

Postoperative care: Avoiding complications

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(supported by grants from Adolor and Glaxo Smith Kline)

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

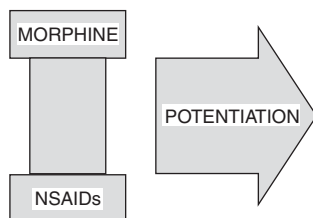
- Expected by majority of patients
- Significantly under treated
- National guidelines not clearly effective
- PCA, continuous epidural analgesia, peripheral blocks effective
- Technical weaknesses with PCA
- Multimodal analgesic techniques may improve outcome
- Health care workers' education essential

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 and nodal dissection

Standardized postop patient-controlled analgesia (PCA) orders?

For PCA Dosing Guidelines see page 2

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

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**CASE MANAGEMENT**

- Does she require perioperative beta blockade?
- Should her blood sugar level be treated preoperatively?
- Does she need any more tests?

- 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

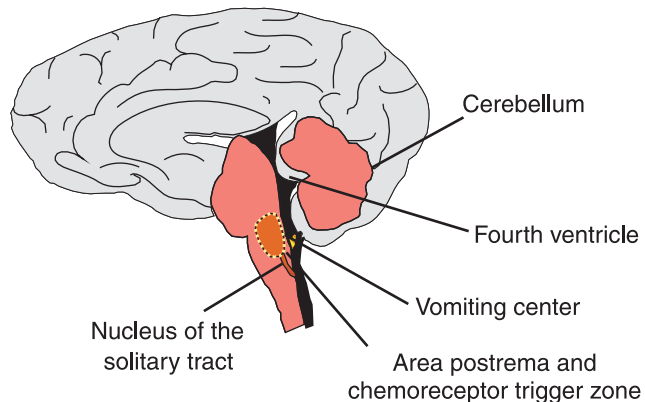
68 y/o female-cancerous colon polyp—scheduled for elective laparoscopic sigmoidectomy

- 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



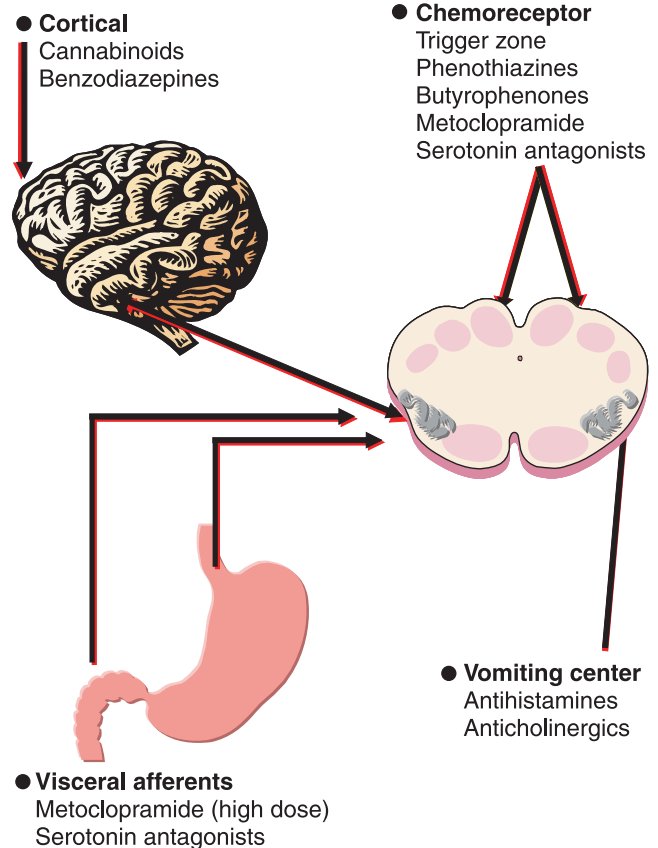
Kovac AL. Drugs 2000;59:213-243.

SURGICAL AND ANESTHETIC FACTORS INCREASING PONV RISK

- Surgical site and procedure⁽¹⁻³⁾
 - Duration of surgery
 - OB/GYN
 - Ophthalmic
 - Abdominal
 - Laparoscopy
 - ENT
 - Head & neck and oral
 - Plastic
- Anesthetic factors
 - General anesthesia⁽²⁾
 - Premedications⁽¹⁾
 - Anesthetic agents⁽¹⁾
 - Use of opioids⁽¹⁾
 - Lack of preoperative fasting⁽¹⁾
 - Nasogastric suctioning⁽¹⁾
 - Postoperative pain¹

1. Kovac AL. Drugs. 2000;59:213-243.
2. Sinclair DR, et al. Anesthesiology. 1999;91:109-118.
3. Gan TJ, et al. Anesth Analg 2003;97:62-71.

PROPOSED SITES OF ACTION: ANTIEMETIC DRUG CLASSES



Tortorice and O'Connell. Pharmacotherapy. 1990;10:129-145;
Simpson and Hicks. J Pharm Pharmacol 1996;48:774-781.

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

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

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; IIB), transdermal scopolamine (IIB)

Adapted with permission from Gan T, et al. *Anesth Analg* 2003;97:62-71.

*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

Initial therapy	Treatment	Level of evidence
No prophylaxis or dexamethasone	Administer low-dose 5-HT ₃ antagonist*	IIA
5-HT ₃ antagonist* plus second agent†	Use drug from different class	V
Triple therapy with 5-HT ₃ antagonist* plus 2 other agents† when PONV occurs	Do not repeat initial therapy	IIIA
< 6 hours postop (In PACU)	Use drug from different class	V
	Use propofol, 20 mg prn	IIIB
Triple therapy with 5-HT ₃ antagonist* plus 2 other agents† when PONV occurs	Repeat 5-HT ₃ antagonist* and droperidol‡ (not dexamethasone or transdermal scopolamine)	V
> 6 hours postop	Use drug from different class	V

*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. Adapted with permission from Gan T, et al. *Anesth Analg* 2003;97:62-71.

CLINICAL CASE PRESENTATION

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

- Due to PONV, patient unable to ambulate first POD (usual routine)
- What factors may increase this patient's risk for venous thromboembolism?
- At risk for complications from DVT?

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

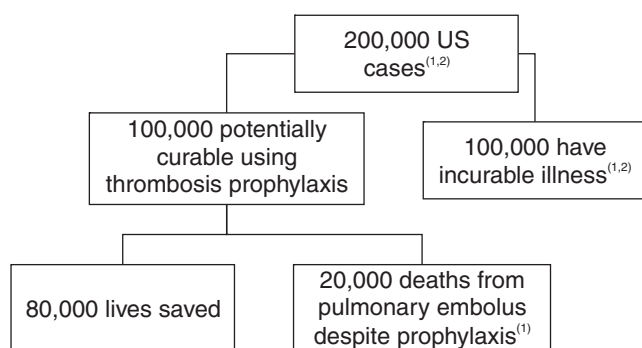
Geets WH, et al. *Chest* 2001;119:132S-175S.

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

Kleinbart J, et al. Prevention of venous thromboembolism. In: Making health care safer: A critical analysis of patient safety practices. AHRQ Pub. No. 01-E058; 2001.

ANNUAL INCIDENCE OF FATAL PULMONARY EMBOLISM



1. Anderson FA Jr, et al. Arch Intern Med 1991;151:933-938.
2. Hirsh J, Hoak J. Circulation 1996;93:2212-2245.

STRATEGIES FOR PRIMARY AND SECONDARY PREVENTION OF VTE

- Pharmacologic
 - LMWH (eg, enoxaparin, dalteparin)^(1,2)
 - Unfractionated heparin (UFH)^(1,2)
 - Oral anticoagulants (eg, warfarin)⁽¹⁾
 - Antiplatelet (eg, aspirin)⁽¹⁾
 - Pentasaccharide (eg, fondaparinux)⁽²⁾
 - Direct thrombin inhibitors (eg, bivalirudin, argatroban)⁽²⁾
- Mechanical
 - Intermittent pneumatic compression⁽¹⁾
 - Graduated elastic compression stockings⁽¹⁾

1. Geerts WH, et al. Chest. 2001;119:132S-175S.
2. Nutescu E, Racine E. Am J Health-Syst Pharm 2002;59:S7-S14.

HEPARIN ADMINISTRATION

- Treatment⁽¹⁾
 - acute venous thrombosis
 - pulmonary embolus
 - atrial fibrillation with embolization
- Prophylaxis⁽²⁾
 - pregnant women
 - postoperative patients
 - during arterial/cardiac surgery
- Anticoagulant for blood transfusion, extracorporeal circulation, dialysis, indwelling catheters, blood samples

1. Hirsch J, et al. Arterioscler Thromb Vasc Biol 2001;21:e9-e33.
2. Majerus PW, et al. In: Hardman JG, Limbird LE, eds. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York: McGraw-Hill; 2001.

RISKS AND CONSEQUENCES OF HEPARIN ADMINISTRATION

Risks

- Bleeding
- Heparin-induced thrombocytopenia (HIT)
- Heparin-induced thrombocytopenia thrombotic syndrome (HITS)

Heparin failure

- Progression/recurrent DVT

RISK OF HIT WITH HEPARIN ADMINISTRATION

Approaches 5% per day⁽¹⁾

Greatest in patients undergoing cardiac or orthopedic surgery⁽¹⁾

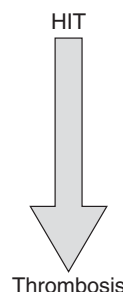
Higher in patients receiving UFH vs low molecular weight heparin (LMWH)^(1,2)

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

1. Warkentin TE. J Crit Illness. 2002;17:172-178.
2. Warkentin TE, et al. N Engl J Med 1995;332:1330-1335.

CLINICAL FEATURES OF HIT

- Thrombocytopenia, occurring 4-14 days after starting heparin (or hrs if previously received)⁽¹⁾
 - Fall in platelet count of > 50%⁽²⁾
 - Platelet count 20,000-150,000/ μ L; median 50,000/ μ L⁽²⁾
- Arterial or venous thrombosis occurs in 30-50% of HIT cases⁽³⁾



1. DeBois WH, et al. Perfusion. 2003;18:47-53.
2. Van Cott DM, Laposata M. The Laboratory Test Handbook. 2001:327-358.
3. Lee D, Warkentin TE. Available at: www.tigc.org/eguidelines/hit04.htm. Accessed August 12, 2004.

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

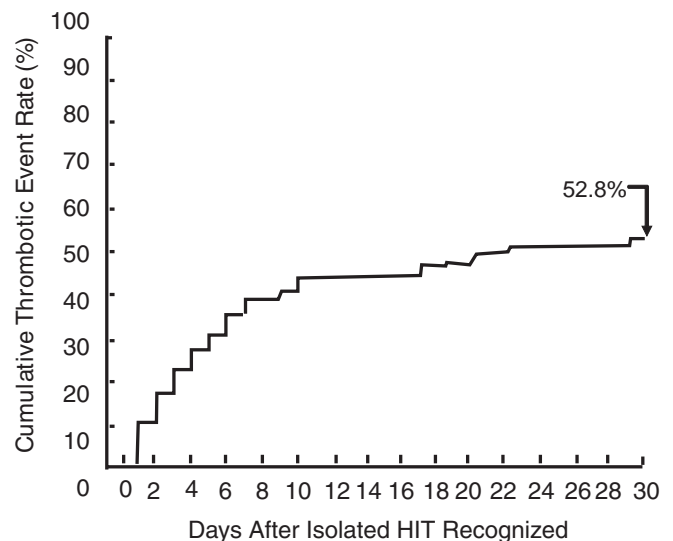
1. Greinacher A, et al. *Blood*. 2000;96:846-851.
2. Lewis BE, et al. *Circulation*. 2001;103:1838-1843.

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



Used with permission from Warkentin TE, Kelton JG. *Am J Med* 1996;101:502-507.

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⁾

1. DeBois WH, et al. *Perfusion* 2003;18:47-53.
2. Warkentin TE. *Br J Haematol* 2003;121:535-555.
3. Chong BH. *J Thromb Haemost* 2003;1:1471-1478.

CLINICAL CASE PRESENTATION

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

Could HIT have been avoided in this patient?

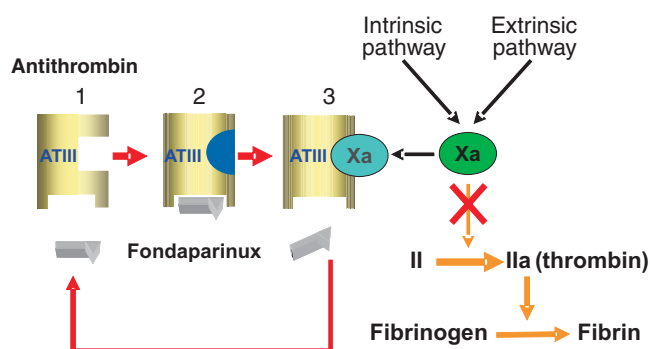
Patient was correctly identified to be at high risk for DVT/PE because of:

- prior history of DVT
- age
- 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



ATIII = antithrombin III.

Adapted with permission from Turpie AGG, et al. *N Engl J Med* 2001;344:619-625.

FONDAPARINUX: FIRST IN A NEW CLASS OF SYNTHETIC INHIBITORS OF FACTOR XA

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

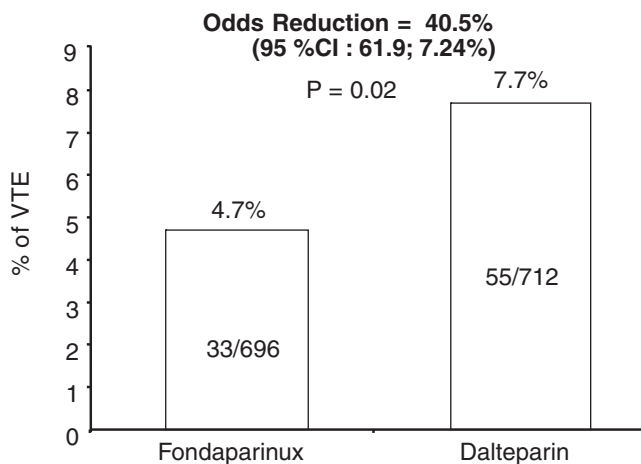
- Treatment of acute PE in conjunction with warfarin when initial therapy is administered in hospital

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.

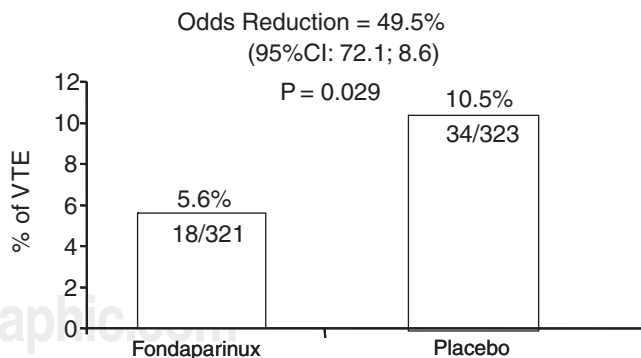
FONDAPARINUX PROPHYLAXIS IN ABDOMINAL CANCER SURGERY PATIENTS



All VTE up to Day 10.

Agnelli D, Berqvist D, Cohen A, et al. *Blood*. 2003;102:abstract 40.

FONDAPARINUX PROPHYLAXIS IN ACUTELY ILL MEDICAL PATIENTS: PRIMARY EFFICACY OUTCOME VTE UP TO DAY 15



Cohen AT, Davidson BL, Gallus AS, et al. *Blood*. 2003;102:abstract 42.

FONDAPARINUX PROPHYLAXIS: DOSAGE 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-Synthelabo 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 mechanisms⁽¹⁾
- POI: uncomplicated ileus following surgery, resolving spontaneously within 2-3 days⁽¹⁾; primary ileus that is a response to surgical trauma, often considered inevitable⁽²⁾
- Paralytic POI: form of POI lasting >3 days after surgery⁽¹⁾

1. Livingston EH, Passaro EP Jr. *Dig Dis Sci* 1990;35:121-132.
2. Luckey A, et al. *Arch Surg* 2003;138:206-214.

MANIFESTATIONS OF POI

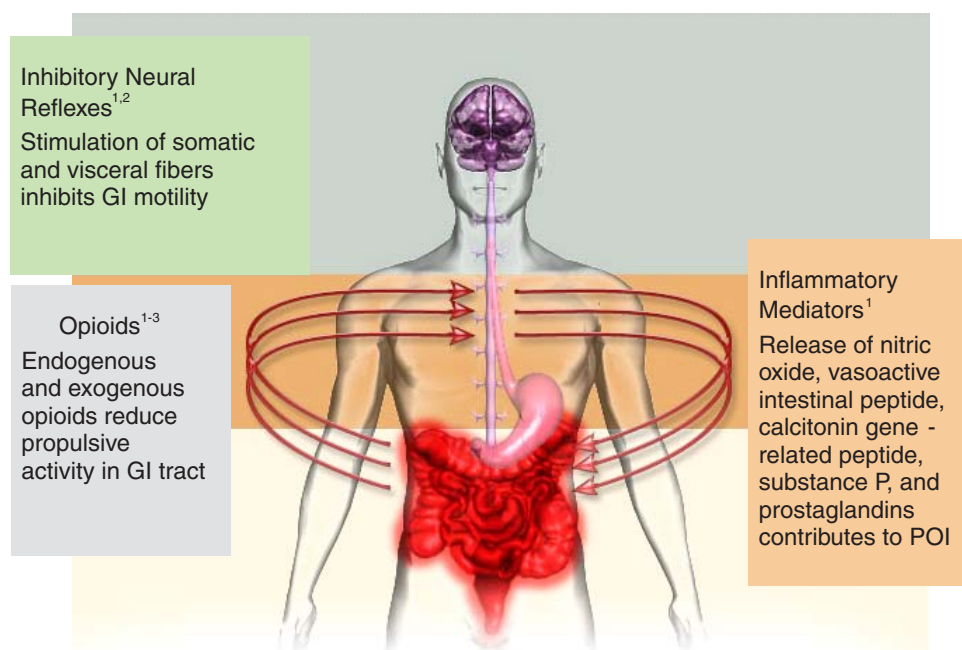
- Abdominal distension^(1,2)
- Cramping^(1,2)

- Delayed passage of flatus and defecation^(1,2)
- Pain and discomfort^(1,2)
- Nausea and vomiting⁽¹⁾
- Pulmonary morbidity^(2,3)
- Delayed nourishment, causing:
 - *Hypoalbuminemia*
 - *Compromised wound healing*
 - *Reduced immune function*
- Increased length of stay/increased costs



Image used with permission from Gastrointestinal Learning File®, produced by the American College of Radiology, Virginia, © 1998.

1. Bungard TJ, et al *Pharmacotherapy*. 1999;19:416-423.
2. Kehlet H, et al. *Am J Surg*. 2001;182(Suppl):3S-10S.
3. Behm B, Stollman N. *Clin Gastroenterol Hepatol*. 2003;1:71-80.

POI: PATHOGENESIS IS MULTIFACTORIAL

NO = nitric oxide

VIP= vasoactive intestinal peptide

CFRP = calcitonin gene-related peptide

1. Holte K, et al. *Drugs* 2002;62:2603-2615.
2. Behm AJ, et al. *Clin Gastroenterol Hepatol* 2003;1:71-80.
3. Bauer B, et al. *Curr Opin Crit Care* 2002;8:152-157.

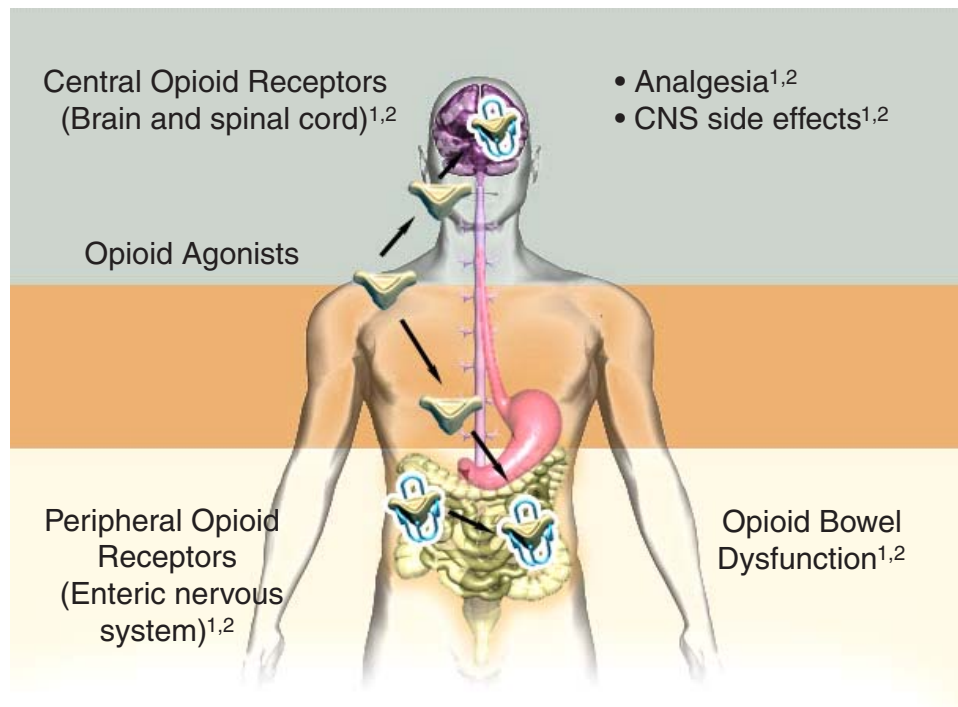
EFFECTS OF EXOGENOUS OPIATES ON THE GI TRACT

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

Adapted from Kurz A, Sessler DI. *Drugs* 2003;63:649-671.

Pappagallo M. *Am J Surg* 2001;182:11S-18S.

CENTRAL VS PERIPHERAL OPIOID EFFECTS



1. Spiller RC. *Curr Opin Gastroenterol* 2003;19:103-105.
2. Holte K, Kehlet H. *Drugs* 2002;62:2603-2615.

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
- 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

1. Kurz A, Sessler DI. *Drugs* 2003;63:649-671.
2. Taguchi A, et al. *N Engl J Med* 2001;345:935-940.

POI CURRENT TREATMENT MODALITIES

- Physical agents^(1,2)
 - Nasogastric tube
 - Early postoperative feeding
 - Gum chewing
- Perioperative care plan(s)^(1,2)
 - Fluid/sodium restriction
 - Multimodal clinical pathways

1. Luckey A, et al. *Arch Surg* 2003;138:206-214.
2. Baig MK, Wexner SD. *Dis Colon Rectum* 2004;47:516-526.

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

Kurz A, Sessler DI. *Drugs* 2003;63:649-671.

METHYLNALTREXONE

- μ -opioid receptor antagonist⁽²⁾
- Does not readily cross the blood-brain barrier⁽¹⁾
- 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 opioid withdrawal⁽²⁾
- Has not been evaluated in the postoperative setting

1. Luckey A, et al. *Arch Surg* 2003;138:206-214.
2. Yuan C-S, et al. *JAMA* 2000;283:367-372.

ALVIMOPAN

- Peripherally acting μ -opioid receptor antagonist⁽¹⁾
- Highly selective for μ -opioid receptor over δ and κ receptors^(1,2)
- Higher potency at μ -opioid receptor than morphine and methylnaltrexone⁽²⁾
- Because of large molecular weight and its polarity, does not readily cross the blood-brain barrier; thus, does not block central opioid receptors^(1,2)
- High therapeutic index⁽²⁾
- Favorable side-effect profile⁽²⁾

1. Azodo IA, et al. *Curr Opin Investigating Drugs* 2002;3:1496-1501.
2. Schmidt WK. *Am J Surg* 2001;182:27S-38S.

TIME TO HOSPITAL DISCHARGE ORDER WRITTEN

Alvimopan 12 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

*Calculated from the Cox proportional hazards model.
Wolff BG, et al. *Ann Surg* 2004;240:728-735.

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%)

Wolff BG, et al. *Ann Surg* 2004;240:728-735.

ECONOMIC CONSIDERATIONS WITH POI

- Most common reason for delayed discharge after abdominal surgery⁽¹⁾
- Healthcare costs in US estimated at \$750 million to \$1 billion per year⁽¹⁾, due to⁽²⁾:
 - NG intubation
 - IV hydration
 - Extra nursing care
 - Longer hospital stay
 - Additional laboratory testing
- Possible cost benefits of alvimopan, with selected patients, due to⁽³⁾:
 - Shortened hospital stay
 - Reduced use of resources
 - Fewer complications
 - Fewer readmissions

1. Luckey A, et al. *Arch Surg* 2003;138:206-214.
2. Livingston EH, Passaro EP Jr. *Dig Dis Sci* 1990;35:121-132.
3. Leslie JB. *Annals Pharmacother* 2005. In press.

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

