

Postoperative ileus: New Considerations



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Definition

- ▶ POI is a transient cessation of coordinated bowel motility after surgical intervention
- ▶ It prevents effective transit of intestinal contents or tolerance of oral intake



Etiology

- ▶ Sympathetic reflexes:
 - ▶ Ultrashort reflexes confined to gut wall
 - ▶ Short reflexes involve prevertebral ganglia efferent stimuli to the bowel
 - ▶ Long reflexes involve afferent stimuli to the cord



Etiology

- ▶ Motilin, substance P, VIP, cytokines
- ▶ Stimulated by local factors and body response to trauma
- ▶ Inhibition diminishes ileus
- ▶ Opioids:
 - ▶ Exogenous and endogenous
 - ▶ Decrease propulsive movement
 - ▶ Act on myenteric plexus at mu receptors
 - ▶ Jejunum > ileum



Endogenous morphine levels after laparoscopic *versus* open colectomy

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- Higher levels of endogenous morphine were significantly related to delayed gastrointestinal recovery and length of hospital stay

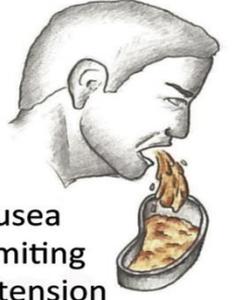




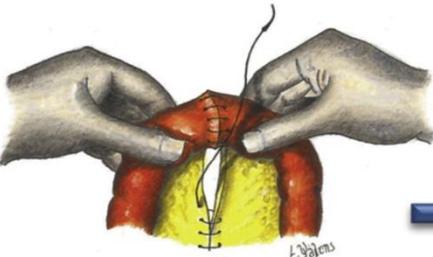
Somatic and visceral trauma

Activation of mast cells, monocytes and macrophages

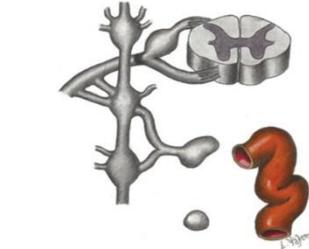
- Histamine
- TNF- α
- Prostanoids
- Interleukins
- Reactive oxygen species



- Nausea
- Vomiting
- Distension
- Absolute constipation



Gut handling and anastomosis



Sympathetic stimulation

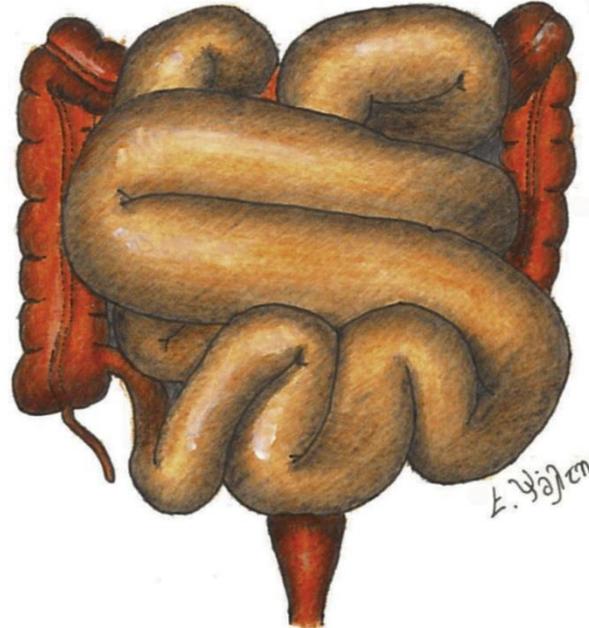
Interference with electromechanical coupling

Intestinal oedema and stretch \rightarrow STAT-3 activation and \downarrow MLC phosphorylation

Activation of opioid receptors; decreased intestinal motility

Changes in gut peptides: motilin, VIP, substance P

Postoperative ileus



Fluid overload



Opioid analgesia



Risk factors

Risk factors for postoperative ileus.

Risk factor	Possible mechanisms
Increasing age [22,24]. Male gender [17].	Reduced overall capacity for the body to recover from surgical insult [24]. Increased inflammatory response to surgery [19]. Increased pain threshold in males [16], resulting in higher catecholamine release [20].
Low preoperative albumin [24]. Acute and chronic opioid use [15,22]. Previous abdominal surgery [22]. Pre-existing airways/peripheral vascular disease [17]. Long duration of surgery [15,17]. Emergency surgery [16,19] Blood loss and need for transfusion [15,17,22,24]. Procedures requiring stomas [19].	Increased oedema and stretch of gut μ -opioid receptor stimulation ameliorates peristalsis [18,23]. Increased need for adhesiolysis, increased bowel handling Reduced physiological reserve Increased bowel handling [21] and opiate use Increased inflammatory and catecholamine response; secondary causes of POI Increased crystalloid administration resulting in oedema Oedema in abdominal wall muscle and cut bowel



Prevention

- ▶ General anesthesia: no effect
- ▶ Regional anesthesia: no effect
- ▶ Epidural:
 - ▶ Block afferent and efferent inhibitory reflexes
 - ▶ Thoracic vs. lumbar
 - ▶ Bupivacain vs. opioids
- ▶ Routine NG
 - ▶ Increases morbidity
 - ▶ Doesn't diminish duration of ileus
 - ▶ In treatment of established ileus



Prevention

- ▶ Mobilization:
 - ▶ Not demonstrated to diminish duration of postoperative ileus
- ▶ Early feeding:
 - ▶ Most of recent studies showed significant decrease of postoperative ileus
- ▶ Laparoscopic surgery:
 - ▶ Less stress, less endo morphine, smaller incision
 - ▶ Minimal improvement over open if early feeding in both



Salt and water overload

- ▶ Surgery causes an increase in ADH, cortisol and aldosterone leading to salt and water retention
- ▶ Liberal perioperative fluid  2–3 kg wt gain, with redistribution of fluid to the interstitial space
- ▶ Oedema can also increase the risk of POI and anastomotic leak
- ▶ The Na⁺/H⁺ ion exchange protein (NHE) is activated by oedema-induced mechanical stretch.
- ▶ NHE reduces contractility, providing a clue to the mechanism behind the inhibition of peristalsis resulting from oedema-induced mechanical stretch



Alvimopan

- ▶ μ -opioid receptors are the primary mediators of opioid analgesic effects in the central nervous system, and also the origin of gastrointestinal side effects
 - ▶ Alvimopan is a peripherally acting μ -opioid receptor antagonist, does not cross the BBB
 - ▶ A meta-analysis alvimopan vs. placebo on POI after major abdominal surgery
 - ▶ alvimopan accelerated recovery of GIT by 1.3 days Hazard Ratio (HR) 1.16 to 1.45 d, $P < 0.00001$
- E.K. Tan, et al. *Aliment Pharmacol Ther*, 25 (2007)
- ▶ Postoperative analgesic effects were not diminished



Intervention	Mechanism	Benefit	
Salt and fluid overload	↓ gut oedema and stretch	++	POI
Carbohydrate loading	↓ insulin resistance	±	
Routine nasogastric tubes	Prophylactic drainage of stomach	–	
Intravenous lidocaine	Anti-inflammatory; opioid-sparing	+	
Coffee	Stimulatory effect	+	
Chewing gum	Stimulatory effect	+	
NSAIDs	Opioid sparing; anti-inflammatory	++	
Early enteral nutrition	Anabolic; ↓ insulin resistance; stimulatory	++	
Laparoscopic surgery	↓ tissue trauma; ↓ bowel handling; ↓ inflammatory reaction	++	
Alvimopan	μ-opioid receptor antagonist	++	
Mid-thoracic epidural anaesthesia	↓ inflammatory response ↓ sympathetic stimulation ↓ opioid requirement	++	
Early mobilisation	? anabolic effect	+ / ±	
Nicotine	Colonic prokinetic	+	
Daikenchuto	Anti-inflammatory on acetylcholine receptors	+	
Magnesium sulphate	Anaesthetic effect	+	
Prokinetics	Prokinetic effect	±	



Novel therapeutic strategies

- ▶ Neural blockade with local anaesthetic or antagonists
- ▶ Suppression of the inflammatory cascade
 - ▶ systemic administration of corticosteroids
 - ▶ focused approach whereby specific pathways in the response to the surgical insult may be targeted



Novel therapeutic strategies

- ▶ Manipulation of gastrointestinal neuropeptides
 - ▶ Octreotide inhibits the release of many GIT hormones via direct action on neurons in the ENS
 - ▶ Octreotide, in a canine model, accelerated postoperative GIT transit at low doses
 - ▶ In healthy human volunteers Octreotide accelerated gastric emptying but delayed mouth-to-caecum transit time



Novel therapeutic strategies

- ▶ A more generalized approach to the manipulation of gastrointestinal neuropeptides in the postoperative period may be achievable by gum chewing.
- ▶ It was initially postulated that this 'sham feeding' would stimulate the cephalic phase of digestion and produce a neurohormonal milieu conducive to gut recovery



Novel therapeutic strategies

- ▶ Oral water-soluble hyperosmotic contrast media, such as gastrografin, have been shown to be of therapeutic benefit by drawing fluid out of the bowel wall into the gut lumen, thereby reducing dysfunction and promoting peristalsis



Conclusions

- ▶ The pathophysiological basis of an ileus is multifactorial and key contributing factors include generation of an inflammatory response, administration of opioids, autonomic dysfunction, disturbances in gastrointestinal hormone activity and electrolyte fluctuations.
- ▶ Novel therapeutic strategies should target individual pathways in the pathogenesis of ileus, such as neural blockade, suppression of inflammation, mechanical reduction of oedema and gut neuropeptide manipulation

