Coverpage:

Official title of the study:

Intraoperative administration of intravenous morphine in patients undergoing laparoscopic cholecystectomy – a retrospective, observational, quality-improvement study.

Document date:

November 21st 2023

NCT number:

None

Purpose:

Primary purpose: To investigate whether intraoperatively administered morphine improves postoperative analgesia.

Secondary purpose: To investigate whether intraoperatively administered morphine increases opioid related adverse effects.

PICO:

Population: adult patients who have undergone elective laparoscopic cholecystectomy

Intervention: change in anesthesia technique to include an intraoperative dose of morphine

Comparison: A) no morphine = patients operated in the year before the change in anesthesia protocol (June 1st 2022 – May 31st 2023)

B) morphine = patients operated in the year following the change in anesthesia protocol (Jan 1st 2024 – Dec 31st 2024)

Outcomes: Primary: use of rescue analgesia in the postoperative ward

Secondary: pain scores on admittance and discharge from postoperative ward, time from end of surgery to admittance to postoperative ward (surrogate measure for emergence from anesthesia), use of rescue antiemetic treatment in the postoperative ward, time in postoperative ward, use of analgesic and antiemetic treatment in the first 24 hours after discharge from postoperative ward, time in hospital.

Background:

Pain following laparoscopic cholecystectomy is complex and stems from several stimuli: e.g. skin-incisions, abdominal distention due to pneumoperitoneum and irritation of the phrenic nerve.[1] Postoperative pain continues to be a problem despite years of focus on the issue as well as increased use of laparoscopic and minimally invasive, surgical technique. This holds true for laparoscopic cholecystectomy as well. [2,3] Some investigators report that as much as 50-70% of patients experience moderate to intensive pain postoperatively. [4] It is well known that postoperative pain causes increased morbidity and is a primary cause of prolonged length of hospital stay.[1] Multimodal analgesic approach is recommended for this type of surgery. Because use of opioids frequently cause adverse effects an opioid-sparing approach is recommended.[2] However, non-opioid analgesia also has the potential for adverse effects. Even if it is possible to perform opioid-free anesthesia knowledge and evidence is still sparse, and peri- and postoperative opioid rescue analgesia is often necessary.[5,6,7]

We hypothesize, that multimodal analgesia including a perioperative dose of morphine (0,1 mg/kg) given 20 minutes after start of surgery will have beneficial effect on postoperative pain without causing significant increase in opioid related adverse effects.

Design:

Retrospective, observational, data from patient records/register based

Investigation site: Hospital of South West Jutland Esbjerg

Population:

2 groups:

a) No morphine intraoperatively: Patients operated in the year before change in anesthesia protocol
b) Morphine intraoperatively: Patients operated in the year after change in anesthesia protocol

Inclusion criteria:

- Patient having undergone elective laparoscopic cholecystectomy

Exclusion criteria:

- Age under 21 (because these patients are admitted to a separate ward for children and young adults)
- Patients who are unable to give consent to anesthesia
- Patients who cannot participate in pain-scoring by numerical ranking scale (NRS)
- Patients with chronic pain (characterized by patient receiving regular analgesic treatment and patients with active or previous contact to pain clinic)
- Patients with active or previous substance abuse
- Emergency surgery

Outcomes

Primary:

- Use of rescue analgesia (calculation of total morphine equivalents) in the postoperative ward

Secondary:

- Intraoperative opioid use (calculation of total morphine equivalents)
- Time from end of operation to admittance to postoperative ward (surrogate measure of emergence from anesthesia)
- Pain score at admittance to postoperative ward, scale from 0 to 3*
- Pain score at discharge from postoperative ward, scale from 0 to 3*

*Due to retrospective, register based design we cannot use standard numerical ranking scale (NRS), since local practice is to register pain in intervals of NRS: no pain = 0, light pain = 1-3, moderate pain = 4-6, severe pain = 7-10

- Use of rescue antiemetic treatment in the postoperative ward
- Time in postoperative ward
- Analgesic use in surgical ward during first 24 hours if admitted**
- Use of antiemetic treatment in surgical ward during first 24 hours if admitted**

** It is expected that a large proportion of the included patients will be managed as out-patients.

- Total admission time.

Other data collected for statistical analysis:

- Age at operation
- Gender
- ASA-classification
- Co-morbidity
- Height
- Weight
- Smoking habits (smoker/non-smoker)
- Use of alcohol (none, 1-21 units per week, > 21 units per week)
- In-patient/out-patient status
- Anesthesia maintenance (intravenous or inhalational)'
- Dose of fentanyl, remifentanil and morphine
- Use of lidocaine
- Postoperative nausea and vomiting (PONV)-prophylaxis
- Use of vasopressor or inotropes
- Paracetamol and/or NSAIDs gives preoperatively or intraoperatively
- Pre- and postoperative C-reactive protein (CRP)-values, if taken

Analyses:

- Per protocol
    - a) No-morphine vs b) Morphine
    - T-test, statistical difference in:
        - Analgesic use in postoperative ward (primary)
        - Intraoperative analgesic use
        - Pain scores in postoperative ward
        - Time for end of surgery to admittance to postoperative ward

        - Use of rescue antiemetic drugs in postoperative ward
        - Time in postoperative ward
        - Use of opioid analgesia and antiemetic drugs in surgical ward
        - Time in hospital
    - If necessary and possible logistic regression analyses.

Anticipated time schedule:

2023	Protocol, permissions and generation of data collection tool in Redcap
Feb - Sept 2024	Data collection, no-morphine group
Oct 2024 – April 2025	Data collection, morphine group
April 2025 - ?	Data management, analyses, manuscript, publication

Ethics:

Patients are all subject to standard anesthesia care as per the department guidelines (as per approved anesthesia protocol). No experimental drugs or techniques are used.

Written consent to access relevant patient files without direct consent from each patient as per the quality improvement nature of the study has been obtained.

We have consulted our local board of directors (approval date October 28th 2023, Acadre case no 23/47526) as well as the regional ethics committee (approval date July 3rd 2023, case no S-20232000-86).

Perspective:

Laparoscopic cholecystectomy is a frequent procedure. Despite wide attention to the problem, patients undergoing this procedure is still experience considerable postoperative pain. We believe that our findings will improve knowledge in pain management and as such be of benefit to future patients

Bibliography:

[1] Jiang B, Song Y. Pharmacotherapeutic pain management in patients undergoing laparoscopic cholecystectopmy. Adv Clin Exp Med 2022; 31(11): 1275-1288.

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[7] De Oliveira Jr GS. Is there a strong link between intraoperative anesthetic management and postoperative recovery? J Clin Anesth 2019; 53: 81-82.