The analgesic efficacy of perioperative delta-9-THC (Namisol) in patients undergoing major abdominal surgery: a randomized, double blinded, placebo-controlled, parallel design

Published: 08-03-2013
Last updated: 23-04-2024

The primary aim of this study is to investigate the analgesic effect of perioperatively administered Namisol® to reduce postsurgical pain on the day of surgery and in the first five days after major abdominal surgery. A secondary aim is to...

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

Summary

ID

NL-OMON38617

Source
ToetsingOnline

Brief title
NamiSur

Condition

- Other condition
- Gastrointestinal therapeutic procedures

Synonym
pain after surgery

Health condition

postchirurgische pijn

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Pain, Postsurgical, Sensitization, THC

Outcome measures

Primary outcome

The primary study outcome is postsurgical pain intensity during the first five postoperative days, reflected by the primary endpoint: the area under the curve of the VAS scores at rest on the day of surgery and in the first five days after surgery.

Secondary outcome

The secondary outcome is the incidence of persistent postsurgical pain after 6, 12, and 24 weeks after surgery. In addition to the primary and secondary outcomes, several other outcome parameters will be collected. These include the area under the curve of the VAS scores after coughing on the day of surgery and in the first five days after surgery, measures of postsurgical pain intensity during the first 24 postoperative weeks, measures of analgesic efficacy, central nervous system processing and sensitization in the first 5 days and after 6, 12, and 24 weeks after surgery, postoperative sedation level, and immune system response during 72 hours after surgery and after 6 weeks are investigated. In addition, questionnaires are filled out to examine parameters

related to side effects and postoperative recovery.

Study description

Background summary

Early postsurgical pain is a consequence of tissue trauma during surgery, which can lead to hyperalgesia or allodynia. Adequate management of postsurgical pain leads to earlier mobilization, shortened hospital stay, reduced costs, and increased patient satisfaction. Treatment usually involves the use of opioids, which have many side effects. Besides the problem of acute surgical pain, surgery may lead to the development of persistent postsurgical pain.

Based on preclinical research, it is hypothesized that Δ9-THC may improve outcomes of early postsurgical pain due to pain modulatory effects and may lower the incidence of persistent postsurgical pain through modulation of central pain processing, e.g. reduction of central sensitization. From clinical studies, evidence for the value of Δ9-THC in this context is, to date, scarce. Indeed, research in a patient group with a major nociceptive load - i.e. major abdominal surgery - and an extended perioperative treatment schedule has not been performed so far. Both a major nociceptive load and an extended perioperative treatment schedule are necessary for adequate assessment of the analgesic efficacy of Δ9-THC in this context. Thus, the question regarding the perioperative analgesic efficacy of Δ9-THC in major abdominal surgery remains unresolved.

Study objective

The primary aim of this study is to investigate the analgesic effect of perioperatively administered Namisol® to reduce postsurgical pain on the day of surgery and in the first five days after major abdominal surgery. A secondary aim is to investigate the effect of perioperatively administered Namisol® on the incidence of persistent postsurgical pain in the first 24 postoperative weeks.

Study design

A randomized, double-blind, placebo-controlled, parallel-group study design with an perioperative add-on treatment of Namisol or placebo and a follow-up period of 24 weeks.

Intervention

Namisol®, a tablet with standardized Δ9-THC content, or identical matching

placebos will be administered orally to evaluate the analgesic properties of Namisol® administered as add-on perioperative treatment. The study medication is given from the day before surgery (day -1: 5 mg in the afternoon and in the evening) up to the fifth day after surgery (day 0 to +5: 5 mg four times daily).

Study burden and risks

Participation means three or four visits to the outpatient clinic in addition to usual care, including the screening visit. Various measurements, including blood samples (seven additional samples over the entire study period), will be conducted during each visit. The participating patients may experience better pain relief in the postoperative period and may benefit from a reduced incidence of persistent postsurgical pain, but are subject to more intense diagnostics and observation.

The dose administration in the current study is four times daily, which is a higher frequency than the frequency used in earlier studies. Because of this, to reduce unwanted side effects in the perioperative period, a dose of 5 mg is chosen and we chose to start administration of the study medication after hospitalization, to ensure adequate management in case of side effects or adverse events.

Extra precaution is taken considering the opioid potentiating effect: no opioid medication will be administered in the epidural catheter (except during induction of anesthesia) to lessen the risk of respiratory depression during and after surgery. Because these and other possible effects of Namisol® in the perioperative period, if the patient experiences side effects after any dose of Namisol®/placebo and these side effects are, judged by the patient or the investigator, untolerable, the patient will be withdrawn from the study and will be replaced to ensure the safety of the patient.

Contacts

Public
Universitair Medisch Centrum Sint Radboud

Huispost 690
Nijmegen 6500 HB
NL
Scientific
Universitair Medisch Centrum Sint Radboud

Huispost 690

Nijmegen 6500 HB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patient is at least 18 years old on the day the informed consent form will be signed.
2. Patient has persistent or intermittent abdominal pain due to underlying intra-abdominal pathology.
3. If the patient uses concomitant analgesic medication the dosage intake is stable for at least two weeks prior to the day of screening. Stable dose intake is defined as a daily equivalent sum of intake according to medical prescription within a small deviation range as judged by the investigator.
4. Patient is undergoing elective, open abdominal surgery with planned use of an epidural catheter. The surgical procedure has an estimated duration of at least two hours, excluding the time to induce anesthesia.
5. Patient scores I to III in the American Society of Anesthesiologists physical status classification system (ASA I-III).
6. Patient is willing and able to comply with the lifestyle guidelines, scheduled visits, treatment plan, laboratory tests and other trial procedures.
7. 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 is ineligible for the anesthesia protocol, as judged by the investigator.
2. Patient is undergoing (abdominal wall) surgery with mesh implantation.
3. Patient used any cannabinoids (by smoking cannabis or oral intake) for at least one month prior to the day of screening.

4. Patient has (a history of) a medical disorder that, in the opinion of the investigator, may interfere with the study or may pose a risk for the patient.
5. Patient uses amitriptyline or other concomitant medication that, in the opinion of the investigator, may interfere with the study or may pose a risk for the patient.
6. Patient demonstrates clinically significant deviations in the electrocardiogram (ECG) parameters at screening.
7. Patient is at the moment of screening diagnosed with moderate to severe renal impairment as judged by the investigator.
8. Patient is at the moment of screening diagnosed with moderate to severe hepatic failure as judged by the investigator.
9. Patient has a presence or history of major psychiatric illness as judged by the investigator.
10. 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.
11. Patient has a history of sensitivity/idiosyncrasy to THC or diazepam, compounds related to these compounds, or to any other related drug used in the past.
12. Patient demonstrates a positive urine drug screen at screening visit for THC, cocaine, MDMA, or amphetamines.
13. Female patient intends to conceive a child, is pregnant or breastfeeding, or does not use acceptable birth control measures including oral contraceptives, intrauterine devices or mechanical methods during the course of the study.
14. Patient participated in another investigational drug study within 90 days prior to the first dose and/or participated in more than 2 clinical trials in the last 365 days.

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:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-08-2013

Enrollment:	40
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	08-03-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-06-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-09-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-10-2013
Application type:	Amendment
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	EUCTR2012-005808-17-NL
ClinicalTrials.gov	NCT01790555
CCMO	NL43115.091.13