Satisfactory Analgesia Minimal Emesis in Day Surgeries

(SAME-Day study)

A Randomized Control Trial Comparing Morphine and Hydromorphone

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STUDY BACKGROUND
THE PROBLEM?

Around 70% of procedures are being done as DS, with known benefits to patients and hospitals.

Pain and PONV are recognized as the leading factors affecting the quality of services delivered.

Postsurgical pain could be inadequately treated in 30%-60%.

30%-40% of them patients suffer from significant PONV.

A single episode of PONV can prolong the PACU stay by 25 mins.
Opioids remain the main stay of analgesia—despite the use of multimodal analgesia.

Commonly Morphine and Hydromorphone are used.

They exert no ceiling effect for their analgesia; incomplete or inadequate analgesia is related to the appearance of side effects.

Clinical effectiveness, relative to each other, is reflected not just by satisfactory analgesia, but by a combination of ‘satisfactory analgesia with limited side effects’.
DESIGN

Multisite-SJH, MUMC, Juravinski

2 arm, parallel, superiority design

Randomization of patients and blinding of patients, health care providers (physicians and nurses) and research personnel (research coordinator and data analyst).

Stratified based on Site and Type of Surgery (lap vs open)
Intention to treat approach for design and analysis
In patients who undergo DS causing at least moderate pain, hydromorphone (HM) increases the proportion of patients who would demonstrate SAME [analgesia=<4/10 NAS, PONV-<2/5 VDS] as compared to morphine (M), when both are administered intravenously, in equi-analgesic doses, and are compared at 2 hours after surgery in PACU.

HYPOTHESIS
DS of the abdominal and pelvic regions, within the scope of general surgical (GS), gastrointestinal (GI) and gynecological (GYN) specialties

Recruitment at Day Surgery Unit
Requesting for Consent Waiver

**INCLUSION**

Age-18 yrs to 65 yrs;

Ambulatory surgeries producing at least moderate pain—such as cholecystectomy, appendicectomy, ovarian cystectomy, inguinal hernia repair, abdominal wall hernias; and

An ability to communicate in English.

**EXCLUSION**

Allergy to M or HM;

Patient on regular chronic opioid medication;

Patient with uncontrolled systemic disease;

Severe obesity with a BMI >35;

History of drug addiction or dependence;

Any planned regional or nerve block other than local anesthesia infiltration;

Patients with confirmed sleep apnea;

Emergency surgeries and urological surgeries.
Patient in DSU

- First contact
- Patient informed about the study
- Initiate randomization and inform PACU nurse of the sequence number
Patient in DSU

- First contact
- Patient informed about the study
- Initiate randomization and inform PACU nurse of the sequence number

Operating Room

- Routine management as per the protocol
• Only General Anesthetic
• No regional other than local infiltration
• Midazolam 1-2 mg –to be given as appropriate
• Propofol-Induction in titrated doses
• Rocuronium-Muscle relaxant in titrated doses
• Intraop opioids: Remifentanil-bolus or infusion
  Fentanyl-25-50 mcg bolus
  Sufentanil-5-20 mcg bolus
• No long acting opioids to be given during the surgery
• No NSAIDS
• Antiemetic prophylaxis with Dexamethasone 4mg soon after induction in all patients, except with history of allergy.
• LA infiltration: 20-30 mls of 0.25% bupivacaine

OPERATING ROOM PROTOCOL
Patient in DSU
- First contact
- Informed about the study
- Initiate randomization and collect medication as per the sequence

Operating Room
- Routine Management as per the Protocol

PACU
- Application of Randomized Protocol by the PACU nurse
- Primary Outcomes Recorded
PACU PROTOCOL

1st dose within 5 minutes after coming to PACU:

0.05mg/kg morphine units (rounding off to the nearest 1 ml or 0.5 ml).

Repeat doses: 0.03 mg/kg morphine units every 5-10 minutes to titrate for analgesia and side effects

For example: 70 kg man=3.5 mg morphine units 1st dose and 2 mg morphine units subsequently
67 kg patient will also get 3.5 mg morphine units as the 1st bolus and 2 mg morphine units as the subsequent bolus

Titrate to have analgesia: NAS =<4/10.

If Nausea-Vomiting observed: record it
Treat it with anti-emetics
(Ondansetron 1-4 mg IV, Dimenhydrinate 25-50 mg)

If patient is too sedated (<3-Ramsey Sedation Scale)- withhold the next dose and restart if the score is >3

If respiratory depression present, withhold the next dose, treat with Naloxone if necessary.

Ketorolac IV 15-30 mg as rescue medication if patient does not tolerate the study opioid or if the patient does not satisfy the success of satisfactory analgesia at 2 hrs
Patient in DSU
• First contact
• Informed about the study
• Initiate randomization and collect medication as per the sequence

Operating Room
• Routine Management as per the Protocol

PACU
• Application of Randomized Protocol
• Primary Outcomes Recorded

DSU
• Routine Management as per the protocol
• Outcomes completed

Patient discharged home
Approximately 20% of patients suffer from inadequate analgesia with PONV using morphine.

For a 2 sided test: alpha of 0.05 and a power of 90%, and with an estimated effect size of 10% (p1= 80% and p2= 90%), a sample size of 266 per group was calculated.

We expect minimal loss through attrition as the study involves a follow up of few hours.

The expected recruitment is approximately 20 cases per month at each of the 3 sites. We expect the trial to run for 10-12 months.
<table>
<thead>
<tr>
<th>OUTCOME MEASURE</th>
<th>TYPE</th>
<th>MEASUREMENT</th>
<th>TIME OF MEASUREMENT</th>
<th>ANALYSIS METHOD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
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<tr>
<td>Satisfactory Analgesia with minimal PONV</td>
<td>Binary</td>
<td>NAS=&lt;4/10 VDS&lt;2/5</td>
<td>At 2hrs or at the time of discharge from PACU</td>
<td>Chi-square</td>
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<tr>
<td><strong>Severe Itching</strong></td>
<td>Binary</td>
<td>VAS&gt;5/10</td>
<td>At 2hrs or at the time of discharge from PACU</td>
<td>Chi-square or Fisher’s test (as appropriate)</td>
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<tr>
<td><strong>Severe Sedation</strong></td>
<td>Binary</td>
<td>Ramsey Score &gt;3/6</td>
<td>At 2hrs or at the time of discharge from PACU</td>
<td>Chi-Square or Fisher’s test (as appropriate)</td>
</tr>
<tr>
<td><strong>Severe Respiratory Depression</strong></td>
<td>Count</td>
<td>All cases needing treatment as counts</td>
<td>At 2hrs or at the time of discharge from PACU</td>
<td>Chi-square or Fisher’s test (as appropriate)</td>
</tr>
<tr>
<td><strong>Use of Ketorolac</strong></td>
<td>Continuous</td>
<td>Total dose used per patients as a rescue therapy</td>
<td>At 2hrs or at the time of discharge from PACU</td>
<td>T test</td>
</tr>
<tr>
<td><strong>Mean dose of Analgesic Used</strong></td>
<td>Continuous</td>
<td>Dose of Analgesic used per patient in EMU</td>
<td>At the time of hospital discharge</td>
<td>T test</td>
</tr>
<tr>
<td><strong>Patient Satisfaction</strong></td>
<td>Continuous</td>
<td>Mean Score calculated between 0 to 5 scale</td>
<td>At the time of hospital discharge</td>
<td>T test</td>
</tr>
<tr>
<td><strong>Time to discharge from PACU</strong></td>
<td>Continuous</td>
<td>Mean time in hrs</td>
<td>At 2hrs or at the time of discharge from PACU</td>
<td>T test</td>
</tr>
<tr>
<td><strong>Time to discharge from the hospital</strong></td>
<td>Continuous</td>
<td>Mean time in hrs</td>
<td>At the time of hospital discharge</td>
<td>T test</td>
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<tr>
<td>BASELINE</td>
<td>SURGICAL DETAILS</td>
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<tr>
<td>Age</td>
<td>Type of surgery (gastrointestinal or gynecological)</td>
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<tr>
<td>Gender</td>
<td>Actual surgical procedure</td>
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<tr>
<td>Weight in kgs</td>
<td>Duration of the procedure</td>
<td></td>
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<tr>
<td>Height in cms</td>
<td>Laparoscopic or open surgery</td>
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<tr>
<td>Previous history of severe PONV</td>
<td>Antiemetics (dexamethasone) used prior to, or during the procedure and its dose</td>
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<tr>
<td>Smoking</td>
<td>Any other drugs used during the surgery</td>
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PRESENT UPDATE

Initial funding-CARF

REB-provisional provided

Consent waiver-request declined –but need to reapply

Formal –no objection from surgical colleagues to be requested

Pharmacy –discussed, final plan regarding medication and dispensing

PACU and DSU-formal no objection requested as part of REB application

To identify personnel (PACU) to be involved in the study
HIGHLIGHTS and CHALLENGES

Pragmatic and Important question to be answered

Similar to present standard of care, but controlled to study framework and methods

Practically feasible-
HIGHLIGHTS and CHALLENGES

Preoperative antiemetic prophylaxis?

Local anesthetic infiltration

DSU analgesia provision-oral opioids: percocet or tylenol 2 or tylenol

Pharmacy-vial vs syringe; 20 mls to 40 mls

Other Outcomes-pain over 24 hrs and pain at 2, 4 and 6 months?

Need for consent?

Any other methodological concerns?
THANKS