Pathogenesis and clinical and economic consequences of postoperative ileus

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Abstract: Postoperative ileus (POI) occurs frequently in patients undergoing major abdominal surgery; and only recently has there been renewed interest in understanding the pathogenesis, etiology, clinical manifestations, and clinical and economic consequences related to POI. This interest has been spurred by the potential access to novel pharmaceutical options for the management of POI. POI has a complex and multimodal pathophysiology including neurogenic, inflammatory, hormonal, and pharmacologic components. The clinical manifestations are clinically obvious and include abdominal distention, pain, nausea, vomiting, and inability to pass stools or tolerate a solid diet. Prolonged ileus has been defined as persistence of these symptoms for more than 4 days after major abdominal surgery; however the goal should be to reduce the incidence of these symptoms immediately after surgery. Clearly, the magnitude of the surgical stress and usage of opioid analgesia are the predominant causes of POI. The unappreciated sequelae of POI include increased rates in adverse surgical wound healing, reduced ambulation, atelectasis, pneumonia, urinary infections, and deep vein thrombosis. The secondary impact of these complications includes increased hospital length of stay, resource use, and healthcare costs. POI is common and the impact is underestimated. The addition of alvimopan as the first in class µ-opioid inhibitor has demonstrated consistent benefit in reducing the incidence and impact of POI with reductions in length of hospital stay. POI is a common, and underappreciated complication of major abdominal surgery, and clinicians should be aware of the clinical care options, including novel pharmaceutical agents, that can successfully reduce the incidence of this postoperative complication.

Keywords: alvimopan, postoperative ileus, abdominal surgery

Introduction

Postoperative ileus (POI) is perceived as an unavoidable outcome of major abdominal surgery, primarily due to poorly understood multifactorial pathophysiology. POI is multifactorial in origin and causative factors include neurogenic, inflammatory, hormonal and pharmacologic influences. The neurogenic component relates to the pain induced neural reflexes which in turn result in sympathetic hyperactivity and inhibition of gastrointestinal (GI) motility. Surgical manipulation contributes further by activating a number of inflammatory cascades, primarily via the arachidonic acid cascade. These mediators cause the release of endogenous opioid peptides which further exacerbate the effects of exogenous opioid analgesics (administered for analgesia) on inhibition of bowel function. The hormonal influence on ileus is primarily mediated via corticotropin-releasing hormone as a response to the tissue trauma. POI may also occur following minimally invasive surgical procedures, despite obvious reductions in
surgical trauma and manipulation of the bowel, possibly due
to the effects of opioid analgesics mediated by stimulation of
GI opioid receptors by exogenous opioids. The opioid nega-
tive effect on GI motility is believed to occur due to stimula-
tion of µ-opioid receptors in the bowel, leading to inertia in
the gut. Relief of POI-related pain is a two edged sword
as the surgeon balances adequate analgesia with additional
impairment of GI motility. However the recent availability of
alvimopan, a first in class oral µ-opioid receptor antagonist,
offers the potential of effective prophylaxis against postop-
erative ileus. POI is not life-threatening, but patients with
POI typically experience substantial discomfort.

Ileus after abdominal surgery can last a long time despite
the use of what is referred to as a fast-track protocol, with
early ambulation and gradual resumption of oral intake of
liquids followed by solid food to accelerate a return to normal
GI function. In 149 patients undergoing major abdominal
surgery who were encouraged to ambulate and take oral liq-
uids on the first postoperative day and eat solid food on the
second postoperative day, more than 4 days elapsed before GI
function returned to normal in half of the patients and 25% of
patients had not regained normal GI function after more than
6 days had elapsed. Opioid analgesic use for postoperative
pain has been shown to correlate with the time to return of
normal bowel function after surgery.

Consequences
Although not life-threatening, POI can prolong postopera-
tive recovery, increase hospital length of stay and healthcare
resource utilization and costs. The resultant abdominal
distention increases the risk of hernia formation and wound
dehiscence, while nausea and vomiting impacts resumption of
enteral nutrition and increases the risk for malnutrition and
impaired wound healing. The need for nasogastric decom-
pression and prolonged venous access inhibit ambulation
which may increase rates of pulmonary complications and
thromboembolus. The morbidities associated with POI and
the added care required places greater economic burdens
on the healthcare system. The prolonged hospitalization
associated with POI is an important issue at hospitals with
a limited number of beds and high demand for inpatient
services. Efforts to minimize POI and hospital lengths of
stay without increasing the risk of post-discharge readmis-
sion have the potential to improve the financial bottom line
for hospitals, private and governmental health insurers, and
society at large. Approximately 161,000 Medicare recipients
undergo major intestinal or rectal resection each year which
consumes an estimated 1.8 million hospital days at a cost of
$1.75 billion. Safely shortening this length of stay would
produce significant dividends.

Role of enhanced recovery programs
A multi-modal approach has been developed to improve post-
operative morbidity, including POI, in surgical patients. Patient
education is an important component of fast-track protocols
to accelerate recovery of normal GI function and should include
an understanding of how important attempting early ambulation and
early enteral nutrition is to the care plan. They should also understand the components of
effective pain with both narcotic and non-steroidal combina-
tions of oral medications. The newly available peripherally
selective µ-opioid receptor antagonist alvimopan offers an
additional adjunct to the minimization of POI rates.

Potential role of alvimopan
A recent pooled analysis of 3 of the prospective, random-
ized and blinded alvimopan trials confirmed that a 12 mg
dose provided optimal reduction in GI morbidity and return
of GI function. These benefits are clinically relevant and
important to clinicians when arranging discharge plans. An
interesting additional benefit of alvimopan was a significant
decrease in the incidence of POI as a serious adverse event
coupled with a reduction in the proportion of patients who
had prolonged hospital stay or readmission. These benefits
translated into a 50% reduction in the proportion of patients
defined as having prolonged hospital stay.

Alvimopan has been generally well tolerated in the
available trials without producing a negative impact on narc-
ocic analgesic effects as demonstrated by pain scores. These
trials all included a program of early oral nutrition and ambu-
lation and therefore the reduction in time to discharge order
written compared to placebo confirmed the additional benefit
of alvimopan even in an enhanced recovery program.

Conclusion
The clinical and economic consequences of POI are substantial.
Ensuring that patients undergoing major abdominal surgery
understand the preoperative and postoperative care regimen
can minimize these consequences.

Disclosure
The author declares no conflicts of interest.

References
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