The safety, tolerability, and analgesic efficacy of Δ9-THC (Namisol®) in chronic pancreatitis patients suffering from persistent abdominal pain

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Primary Objective: - To investigate the efficacy of Namisol® after a single dose of Δ9-THC on the experienced pain intensity (measured by the VASpain in rest and on movement) in patients with chronic pancreatitis.Secondary Objectives:- To...

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

Summary

ID

NL-OMON35767

Source
ToetsingOnline

Brief title
Δ9-THC in chronic pain

Condition

- Other condition
- Exocrine pancreas conditions

Synonym
chronic pancreas inflammation, Chronic pancreatitis

Health condition

viscerale pijn

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Abdominal pain, Cannabis, Chronic pancreatitis, Tetrahydrocannabinol

Outcome measures

Primary outcome

Pain intensity:

- VAS in rest

- VAS on movement

Secondary outcome

Nociceptive parameters:

• EEG

- Event related potetentials to noxious electrical stimuli

- FFT spontaneous EEG

• QST

- Pressure pain tolerance thresholds

- VAS to noxious electrical stimuli

• DNIC

Pharmacokinetics:

- Cmax, AUClast, AUC*, tmax, *z, and t1/2term for THC, 11-OH-THC and THC-COOH

Pharmacodynamics:

- VASBond,

- VASBowdle

- Body sway

Safety en tolerability:

- Vital signs (ECG, HRV, HF, BP)

- Safety laboratory

- Adverse events

Study description

Background summary

The most important symptom in chronic pancreatitis (CP) is abdominal pain. Pancreatic pain 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 and reliable pharmacokinetic profile, provides the opportunity to test the analgesic potential of Δ9-THC in favourable conditions.

Study objective

Primary Objective:
- To investigate the efficacy of Namisol® after a single dose of Δ9-THC on the experienced pain intensity (measured by the VASpain in rest and on movement) in patients with chronic pancreatitis.

Secondary Objectives:
- To investigate the efficacy of Namisol® after a single dose of Δ9-THC on

nociceptive pain mechanisms (measured by EEG, QST, and DNIC) in patients with chronic pancreatitis.
- To evaluate the safety and tolerability of Namisol® after a single dose of Δ9-THC in patients with chronic pancreatitis.
- To evaluate the pharmacokinetics (PK) of Namisol® after a single dose of Δ9-THC in patients with chronic pancreatitis.
- To evaluate (undesirable) pharmacodynamic (PD) effects of Namisol® after a single dose of Δ9-THC in patients with chronic pancreatitis.

Study design

A randomized, single-dose, double-blinded, placebo-controlled, 2-way cross-over trial. Patients will visit the UMC St Radboud for two study days and will receive a single dose Namisol® or placebo. Pain (objectively and subjectively measured) and other parameters will be repeatedly measured after intake of study medication.

Intervention

Namisol® (8 mg) with standardized Δ9-THC content or active placebo (5 mg Diazepam in non-opioid users/ 10 mg Diazepam in opioid users) will be administered orally in a double dummy 2-way cross-over design.

Study burden and risks

The risk of participation includes the possible side-effects of the study drug (i.e. tachycardia, feeling high, changed perception of time, disturbance in attention, drowsiness, nausea) and findings during test (i.e. positive test result for hepatitis B, hepatitis C or HIV).

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

1. Patient is 18 years or older on the day the informed consent form will be signed.
2. Patient is male.
3. Patient has chronic pancreatitis, diagnosed using the Marseille and Cambridge Classification System (addendum II).37
4. Patient suffers from chronic abdominal pain typical for pancreatitis, meet the criteria for chronic pain according ISAP (intermittent or persistent pain on a daily basis in at least 3 months)38, and consider their pain must as severe enough for medical treatment (average NRS >= 3).
5. Patient in de opioid subgroup takes stable doses of opioids, e.g. morphine or tramadol, for the past 2 months on the day of screening. Stable dose intake is defined as a daily equivalent sum of opioid intake according medical prescription within a small deviation range as judged by the (principal) investigator.
6. Patient in the non-opioid group does not take any opioids for the past 2 months on the day of screening.
7. Patient is willing and able to comply with the scheduled visits, treatment plan, laboratory tests and other trial procedures.
8. Patient is able to speak, read and understand the local language of the investigational site, is familiar with the procedures of the study, and agrees to participate in the study program by giving oral and written informed consent prior to screening evaluations.

Exclusion criteria

1. Patient used any cannabinoid (by smoking cannabis or oral intake) for at least one year on the day of screening.
2. Patient is insulin dependent for more than 5 years on the day of screening.

3. Patient does not feel a pinprick test in the lower extremities, due to affected sensory input (e.g. neuropathy as a result of diabetes mellitus).
4. Patient has a body mass index (BMI) below 18 or above 31.2 kg/m2.
BMI (kg/m²) = weight (kg) / (height * height) (m2)
5. Patient suffers from serious painful conditions other than chronic pancreatitis or had any major pre-existing chronic pain syndrome.
6. Patient has a (history of) a significant medical disorder that, in the opinion of the investigator, may interfere with the study or may pose a risk for the patient.
7. Patient uses any kind of concomitant medication that, in the opinion of the investigator, may interfere with the study or may pose a risk for the patient (e.g. HIV antivirals).
8. Patient gets enteral feeding.
9. Patient takes amitriptyline on a daily basis.
10. Patient takes more than 20 mg benzodiazepines 6 hours prior or following intake of study medication (11 hour am) according prescription.
11. Patient demonstrates deviating electrocardiogram (ECG) parameters at screening, e.g. heart rate >100 bpm, QRS duration >120 msec, QTc interval >450 msec, PR interval >210 msec, any clinically significant rhythm abnormality.
12. Patient is previously diagnosed with moderate to severe renal impairment, e.g. creatinine values > 2x ULN and/or a significant change of their normal values.
13. Patient is previously diagnosed with moderate to severe hepatic failure or show significant clinical abnormalities in biochemistry blood sample as judged by the investigator.
14. Patient has a presence or history of major psychiatric illness as judged by investigator, e.g. major depression, schizophrenia.
15. Patient has experienced an epileptic seizure in the past.
16. Patient demonstrates clinically significant laboratory abnormalities that in the opinion of the investigator may increase the risk associated with trial participation or may interfere with the interpretation of the trial results.
17. Patient has a history of sensitivity / idiosyncrasy to THC, compounds chemically related to these compounds, or to any other related drug used in the past.
18. Patient has a known or suspected lactose intolerance.
19. Patient shows a positive alcohol breath test at screening or admission and/or is unable/unwilling to refrain from alcohol use from 48 hours before each study day until the last blood sample has been drawn.
20. Patient demonstrates a positive urine drug screen at screening visit for THC, cocaine, MDMA, and amphetamines.
21. Patient demonstrates a positive test result on hepatitis B surface antigen, hepatitis C antibody or HIV antibody test.
22. Patient is unwilling or unable to comply with the lifestyle guidelines.
23. Patient intends to conceive a child during the course of the study.
24. Patient participates in another investigational drug study within 90 days prior to the first dose and/or participates in more than 2 clinical trials in the last year.
25. Patient has a clinical significant exacerbation in illness within two weeks of participating in this study.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-10-2011
Enrollment:	24
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	29-03-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	26-07-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	11-07-2013
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	EUCTR2011-000647-24-NL
ClinicalTrials.gov	NCT01318369
CCMO	NL35471.091.11