Post-Operative Pain prevention after hepato-pancreato-biliary surgery: continuous sUbfascial infiltration or ePidural analgesia? a randomized controlled non-inferiority multicenter trial

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Primary Objective: To study whether CSWI+PCA provides similar analgesia after laparotomies for HPB conditions as compared to PCEA measured as the OBAS score, a composite endpoint composed of pain score, patient satisfaction and opioid related side...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON42243

Source
ToetsingOnline

Brief title
POP-UP study

Condition

- Hepatic and hepatobiliary disorders
- Gastrointestinal therapeutic procedures

Synonym
post-operative pain, post-operative pain after HPB- operations

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: analgesia, epidural, hepato-pancreato-bilairy surgery, wound infiltration

Outcome measures

Primary outcome

Primary endpoint:

Overall benefit of analgesic score (OBAS score). Measured on postoperative day

1-5.

Secondary outcome

Secondary endpoints:

- Total operative time. (operation time / pre-operative time)

- Length of hospital stay / readiness for discharge

- Failure of analgesic technique

- Pain after 12/24/72 hours, during rest and movement (VAS score)

- Cumulative opioid consumption

- Hypotension with the need for additional fluid boluses during and after

surgery and noradrenaline dependency

- Days CSWI/PCEA needed

Side effects up to 30 days, including:

- Prolonged post-anaesthesia care unit / Intensive care unit stay

- Duration of indwelling urinary catheter (days)

- Pruritus, post-operative nausea and vomiting

- Complications related to anaesthetic technique, f.e. CNS toxicity, epidural

hematoma, epidural abscess, wound infection

- Post-surgical pain after 30 days

Study description

Background summary

Postoperative pain prevention is essential for the recovery of patients after surgery. Effective analgesia may prevent complications such as pneumonia, thromboembolic complications, a prolonged catabolic stage and anxiety among patients. It can facilitate
early mobilization and may result in earlier recovery.1

Continuous Epidural Analgesia (CEA) is the current standard pain treatment after laparotomy for hepato-pancreato-biliary (HPB) conditions and other indications. This is supported by a recent Cochrane systematic review which concluded that CEA is superior to opioid patient controlled analgesia (PCA) in relieving postoperative pain for up to 72 hours in patients undergoing intra-abdominal surgery, but it is associated with a higher incidence of pruritus.2 Other downsides of CEA are a) the time used to place the epidural catheter, b) the small risk of epidural complications (hematoma and abscess)3, c) the postoperative hypotension, frequently requiring additional intravenous fluid boluses which might delay recovery and d) need for indwelling urinary catheter. For these reasons alternatives have been explored.

Patient-controlled epidural analgesia (PCEA) is the current best practice. The benefits compared to CEA are less motor block, less infused volume and patients are likely to require less anaesthetic intervention. PCEA and CEA have a similar safety profile.4 Currently, no randomized trial has used PCEA, the current best practice, in the control arm.

A promising alternative is the continuous i.m. bupivacaine infusion (CSWI) plus patient-controlled analgesia (PCA). In several high UK volume centers for hepato-pancreato-biliary surgery (Basingstoke, Edinburgh, Southampton) this has become the routine approach for all laparotomies. These catheters are placed at the end of the surgery by the surgeon and are connected to pumps. This technique combined with PCA does not have the described downsides of CEA.

In a retrospective study , a reduction in length of hospital stay was seen after major liver resections with the use of the same technique. The pain control by CSWI + PCA was similar to that provided by CEA. On average patients were discharged one day earlier (7 vs 8 days). The morbidity was also lower (26% versus 39%). A drawback of this study is that the patients in the CEA group were all operated by the same surgeon.

Although various studies have showed promising results with the use of CSWI + PCA, a widespread implementation of this technique hasn*t been realized. This could be because of the use of small study groups, which caused underpowered results on secondary outcomes.
In addition, in some of studies, the control arm didn*t use the current best practice. For example CEA wasn*t used during the operation or the method of CEA was without the use of an opioid. Finally, large randomized controlled trials are lacking that focus on one category of surgical procedures.

Our study will have the overall benefit of analgesic score (OBAS) as primary endpoint, instead of only the pain score (VAS). The OBAS is a multi-dimensional quality assessment instrument to measure patients' benefit from postoperative pain therapy.6 In our opinion the OBAS score is a superior measurement in comparison to the VAS scoring system to score the true effectiveness of analgesic therapy. Pain intensity, opioid-related adverse effects and patient satisfaction are merged at the same time.

Study objective

Primary Objective: To study whether CSWI+PCA provides similar analgesia after laparotomies for HPB conditions as compared to PCEA measured as the OBAS score, a composite endpoint composed of pain score, patient satisfaction and opioid related side effects.

Secondary Objective(s): To determine whether CSWI+PCA in comparison to PCEA reduces total operative time.

Other research questions:

- Does CSWI+PCA in comparison to PCEA decrease the length of hospital stay?
- Does CSWI+PCA in comparison to PCEA decrease the occurrence of analgesic technique failure?
- Does CSWI+PCA in comparison to PCEA decrease the need for rescue medication?
- Does CSWI+PCA in comparison to PCEA decrease the occurrence of hypotension with the need for additional fluid boluses and noradrenaline dependency?
- Does CSWI+PCA in comparison to PCEA decrease the number of analgesia related side effects?
- Does CSWI+PCA in comparison to PCEA decrease the usage of indwelling urine catheters?
- Does CSWI+PCA in comparison to PCEA decrease the length of postoperative ICU

stay?
- Does CSWI+PCA in comparison to PCEA decrease the incidence of post-surgical pain?
- Does CSWI+PCA in comparison to PCEA reduce the cumulative opioid consumption?
- Does CSWI+PCA in comparison to PCEA decrease the need for CSWI+PCA or PCEA?

Study design

This is a randomized controlled, non-inferiority, multicenter trial running in both AMC and OLVG comparing two treatment strategies.
Patients who will undergo a laparotomy for HPB conditions will be randomly allocated between A) CSWI+PCA or B) PCEA.

Intervention

CSWI (Bupivacaine)
After the incision 3x10ml bupivacaine 0.25% is injected at three locations in the space between peritoneum and posterior fascia. (total 30 ml)

At the end of surgery wound catheters are placed: two in case of a midline laparotomy, three in case of a right or left subcostal incision.

Catheter positions:
1. Catheter right subcostal region between peritoneum and fascia, tunnelled via rectus sheath to right thorax
2. Subcostal between rectus sheath and peritoneum on right side, tunnelled to similar spot on thorax. This catheter and nr 1 covered with foil.
3. Subcostal between rectus sheath and peritoneum on left side with separate endpoint on skin, rolled and covered with foil.

Each catheter is infused with a bolus of 10ml bupivacaine 0.25% (total 30ml). Next, with one infuser pump per catheter infusion with bupivacaine 0.125% is started 4ml/hr. Max 12ml/u over 24hrs.

In case of midline laparotomy only catheter 2 and 3 are used. In case of 2 catheters the two pumps run at 6ml/hr of bupivacaine 0.125%.

PCA (Morphine)
Bolus dose: 1 ml = 1 mg morphine Lock-out time: 5 minutes, 4-uur maximum dose: 30 ml = 30 mg morphine.

3.1.2 Group B (PCEA) (Control arm)
Current best practice of patient controlled epidural analgesia (PCEA).
The PCEA solution consists of bupivacaine (0,125 %) and sufentanil (1 µg/ml). Running at 6 ml/hr, patients are able to bolus 2ml with a lockout time of 20 minutes.

The 4 hour maximum was set to 1,2 mg bupivacaine/kg.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
- Patients will be receive a telephone call 30 days after surgery. This will take 5-10 minutes. (see F1)
- The OBAS score is asked standard by the acute pain service.
- Since both techniques (CSWI+PCA and PCEA) are already being used in daily practice, there is virtually no additional risk involved.

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

- Patients of 18 years and older
- Elective laparotomy for hepato-pancreato-biliary conditions:
* Pylorus preserving pancreatoduodenectomy (PPPD), Whipple procedure
* Distal pancreatectomy
* Hepatojejunostomy
* Partial liver resection
* Other hepato-pancreato-biliary laparotomies (elective)
- Patients who have signed an informed consent form

Exclusion criteria

- ASA status 4
- Chronic opioid use
- Allergy to local anesthetics or morphine
- Renal / Liver failure
- Contraindications for epidural placement
- INR >1.5 , PPT>1.5, Platelets <80

Study design

Design

Study phase:	4
Study type:	Interventional
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):	21-01-2015
Enrollment:	102

Type:	Actual

Medical products/devices used

Generic name:	Standard Epidural Catheter;Perifix epidural catheter 20G standard
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	10-12-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-04-2015
Application type:	Amendment
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
CCMO	NL50968.018.14