The American Journal of Surgery (2016) 212, 851-856

The American Journal of Surgery®

Clinical Science

Is there value in alvimopan in minimally invasive colorectal surgery?

Deborah S. Keller, M.S., M.D.[a,b,*], Juan-Ramon Flores-Gonzalez, M.D.[a], Sergio Ibarra, M.D.[a], Ali Mahmood, M.D., F.A.C.S., F.A.S.C.R.S.[a,b,c], Eric M. Haas, M.D., F.A.C.S., F.A.S.C.R.S.[a,b,c]

[a]Colorectal Surgical Associates, Houston, TX, USA; [b]Department of Surgery, Houston Methodist Hospital, 7900 Fannin, Suite 2700, Houston, TX 77054, USA; [c]Minimally Invasive Colon and Rectal Surgery, The University of Texas Medical School at Houston, Houston, TX, USA

KEYWORDS:
Laparoscopic colorectal surgery;
Enhanced recovery after surgery;
Postoperative ileus;
Health care outcomes;
Alvimopan

Abstract

BACKGROUND: Alvimopan's goal is to minimize postoperative ileus and optimize outcomes; however, evidence in laparoscopic surgery is lacking. Our goal was to evaluate the benefit of alvimopan in laparoscopic colorectal surgery with an enhanced recovery pathway (ERP).

METHODS: Laparoscopic colorectal cases were stratified into alvimopan and control cohorts, then case-matched for comparability. All followed an identical ERP. The main outcomes were length of stay, complications, readmissions, and costs in the alvimopan and control groups.

RESULTS: About 321 patients were analyzed in each cohort. Operative times were comparable ($P = .08$). Postoperatively, complication rates were similar ($P = .29$), with no difference in ileus ($P = 1.00$). The length of stay (3.69 vs 3.49 days; $P = .16$), readmission (2.8% vs 3.7%; $P = .66$) and reoperation rates (2.2% vs 1.6%; $P = .77$) were comparable for alvimopan and controls, respectively. Total costs were similar ($14,932.47 alvimopan vs $14,846.56 controls; $P = .90$), but the additional costs in the alvimopan group could translate to savings of $27,577 in the cohort.

CONCLUSIONS: Alvimopan added no benefit in patient outcomes in laparoscopic colorectal surgery with an ERP. These results could drive a change in current practice. Controlled studies are warranted to define the cost and/or benefit in clinical practice.

Postoperative ileus (POI) is a frequent complication in patients undergoing major abdominal surgery, with major clinical and economic impacts on the health care system.[1] The etiology is multifactorial, with factors including disruption of the sympathetic and parasympathetic pathways to the gastrointestinal tract, inflammatory changes mediated over multiple pathways, and use of opioids for postoperative pain management.[2] Of an estimated 22 million inpatient surgeries performed annually in the US, an estimated 2.7 million are complicated by POI.[3] In colectomy patients specifically, up to 25% suffer POI.[4] Postoperative ileus is a major driver of delayed hospital discharge, increased length of stay (LOS), and the resulting increased health care utilization.[5,6] The annual economic

The authors declare no conflicts of interest.

Poster Presentation P1222 The American Society of Colon and Rectal Surgeons Annual Conference, May 31, 2015 to June 3, 2015, Boston, MA, USA.

The authors received no financial support, grants, or funding for this study.

* Corresponding author: Tel.: (713) 790-0600; fax: (713) 790-0616.
E-mail address: debby_keller@hotmail.com

Manuscript received May 15, 2015; revised manuscript February 15, 2016

0002-9610/$ - see front matter © 2016 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.amjsurg.2016.02.016

impact of POI has been estimated at $750 million in the United States.[7] Numerous interventions to prevent POI and reduce the subsequent LOS have been implemented in colorectal surgery, including multimodal enhanced recovery pathways (ERPs) that stress early feeding, ambulation, avoidance of nasogastric tube, omission of mechanical bowel prep, gum chewing, optimized fluid management, and opioid sparing analgesia.[8–18] Despite use of enhanced recovery programs and laparoscopic technique, POI remains a significant factor affecting LOS.[19]

One tool used to combat POI is alvimopan. Alvimopan (Entereg; Adolor and GlaxoSmithKline, Exton, PA, USA) is a selective mu opioid receptor antagonist that blocks the effects of opioids on the intestine without interfering with their centrally mediated analgesic effect.[20] In May 2008, the Food and Drug Administration approved alvimopan for accelerating upper and lower gastrointestinal tract recovery after partial colon or small bowel resection with primary anastomosis.[21] High-level evidence supports alvimopan effectively reduces the incidence of POI, time to gastrointestinal recovery, hospital LOS of one full day, and total hospital costs compared with the placebo group in open colorectal surgery.[6,22–28] These studies showed a benefit in open colectomy. The benefit of alvimopan in minimally invasive approaches have not been consistent.[19,29–36] Controlled trials and definitive recommendations for alvimopan in laparoscopic colectomy surgery are lacking. At a cost ranging from $600 to more than $1,000 for the medication course, (depending on the duration of treatment) further study on the effect in laparoscopic colorectal surgery is warranted.[30,37,38]

The goal of this study was to evaluate patient and financial outcomes using alvimopan in laparoscopic colorectal surgery. Our aim was to determine if a benefit exists in postoperative recovery, LOS, and total hospital costs to justify routine use of alvimopan in laparoscopic colorectal surgery with a multimodal opioid-sparing enhanced recovery protocol.

Methods

Review of a prospective departmental database identified elective laparoscopic colorectal cases from 2008 to 2014. Cases were stratified into alvimopan and no alvimopan (control) cohorts. The alvimopan and control groups were matched 1:1 on age, sex, body mass index (BMI), comorbidity (based on American Society of Anesthesiologist score), and surgeon to ensure the cohorts were comparable at baseline. All patients followed an identical ERP except for the use of alvimopan. The ERP elements include no routine nasogastric tubes or drains, pain management with scheduled nonopioids postoperatively and opioids for rescue pain only, early oral analgesia and diet, early ambulation, and defined discharge criteria. No patient-controlled analgesic pumps are routinely used in the ERP. In the alvimopan group, patients were administered 12-mg PO between 1 and 2 hours before surgery, then 6-mg PO twice daily up to 7 days postoperatively or for the duration of their hospital stay. Cases were included if a laparoscopic colorectal resection was performed on an elective basis, via an abdominal approach, and complete medical records were available for analysis. Patients were excluded if emergent cases, less than 18 years of age, stoma closure procedures, explorations without resection, treated outside of the multimodal ERP, or procedures performed through an anorectal approach. To evaluate the impact in the laparoscopic cohort, cases converted to an open approach intraoperatively were excluded from the matching and analysis.

Alvimopan was incorporated into the ERP by all surgeons in November of 2008. Administration was per surgeon preference and availability. All surgeons used the medication for all colorectal diagnoses and procedures, except bowel obstructions. Alvimopan was not administered to patients who had a hypersensitivity to the medication or any components, severe hepatic impairment (Child-Pugh C) or end-stage renal disease. There were also situations in which a preoperative dose could not be administered; for example, medication was unavailable on formulary at one of the major centers until 2013.

Patient demographic, perioperative, and postoperative outcomes were collected. Data fields evaluated included age, sex, BMI, indication for operation, operative procedure, operative time, blood loss, intraoperative complication, postoperative complications, LOS, readmission, reoperation, and mortality rates, and the total, direct, and indirect hospital costs for the episode of care. Cost data were obtained directly from accounting, with direct, indirect, and total costs, as well as the fixed and variable costs for direct and indirect categories were broken out individually. The main outcome measures were the LOS, complications, readmissions, and cost of care in the alvimopan and control groups.

Statistical analyses was performed using descriptive statistics to describe categorical data as percentages or means (±standard deviation), chi-square test for categorical variables, Student t test for continuous variables, or the Mann-Whitney U-test for non-normally distributed data, as appropriate. The level for statistical significance was defined as $\alpha < .05$.

Results

A total of 1,055 laparoscopic colorectal surgery patients were evaluated during the study period. There were 823 patients who met inclusion criteria. From this sample, patients were stratified into the alvimopan and control groups, and matched, 1:1 leaving 321 patients evaluated in each cohort. The patients were well-matched in all demographic parameters. There were no significant differences in age ($P = .41$), sex ($P = .81$), comorbidity by American Society of Anesthesiologist score ($P = .41$), or