namisol® after a stable dose treatment of Δ9-THC on experimental pain mechanisms (measured by EEG, QST, and DNIC) in chronic pancreatitis patients suffering from abdominal pain.
- To investigate the efficacy of Namisol® after a stable dose treatment of Δ9-THC on changes in pain experience (Izbicki), anxiety and depression (HADS), general health (SF-36), pain catastrophizing (PCS), global impression of change (PGIC), pain related anxiety (PASS) in chronic pancreatitis patients suffering from abdominal pain.
- To evaluate the safety and tolerability (adverse events) of Namisol® after a stable dose treatment of Δ9-THC in chronic pancreatitis patients suffering from abdominal pain.
- To evaluate the pharmacokinetics (PK) of Namisol® after a stable dose treatment of Δ9-THC in chronic pancreatitis patients suffering from abdominal pain.
- To evaluate pharmacodynamic (PD) effects (body sway, HF, feeling high) of Namisol® after a stable dose treatment of Δ9-THC in chronic pancreatitis patients suffering from abdominal pain.

Study design

A randomized, double-blind, placebo-controlled, parallel design to evaluate the analgesic properties of Namisol® during a 50-52 days add-on treatment.

Intervention

Namisol® with standardized Δ9-THC content or identical matching placebos will be administered orally to evaluate the analgesic properties of Namisol® during a 52 days add-on treatment to other analgesics. The study consists of two phases: a step-up phase (day 1-5: 3 mg TID; day 6-10: 5 mg TID), and a stable dose phase (day 11-52: 8 mg TID). The dosage may be tapered to at least 5 mg TID, when 8 mg is not tolerated.

Study burden and risks

The risks of participation include the possible side-effects of the study drug (i.e. tachycardia, feeling high, disturbance in attention, drowsiness, nausea) and findings of testing (i.e. positive test result for hepatitis B, hepatitis C or HIV). The patients participating will obtain no direct personal benefit. However, patients receiving active study treatment may experience pain relief during the investigation period. It is the hope that results conducted from the study will provide new insight to pain mechanisms, and future treatment options for CP patients. An alternative pain treatment is highly desirable in particularly this group of patients.

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

• Aged 18 years or older
• Confirmed chronic pancreatitis
• Pain duration exceeding 3 months, and average NRS>=3
• Stable doses intake of analgesics for the past 2 months
• Patient has been informed about the study, understood the information and signed the informed consent form

Exclusion criteria

• Patient took cannabinoids on a regular basis for at least one year
• Patient does not feel a pinprick test in the lower extremities
• Patient has a body mass index (BMI) above 33,0 kg/m2
• Patient has a significant medical disorder that may interfere with the study or may pose a risk for the patient
• Patient uses any kind of concomitant medication that may interfere with the study or may pose a risk for the patient
• Patient takes amitriptyline on a daily basis
• Patient does not tolerate oral intake of medication or liquids, or is refrained from oral intake because of medical reasons
• Patient demonstrates clinical relevant deviations in the electrocardiogram (ECG)
• Patient has an actual moderate to severe renal impairment
• Patient has an actual moderate to severe hepatic impairment
• Patient has a presence or history of major psychiatric illness
• Patient has experienced an epileptic seizure in the past
• Patient demonstrates clinically significant laboratory abnormalities
• Patient demonstrates a positive urine drug screen for THC, cocaine, MDMA, and amphetamines
• Patient demonstrates a positive test result on hepatitis B surface antigen, hepatitis C antibody or HIV antibody test
• Patient has a history of sensitivity / idiosyncrasy to THC
• Patient has a known or suspected lactose intolerance
• Female patient is pregnant or breastfeeding
• Patient intends to conceive a child during the course of the study
• Patient participates in another investigational drug study
• Patient has a clinical significant exacerbation in illness

• Patient is unwilling or unable to comply with the lifestyle guidelines

Study design

Design

Study phase:	2
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):	15-10-2012
Enrollment:	68
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	delta-9-tetrahydrocannabinol
Generic name:	Namisol

Ethics review

Approved WMO Date:	12-03-2012
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-08-2012

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-04-2014
Application type:	Amendment
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	EUCTR2012-000730-19-NL
CCMO	NL39537.091.12
Other	nog niet bekend