Postoperative care: Avoiding complications

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OVERLOOKED COMMON POSTOPERATIVE COMPLICATIONS

• Pain
• Cardiorespiratory problems
• Drug interactions
• Deep vein thrombosis (DVT)
• Pulmonary embolism (PE)
• Heparin-induced thrombocytopenia (HIT)
• Postoperative nausea & vomiting (PONV)
• Opioid-induced emesis (OIE)
• Postoperative ileus (POI)

CASE:

68 y/o female - cancerous colon polyp--scheduled for elective laparoscopic sigmoidectomy. EKG shows non-specific T wave changes, cannot rule out MI, blood sugar 177 mg/dl, mild hypertension treated with hydrochlorothiazide. Body mass index 31. Non smoker. BP 160/95.

CLINICAL CASE PRESENTATION

68 y/o female–cancerous colon polyp–scheduled for elective laparoscopic sigmoidectomy

• The patient received a general oral-tracheal anesthetic (propofol, rocuronium, fentanyl, sevoflurane, O₂ with air, MSO₄, ketorolac)
• OG tube used during surgery but removed prior to extubation
• Laparoscopy converted to open sigmoidectomy because of tumor spread and positive nodes; Foley left in place
• Extubated in OR and transferred to PACU

POSTOPERATIVE PAIN

• Expected by majority of patients
• Significantly under treated
• National guidelines not clearly effective
• PCA, continuous epidural analgesia, peripheral blocks effective
• Technical weaknesses with PCA
• Multimodal analgesic techniques may improve outcome
• Health care workers’ education essential

POSTOPERATIVE PAIN MANAGEMENT

• Multimodal therapies, perioperative care
• Iontophoretic transdermal fentanyl
• Extended release epidural morphine
• RCTs to evaluate implementation of guidelines
• Assessment of postop outcomes (pain intensity, opioid, detoxification, consumption and de-escalation, side effects, return to work)

PRINCIPLES OF PAIN RELIEF

• Plan preoperatively (preemptive)
• Design route of administration to patient’s situation
• Give drugs regularly rather than on request
• Be prepared to change drug, dosage, frequency or route according to response
POSSIBLE MODEL FOR MULTIMODAL APPROACH TO POSTOPERATIVE ANALGESIA

- Reduced doses of both analgesics
- Improved antinociception due to synergistic/additive effects
- Reduced incidence of side-effects of both drugs

CLINICAL CASE PRESENTATION

68 y/o female–cancerous colon polyp–underwent elective OPEN sigmoidectomy nd nodal dissection

Standardized postop patient-controlled analgesia (PCA) orders?

For PCA Dosing Guidelines see page 2

<table>
<thead>
<tr>
<th>Medication</th>
<th>Morphine 5 mg/ml</th>
<th>Fentanyl 10 micrograms/ml</th>
<th>Hydromorphone 0.2 mg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incremental Dose (ID)</td>
<td>________ mg</td>
<td>________ micrograms</td>
<td>________ mg</td>
</tr>
<tr>
<td>* Average starting dose 1 mg</td>
<td>* Average starting dose 10 micrograms</td>
<td>* Average starting dose 0.2 mg</td>
<td></td>
</tr>
<tr>
<td>Lockout Interval (LO)</td>
<td>________ minutes</td>
<td>________ minutes</td>
<td>________ minutes</td>
</tr>
<tr>
<td>* Average lockout 8 minutes</td>
<td>* Average lockout 6 minutes</td>
<td>* Average lockout 8 minutes</td>
<td></td>
</tr>
<tr>
<td>Four-hour limit</td>
<td>________ mg/4 hours</td>
<td>________ micrograms/4 hours</td>
<td>________ mg/4 hours</td>
</tr>
<tr>
<td>* Average limit 24 mg/4 hours</td>
<td>* Average limit 240 micrograms/4 hours</td>
<td>* Average limit 4.8 mg/4 hours</td>
<td></td>
</tr>
<tr>
<td>Continuous Infusion (CI)</td>
<td>________ mg/hr</td>
<td>________ micrograms/hr</td>
<td>________ mg/hr</td>
</tr>
<tr>
<td>Caution in opioid naive</td>
<td></td>
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</tr>
</tbody>
</table>

CARDIAC COMPLICATIONS

- Identifiable risk factors (major, unstable angina, acute MI, CHF, intermediate, mild angina, DM, renal failure, old MI, minor, old age, history of stroke, abnormal EKG)
- Surgical severity
- Duration of procedure
- Perioperative beta blocker therapy

RESPIRATORY COMPLICATIONS

- Anesthetic overdose (opioids, muscle relaxants)
- Obstructive sleep apnea
- Asthma
- Chronic obstructive pulmonary disease
- Preexisting condition (smoking)

CASE MANAGEMENT

- Is she at high risk for postoperative respiratory problems?
- How long should she receive supplemental oxygen?
- Is she a candidate for PCEA, PCA?
- Should she be followed with pulse oximetry in the ward?
- Any precautions?
CLINICAL CASE PRESENTATION

68 y/o female-cancerous colon polyp—scheduled for elective laparoscopic sigmoidectomy

- The patient had postoperative nausea and vomiting (PONV) after previous D&Cs
- Is she at risk for PONV following elective sigmoidectomy?

NAUSEA AND VOMITING INDUCED BY SURGERY OR ANALGESIA

Triggers for nausea and vomiting:

- Surgery
- General anesthesia
- Opioids

SURGICAL AND ANESTHETIC FACTORS INCREASING PONV RISK

- Surgical site and procedure\(^{1-3}\)
  - Duration of surgery
  - OB/GYN
  - Ophthalmic
  - Abdominal
- Anesthetic factors
  - General anesthesia\(^2\)
  - Premedications\(^1\)
  - Anesthetic agents\(^1\)
  - Use of opioids\(^1\)
  - Laparoscopy
  - ENT
  - Head & neck and oral
  - Plastic
- Lack of preoperative fasting\(^1\)
- Nasogastric suctioning\(^1\)
- Postoperative pain

EVIDENCE RATING SCALE

- I Large, randomized, controlled trial
- II Systematic review
- III Small, randomized controlled trial
- IV Nonrandomized trial, case report
- V Expert opinion
- A Good evidence, B Fair evidence, C Insufficient evidence

ANTIEMETIC THERAPY FOR PONV PROPHYLAXIS IN ADULTS

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Dose (evidence)</th>
<th>Timing (evidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ondansetron</td>
<td>4-8 mg IV (IA)</td>
<td>At end of surgery (IIIA)</td>
</tr>
<tr>
<td>Dolasetron</td>
<td>12.5 mg IV (IA)</td>
<td>At end of surgery (IIIA)</td>
</tr>
<tr>
<td>Granisetron</td>
<td>0.35-1 mg IV (IA)</td>
<td>At end of surgery (IIIA)</td>
</tr>
<tr>
<td>Tropisetron</td>
<td>5 mg IV (IA)</td>
<td>At end of surgery (VA)</td>
</tr>
<tr>
<td>Dexamethasone*</td>
<td>5-10 mg IV (IIIA)</td>
<td>Prior to induction (IIIA)</td>
</tr>
<tr>
<td>Droperidol</td>
<td>0.625-1.25 mg IV (IA)</td>
<td>At end of surgery (IIA)</td>
</tr>
</tbody>
</table>


**Other therapies:** Diphenhydramine (1-2 mg/kg IV; IIA), ephedrine (0.5 mg/kg IM; IIB), prochlorperazine (5-10 mg IV; IIIA), promethazine (12.5-25 mg IV; IIIB), transdermal scopolamine (IIB)

*FDA black box warning

**CLINICAL CASE PRESENTATION**

68 y/o female – cancerous colon polyp – scheduled for elective laparoscopic sigmoidectomy

- The patient received multimodal PONV prophylaxis with ondansetron (4 mg), dexamethasone (10 mg); she had no PONV until she vomited the following morning
- Is it PONV or opioid-induced emesis (OIE) from the PCA the patient has been using?
- Suggested treatment of this «common complication»? Replace OG tube?

**GUIDELINES FOR PONV MANAGEMENT IN ABSENCE OR FAILURE OF PROPHYLAXIS**

<table>
<thead>
<tr>
<th>Initial therapy</th>
<th>Treatment</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>No prophylaxis or dexamethasone</td>
<td>Administer low-dose 5-HT₃ antagonist*</td>
<td>IIA</td>
</tr>
<tr>
<td>5-HT₃ antagonist* plus second agent†</td>
<td>Use drug from different class</td>
<td>V</td>
</tr>
<tr>
<td>Triple therapy with 5-HT₃ antagonist* plus 2 other agents† when PONV occurs &lt; 6 hours postop (In PACU)</td>
<td>Do not repeat initial therapy Use drug from different class Use propofol, 20 mg prn</td>
<td>IIIA V IIIB</td>
</tr>
<tr>
<td>Triple therapy with 5-HT₃ antagonist* plus 2 other agents† when PONV occurs &gt; 6 hours postop</td>
<td>Repeat 5-HT₃ antagonist* and droperidol‡ (not dexamethasone or transdermal scopolamine) Use drug from different class</td>
<td>V</td>
</tr>
</tbody>
</table>

*Low-dose 5-HT₃ antagonist dosing: ondansetron 1.0 mg; dolasetron 12.5 mg; granisetron 0.1 mg; tropisetron 0.5 mg; †Alternative therapies for rescue: droperidol 0.625 mg IV; dexamethasone (2-4 mg IV); promethazine 12.5 mg IV; ‡FDA black box warning.


**RISK FACTORS FOR VENOUS THROMBOEMBOLISM (VTE)**

- Increasing age
- Immobilization
- Paralytic stroke
- Previous VTE
- Cancer
- Chemotherapy
- Major surgery (particularly of the abdomen, pelvis, or lower extremities
- Obesity
- Varicose veins
- Trauma (particularly pelvic, hip, or leg fracture)
- Cardiac dysfunction
- Indwelling central venous catheter
- Inflammatory bowel disease
- Nephrotic syndrome
- Pregnancy
- Estrogen use
- Spinal cord injury
- Serious medical illness


**EPIDEMIOLOGY OF VTE**

- 23 million operations in US each year
  - Without prophylaxis:
    - DVT occurs in 20% of operations; 50% of orthopedic operations
    - PE occurs in 1-2% of major operations; 30% of orthopedic procedures
- 31 million medical patients each year in US
  - Without prophylaxis, 16% will develop DVT

ANNUAL INCIDENCE OF FATAL PULMONARY EMBOLISM

- 200,000 US cases
- 100,000 potentially curable using thrombosis prophylaxis
- 100,000 have incurable illness
- 80,000 lives saved
- 20,000 deaths from pulmonary embolus despite prophylaxis


RISKS AND CONSEQUENCES OF HEPARIN ADMINISTRATION

- Risks
  - Bleeding
  - Heparin-induced thrombocytopenia (HIT)
  - Heparin-induced thrombocytopenia thrombotic syndrome (HITTS)

- Heparin failure
  - Progression/recurrent DVT

RISK OF HIT WITH HEPARIN ADMINISTRATION

Approaches 5% per day

- Greatest in patients undergoing cardiac or orthopedic surgery
- Higher in patients receiving UFH vs low molecular weight heparin (LMWH)
- Patients who have received heparin within the past 3-6 months for at greater risk for developing HIT; ask patients about prior recent hospitalizations and heparin use


CLINICAL FEATURES OF HIT

- Thrombocytopenia, occurring 4-14 days after starting heparin (or hrs if previously received)
- Platelet count of > 50% (2)
- Platelet count 20,000-150,000/μL; median 50,000/μL
- Arterial or venous thrombosis occurs in 30-50% of HIT cases


CLINICAL CASE PRESENTATION

68 y/o female - cancerous colon polyp – scheduled for elective laparoscopic sigmoidectomy
Patient prophylaxed with subcutaneous heparin 5,000 units preop q 12 hours

- Noted patchy dark areas on all extremities on POD 3
- Consults?

**Clinical Sequelae in HIT**

- Death: 20-30%\(^{(1,2)}\)
- Amputation: 10%\(^{(1,2)}\)
- New thrombosis: 30-50%\(^{(1,2)}\)

Gangrenous changes due to HIT complications


**Clinical Case Presentation**

68 y/o female – cancerous colon polyp – scheduled for elective laparoscopic sigmoidectomy

- HIT/HITTS successfully diagnosed
- Argatroban therapy initiated
  - No initial bolus
  - Infusion: 2 µg/kg/min targeted a PTT range 1.5-3 x baseline
  - Continued until platelet count returned to near normal
  - When platelet count was near normal, patient started on low doses of warfarin

**14-Year Study of HIT: Results After Heparin Discontinuation**


**HIT Treatment Strategy**

- Discontinue all heparin (occult sources: line flushes; heparin-bonded central lines; hyperalimentation…\(^{(1)}\)
- Ongoing antithrombotic therapy:
  - No warfarin acutely\(^{(2)}\)
  - Direct thrombin inhibitors\(^{(2)}\)
    - Lepirudin (rHirudin): direct IIa inhibitor; effective, but antigenic
    - Argatroban: arginine-based
  - Long term: warfarin, once platelet counts are recovering; start with low dose\(^{(3)}\)

CLINICAL CASE PRESENTATION

68 y/o female with cancerous colon polyp, scheduled for elective laparoscopic sigmoidectomy

Could HIT have been avoided in this patient?

Patient was correctly identified to be at high risk for DVT/PE because of:
- prior history of DVT
- cancer
- obesity
- immobilization
- lower abdominal procedure

Prophylaxis could have been initiated earlier with a direct thrombin inhibitor.

Heparin was administered but selective factor Xa inhibitors may offer an alternative approach.

SYNTHETIC INHIBITORS OF FACTOR XA: TARGETED MECHANISM OF ACTION

Fondaparinux is currently approved for:
- Prophylaxis of DVT, which may lead to PE in patients undergoing:
  - Hip fracture surgery, including extended prophylaxis
  - Hip replacement surgery
  - Knee replacement surgery
  - Abdominal surgery in patients who are at risk for thromboembolic complications
- Treatment of acute DVT in conjunction with warfarin

Fondaparinux studies have been completed or are ongoing for:
- VTE prophylaxis in medically ill patients (eg CHF, acute respiratory illness, acute infectious or inflammatory disease)
- Acute coronary syndrome

Arixtra® (fondaparinux) full prescribing information. Organon Sanofi-Synthelabo LLC; 2005.

FONDAPARINUX PROPHYLAXIS IN ABDOMINAL CANCER SURGERY PATIENTS

Odds Reduction = 40.5%
(95%CI: 61.9; 7.24%)
P = 0.02

FONDAPARINUX PROPHYLAXIS IN ACUETELY III MEDICAL PATIENTS: PRIMARY EFFICACY OUTCOME VTE UP TO DAY 15

Odds Reduction = 49.5%
(95%CI: 72.1; 8.6)
P = 0.029

FONDAPARINUX PROPHYLAXIS:  
DOSE AND ADMINISTRATION

DVT Prophylaxis following abdominal surgery

- Recommended dose: 2.5 mg administered by SC injection once daily after hemostasis has been established
- Initial dose should be given 6 to 8 hours after surgery
- Administration before 6 hours after surgery has been associated with an increased risk of major bleeding
- Usual duration of administration is 5 to 9 days; up to 10 days has been administered

Arixtra® (fondaparinux) full prescribing information. Organon Sanofi-Synthélabo LLC; 2005.

CLINICAL CASE PRESENTATION

68 y/o female with cancerous colon polyp underwent elective OPEN sigmoidectomy and nodal dissection

- Continued NPO with moderate nausea, rare vomiting, and adequate pain control via PCA morphine
- Abdominal sounds quiet; mild distention, no flatus passage
- On POD 4, the patient’s family is concerned that she has not left the hospital «as planned»

POI: DEFINITION

- Ileus: functional inhibition of propulsive bowel activity, irrespective of pathogenetic mechanisms1
- POI: uncomplicated ileus following surgery, resolving spontaneously within 2-3 days1; primary ileus that is a response to surgical trauma, often considered inevitable2
- Paralytic POI: form of POI lasting >3 days after surgery1


MANIFESTATIONS OF POI

- Abdominal distension1,2
- Cramping1,2

- Delayed passage of flatus and defecation1,2
- Pain and discomfort1,2
- Nausea and vomiting1
- Pulmonary morbidity2,3
- Delayed nourishment, causing1,2

POI: PATHOGENESIS IS MULTIFACTORIAL

NO = nitric oxide
VIP = vasoactive intestinal peptide
CFRP = calcitonin gene-related peptide


EFFECTS OF EXOGENOUS OPIATES ON THE GI TRACT

<table>
<thead>
<tr>
<th>Site of action</th>
<th>Pharmacologic action</th>
<th>Clinical effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>Decreased gastric motility</td>
<td>Anorexia</td>
</tr>
<tr>
<td></td>
<td>Increased pyloric tone</td>
<td>Nausea and vomiting</td>
</tr>
<tr>
<td>Small intestine</td>
<td>Decreased pancreatic and biliary secretion</td>
<td>Delayed digestion</td>
</tr>
<tr>
<td></td>
<td>Reduced propulsion</td>
<td>Delayed absorption of medications</td>
</tr>
<tr>
<td></td>
<td>Increased fluid absorption</td>
<td>Hard, dry stool</td>
</tr>
<tr>
<td>Large intestine</td>
<td>Decreased propulsion</td>
<td>Straining, incomplete evacuation, bloating, abdominal distension, constipation</td>
</tr>
<tr>
<td></td>
<td>Increased nonpropulsion contractions</td>
<td>Spasm, abdominal cramps, pain</td>
</tr>
<tr>
<td></td>
<td>Increased fluid absorption</td>
<td>Hard, dry stool</td>
</tr>
<tr>
<td></td>
<td>Increased anal sphincter tone</td>
<td>Incomplete evacuation</td>
</tr>
</tbody>
</table>

Adapted from Kurz A, Sessler DI. Drugs 2003;63:649-671.
POI: PERIPHERAL OPIOID ANTAGONISM

- Most patients require opioids
- Opioids inhibit GI propulsive motility\(^2\)
- Naloxone and naltrexone reduce opioid bowel dysfunction but reverse analgesia\(^1\)
- An ideal POI treatment is a peripheral opioid receptor antagonist that reverses GI side effects without compromising postoperative analgesia\(^2\)
  - Alvimopan
  - Methylnaltrexone


POI CURRENT TREATMENT MODALITIES

- Early ambulation
- Preoperative suggestions
- Surgical technique\(^{1,2}\)
  - Laparoscopy
- Anesthesia and analgesia\(^{1,2}\)
  - Epidural
  - NSAIDs
- Pharmacologic\(^{1,2}\)
  - Prokinetic agents (laxatives)
  - Opioid antagonists
  - Homeopathy
  - Other agents
- Perioperative care plan(s)\(^{1,2}\)
  - Fluid/sodium restriction
  - Multimodal clinical pathways

**NALOXONE**

- Competitive μ-opioid receptor antagonist
- Readily crosses the blood-brain barrier when given IV
- Reverses the centrally mediated effects of opiates (CNS depression, analgesia, respiratory depression)
- May precipitate opioid withdrawal
- If given PO, decreases opioid-induced constipation
- Higher PO doses lead to increased symptoms of opiate withdrawal
- The efficacy of PO naloxone for POI is currently under investigation


**METHYLNALTREXONE**

- μ-opioid receptor antagonist
- Does not readily cross the blood-brain barrier
- If given IV, its effects are limited mainly to GI tract
- Has been shown to decrease opioid-induced constipation without affecting pain control or precipitating opiate withdrawal
- Has not been evaluated in the postoperative setting


**ALVIMOPAN**

- Peripherally acting μ-opioid receptor antagonist
- Highly selective for μ-opioid receptor over δ and κ receptors
- Higher potency at μ-opioid receptor than morphine and methylnaltrexone
- Because of large molecular weight and its polarity, does not readily cross the blood-brain barrier; thus, does not block central opioid receptors
- High therapeutic index
- Favorable side-effect profile


**TIME TO HOSPITAL DISCHARGE ORDER WRITTEN**

Alvimopan 6 mg vs placebo
- Hazard ratio* = 1.25 (p = .07)
- Approximately 13 hours earlier than placebo

Alvimopan 12 mg vs placebo
- Hazard ratio* = 1.42 (p = .003)
- Approximately 20 hours earlier than placebo


**OTHER RESULTS FROM THE ALVIMOPAN PHASE III STUDY #1**

- Incidence of nasogastric tube insertion after surgery
  - Alvimopan 6 mg (8.4%)
  - Alvimopan 12 mg (4.8%; p = .004)
  - Placebo (14.8%)
- Incidence of hospital readmissions within 10 days of discharge
  - Alvimopan 6 mg and 12 mg (~4%)
  - Placebo (~8%)


**ECONOMIC CONSIDERATIONS WITH POI**

- Most common reason for delayed discharge after abdominal surgery
- Healthcare costs in US estimated at $750 million to $1 billion per year, due to:
  - NG intubation
  - IV hydration
  - Extra nursing care
  - Longer hospital stay
  - Additional laboratory testing
  - Possible cost benefits of alvimopan, with selected patients, due to:
    - Shortened hospital stay
    - Reduced use of resources
    - Fewer complications
    - Fewer readmissions


**CLINICAL CASE PRESENTATION**

68 y/o female with cancerous colon polyp underwent elective OPEN sigmoidectomy and nodal dissection

- POI managed «conservatively» with continued IV fluid therapy, replacement of NG tube, increased ambulation, and laxatives
POI continued for 3 additional days with flatus passage
POD 7
Patient discharged to home on POD 10

SUMMARY

Consequences of overlooking common postoperative complications:
- Possibly preventable medical sequelae; among them PONV, DVT/PE, HIT/HITTS, and POI
- Delayed discharge from hospital
- Increased nursing care and laboratory testing

SUMMARY (CONT.)

Need for early recognition and treatment of postoperative complications
- Prophylaxis or treatment of PONV with 5-HT₃ receptor antagonists and other therapies effectively reduces PONV incidence
- Prophylaxis and treatment of DVT/PE can prevent serious sequelae and recurrences
- Direct thrombin inhibitors reduce incidence of HIT-related thrombotic complications
- Peripheral opioid antagonists are emerging POI therapy that block GI opioid µ receptors while maintaining analgesic effects