Postoperative pain relief following pancreaticoduodenectomy: Triple P (PostPainPan) Study

Published: 21-06-2018
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- Primary objective: To compare the efficacy of postoperative pain treatments with sublingual sufentanil micro-tablets versus intravenous patient controlled analgesia with morphine or epidural analgesia in patients following pancreaticoduodenectomy...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON55379

Source
ToetsingOnline

Brief title
Triple P (PostPainPan) study

Condition

- Other condition

Synonym
Postoperative pain

Health condition

postoperatieve pijn

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Grunenthal

Intervention

Keyword: Analgesia, Pain, Pancreaticoduodenectomy, Postoperative, Sufentanil

Outcome measures

Primary outcome

The main end-point of the study will be *mean pain score during postoperative

day 1-3 and mean day pain satisfaction on day 1-3.

Secondary outcome

Mean daily pain scores beyond day 3 (day 0-dicharge)

- Mean daily satisfaction scores beyond day 3 (day 0-dicharge)

- Hemodynamics during and following surgery

- Overall Benefin of Analgesia Score day 1, 2 en 3

- Blood loss

- Surgery time

- Anesthesia time

- Anesthetics used during surgery (propofol/sevoflurane/ketamine, remifentanil/

sufentanil, rocuronium/sugammadex)

- Vasoactive medication during an following surgery

(noradrenaline/phenylephrine/ephedrine/atropine)

- Fluid balances and weight during peri- and postoperative period

- Duration of postoperative analgesia treatment (IV PCA M, EA and SST)

- Rescue pain medication (reason, type, dose and duration)

- Occurrence of nausea, vomiting, pruritis.

- Complications during surgery (anesthetic and surgical complications)

- General postoperative complications (e.g. anastomotic leakage, infectious complications)

- Pancreatic surgery specific complications as defined by the International Study Group of Pancreatic Surgery (Postoperative Pancreatic Fistula, Postpancreatectomy Hemorrhage, Bile Leakage, Delayed Gastric Emptying, Chyle Leak)

- Reinterventions/Clavien-Dindo classification

- Laboratory findings during peri- and postoperative period

- Unplanned (re)admission to the ICU

- PACU stay/ICU stay/hospital stay

- Unplanned 30-day hospital readmission

- Mortality within 30-days.

Study description

Background summary

Pancreaticoduodenectomy (PD) is the treatment of choice for a myriad of (non-) malignant diseases of the pancreas, duodenum and periampullary region. PD is performed under general anesthesia and in a restricted number of hospitals in the Netherlands.In this procedure the head of the pancreas and part of the duodenum are removed. There are various methods for postoperative pain control with varying levels of postoperative pain scores and patient satisfaction.
Result from the Leids Universitatir Medisch Centrum (LUMC) show that the percentage of PD patients with a postoperative pain score > 4 (on an 11-point scale from 0, no pain to 10, most extreme pain imaginable) for patients that received an epidural analgesia (EA) and those that received another form of postoperative pain treatment (most importantly intravenous patient controlled analgesia with morphine) differ from each other. While the percentage of

patients not receiving an epidural had higher pain scores on day 0 (day of surgery), the opposite was true on day 3-4, the percentage was higher for patients that had received an epidural. For patients treated with intravenous patient controlled analgesia with morphine, initial pain score where high and later pain scores were low.

In Europe a new form of pain treatment has become available since 2 years, namely postoperative sublingual sufentanil tablets (SST). SST consists of patient-controlled had held device that delivers 15 mug sufentanil micro-tablets at a minimum of 20 min interval. It is currently used as standard of care in multiple hospitals in the Netherlands. In a recent retrospective cohort analysis of 300 patients of patients from several hospitals in the Netherlands including LUMC, Reinier de Graaf Hospital and Maasstad Hospital, we observed low average pain scores following SST treatment in patients after large abdominal and orthopedic surgery (70% of patients with a pain score < 4 on the first postoperative day). We relate this to the pharmacokinetic and pharmacodynamic properties of sublingual sufentanil. The drug is highly lipophilic and is rapidly absorbed after which it passes the blood-brain barrier within minutes (t*ke0 about 6 min). Due to the sublingual formulation peak concentrations are relatively low and consequently, concentration dependent side effect -such as acute respiratory depression- do not occur. Due to its rapid onset of action, there is little delay in pain relief between the moment of administration and the onset of pain reduction. Hence, we like to ascertain the lack of disadvantage, i.e. non-inferiority of SST versus intravenous patient controlled analgesia with morphine or EA in our population of PD patients. We will thereto compare the pain data obtained from these three standardized pain treatments in our hospitals in pancreaticoduodenectomy patients.

Study objective

- Primary objective: To compare the efficacy of postoperative pain treatments with sublingual sufentanil micro-tablets versus intravenous patient controlled analgesia with morphine or epidural analgesia in patients following pancreaticoduodenectomy in terms of pain intensity and patient satisfaction.
- Secondary objectives: To compare outcome parameters between treatment groups.

Study design

This is an investigator-initiated, open-label, strategy, randomized controlled trial in which patients will be randomized to receive either an (epidural catheter prior to surgery for postoperative pain treatment or intravenous patient controlled analgesia with morphine) or the sublingual sufentanil system postoperatively.

Intervention

The anesthetics (type and dose) given during general anesthesia will be left to the discretion of the attending anesthesiologist and/or resident.
Patients randomized to the epidural group will receive an epidural catheter according to local protocol. At LUMC, following induction the epidural analgesic medication will be administered (ropivacaine 0.75%) as bolus 6-12 mL followed by a continuous infusion (ropivicaine 0.2%/sufentanil 0.75 mug/mL; 6-10 mL/h; with the possibility of giving an additional bolus). In the PACU (recovery/ward) pain will be assessed using the 11-point numerical rating scale (NRS; from 0, no pain to 10, most extreme pain imaginable) at regular intervals. In case of pain score > 4, epidural bolus infusions will be permitted and the patient controlled epidural analgesia (PCEA 1-2 mL bolus, 20-min lockout) system will be started according to local protocol. Additionally, all patients will receive 4 times daily paracetamol 1000 mg and an NSAID/metamizol if allowed according to local protocol.
Patients randomized to the SST will receive long-acting intravenous opiates (e.g. morphine) prior to the end of surgery. In the PACU pain will be assessed using the 11-point numerical rating scale (NRS; from 0, no pain to 10, most extreme pain imaginable). In case of pain score > 4, an opiate will be given according to local protocol. When pain scores are 4 or less, the SST system will be started. Additionally all patients will receive 4 times daily paracetamol 1000 mg ± an NSAID/metamizol 3 times daily.
In case of insufficient pain relief during the course of treatment, patients may receive rescue pain relief according to local protocol, i.e. conversion to IV PCA Morphine or to EA; if this does not help, IV ketamine is added (up to 10 mg/h).
After 3-6 days postoperatively both the SST system and the epidural will be terminated and replaced by naproxen/NSAID, paracetamol, an oral or subcutaneous opiate depending on the pain score (and local protocol). At LUMC:
- NRS < 4: paracetamol 4 times daily 1000 mg + naproxen 500 mg 3 times daily;
- NRS 4-6: oxynorm 5 mg p.o. (max. 6 times/day), combined with to paracetamol ± NSAID as mentioned above;
- NRS > 6: morphine s.c. up to 20 mg (max. 6 times/day), combined with to paracetamol ± NSAID as mentioned above.

Study burden and risks

Negligible burden and risks are expected. Possible disadvantages can easily be treated.

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

ASA class 1-3 patients, aged 18 and older that will undergo an elective pancreaticoduodenectomy under general anesthesia.

Exclusion criteria

Patients that are unable to give written informed consent. Patients with a contra-indication for intravenous morphine, epidural analgesia or sublingual sufentanil (e.g. allergies, coagulopathies etc.)

Study design

Design

Study phase:	4
Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-10-2018
Enrollment:	47
Type:	Actual

Ethics review

Approved WMO Date:	21-06-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	27-08-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	04-12-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	17-03-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 22974
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL64936.058.18
OMON	NL-OMON22974

Study results

Date completed:	25-08-2021
Actual enrolment:	47