Obesity Surgery (2019) 29:394–400
https://doi.org/10.1007/s11695-018-3526-z

ORIGINAL CONTRIBUTIONS

Multimodal Postoperative Pain Control Is Effective and Reduces Opioid Use After Laparoscopic Roux-en-Y Gastric Bypass

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Published online: 13 October 2018

Abstract

Background Opioids have been the mainstay for postoperative pain relief for many decades. Recently, opioid-related adverse events and death have been linked to postoperative dependency. Multimodal approaches to postoperative pain control may be part of the solution to this health care crisis. The safety and effectiveness of multimodal pain control regimens after laparoscopic Roux-en-Y gastric bypass (LRYGB) has not been well studied. The primary aim of our study was to determine if an evidence-based, multimodal pain regimen during hospitalization could decrease the total oral morphine equivalent (TME) use after LRYGB.

Study Design We conducted a retrospective cohort study comparing outcomes prior to the implementation of a multimodal pain protocol (December 2010–December 2012) to those after implementation (April 2013–July 2015). The protocol utilized oral celecoxib and scheduled oral acetaminophen for pain control, with opioids used only as needed for breakthrough pain. Data was extracted from an electronic medical record and an institutionally maintained database of all patients undergoing bariatric surgery at a single center.

Results Compared to controls, the multimodal pain regimen significantly reduced TME used and maximum pain scores with no change in mean pain scores. Multimodal pain protocol patients had a shorter length of stay with no increase in bleeding complications or marginal ulcer rates.

Conclusions An opioid-sparing multimodal pain regimen adequately controls pain while reducing TME use. The regimen appears to be safe and was associated with a reduced length of stay in patients undergoing LRYGB.

Keywords Multimodal pain control · Bariatric surgery · Opioid · Acetaminophen · Celecoxib

This manuscript was presented as a poster at ASMBS Obesity Week 2016

Precis Among patients undergoing laparoscopic Roux-en-Y gastric bypass, an opioid-sparing multimodal pain protocol utilizing scheduled oral acetaminophen and celecoxib reduces oral morphine equivalent use and length of stay without compromising pain control compared to an opioid-based regimen.

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Abbreviations

CI	Confidence interval
HCAHPS	Hospital consumer assessment of healthcare providers and systems
LOS	Length of stay
LRYGB	Laparoscopic Roux-en-Y gastric bypass
TME	Total oral morphine equivalent units
NSAIDS	Non-steroidal anti-inflammatory drugs
PCA	Patient-controlled analgesia
POD	Postoperative day
SD	Standard deviation
Pre-MMPP	Prior to opioid-sparing multimodal pain protocol
MMPP	Opioid-sparing multimodal pain protocol

Introduction

Adequate control of postoperative pain is an important measure of the quality of care. Opioids are commonly used for postoperative pain control [1]. While effective, these medications carry the risk of long-term abuse [2, 3]. Between 4 and 9% of opioid naïve patients remain on opioids 1 year after bariatric surgery [4–6], and rates as high as 14% reported up to 7 years post-surgery [5]. Beyond dependency and abuse, opioids have numerous deleterious effects, including respiratory depression, postoperative ileus, nausea, and vomiting [7, 8]. Nausea and vomiting and their sequelae are the most common causes of emergency department visits [9] and hospital readmissions [10–15] following bariatric surgery. Respiratory depression is also dangerous in the bariatric surgery population due to the high incidence of obstructive sleep apnea [16, 17]. Many of these opioid-related adverse drug events are dose dependent [18]. The high risk to benefit ratio with opioids has led to a search for alternative modalities for the management of postoperative pain [19, 20].

The primary aim of this study was to examine the effect of an opioid-sparing multimodal pain protocol (MMPP) on postoperative opioid requirements and pain compared to historical controls in patients undergoing laparoscopic Roux-en-Y gastric bypass (LRYGB). Our secondary aims were to evaluate the impact of the MMPP on surgical outcomes.

Methods

Study Design

We conducted a retrospective cohort study of patients undergoing LRYGB at a single hospital within an integrated health system between December 2010 and July 2015. In April 2013, we implemented a MMPP for bariatric surgery patients. The patients who had LRYGB between December 2010 and December 2012 were the pre-implementation group (Pre-MMPP) while those undergoing LRYGB between April 2013 and July 2015 were the MMPP group. Patients undergoing surgery in the first 3 months of 2013 were excluded as the MMPP was being piloted and was not reliably implemented. This study was approved by our institutional review board (IRB No. 2015-0356).

Participants

All participants undergoing LRYGB during the study period were eligible for inclusion ($n = 885$). Patients were identified from an institutionally maintained database. Patients were excluded for the following reasons:

1) Glomerular filtration rate less than 60 ml/min
2) Missing data required to calculate TME
3) LRYGB during the unreliable implementation period

Data Collection

Demographics, outcomes, emergency department visits, and readmissions were obtained from the database. Pain scores and both intravenous and oral opioid medication usage were obtained from the electronic medical record (EMR). Data extractors were clinical informatics pharmacists who calculated pain medication use from the EMR based on medication drug class. Identical extraction criteria and procedures were used for both cohorts. A single investigator then converted all opioid doses into an oral morphine equivalent using a publicly available online calculator [21]. Six patients using methadone were excluded, due to the complexity of conversion to TME.

Surgical Procedure

All procedures were done at a single center by one of three bariatric surgeons. Perioperative care pathways were standardized for both groups and pathway adherence was greater than 90% [22].

Six laparoscopic ports (two 12 mm and four 5 mm) were used to perform LRYGB. Prior to incision, approximately 20 ml of local anesthetic (0.25% bupivacaine with 1:200,000 epinephrine) was injected equally between the six port sites. Pneumoperitoneum was created and kept at 15 mmHg for the duration of the procedure. An antecolic, antegastric Roux-en-Y gastric bypass with a 50-cm bilio-pancreatic limb and 150-cm Roux limb was performed. The jejuno-jejunostomy and the gastro-jejunostomy were both created using the linear stapler technique. No buttressing material was used with the stapling. A single permanent seromuscular interrupted suture was used to decrease tension on the junction of the gastrojejunostomy staple line, as well as full thickness absorbable suture was placed at all bridging staple lines.

During the study, we did not have a dedicated anesthesia team. Therefore, CRNAs and anesthesiologists varied throughout the study period. Intraoperative anesthesia care routinely utilized Fentanyl and inhalational agents and was not standardized during the study period. There was no use of regional blocks, totally IV anesthesia delivery or opioid-sparing protocols.

Postoperatively patients were started on a stage 1 gastric bypass diet (less than 8 oz per hour of sugar-free clear liquids) and encouraged to ambulate. Postoperative day 1 (POD1) patients were advanced to a stage 2 diet (high-protein liquid diet with protein goal of 60 g and 48–64 oz of fluid). Patients were discharged when tolerating a diet and oral medications.

Pain Management Protocol

Pre-Implementation (Pre-MMPP)

Prior to initiation of the MMPP, opioids were the foundation for postoperative pain control. No pain medications were

given preoperatively. Either morphine or hydromorphone was administered as needed using patient-controlled analgesia (PCA) in the immediate postoperative period. Basal rates of opioid administration were not utilized unless patients were dissatisfied with escalation of the as-needed dosing. Starting POD1 or when tolerating oral intake, patients were started on oral oxycodone every 6–8 h with additional doses available every 2–4 h as needed for breakthrough pain. PCAs were discontinued once the patients could tolerate this oral regimen.

Post-Implementation (MMPP)

The foundational medications for the MMPP were celecoxib (400 mg) and acetaminophen (975 mg). A single dose of each were given in the post-anesthesia care unit prior to surgery. Patients with GFR < 60 or those who were allergic were not given celecoxib. Patients with liver dysfunction or allergy were not given acetaminophen. Opioid-based PCA was used postoperatively under the same guidelines as the Pre-MMPP group. Patients received a scheduled daily dose of oral celecoxib (400 mg) starting on POD1. Oral acetaminophen (975 mg) was given every 8 h while hospitalized. Oral acetaminophen (650 mg) was available as needed every 4 h for breakthrough pain. Total acetaminophen doses were limited to 4000 mg daily. Oral oxycodone (5–10 mg) was utilized as a secondary option for breakthrough pain in patients dissatisfied with their pain control on the primary regimen.

Statistical Analysis

We conducted a univariate analysis comparing the Pre-MMPP and MMPP groups. Categorical variables were compared using either the Chi-square test or the Fisher's exact test, and continuous variables were compared using two sample *t* tests for normal distributions or the Mann-Whitney *U* test for non-parametric data. Results are reported as frequencies and percentages, and means and standard deviations unless otherwise specified. All analyses were conducted in SAS version 9.4 (SAS Institute Inc., Cary, NC). All tests were two-sided and p values less than 0.05 were considered statistically significant.

Results

During the study period, 885 patients underwent LRYGB at our institution. After applying our exclusion criteria, 629 patients remained and were included in the analysis (Pre-MMMP = 384; MMPP = 245). These groups were statistically similar with the exception of mean length of surgery which was 12 min longer in the Pre-MMPP group (169 vs 157 min; $p = 0.001$). (Table 1).

Mean pain scores were similar in both groups. However, MMPP patients had lower maximum pain scores (7.1 vs. 7.7; $p = 0.001$) and required less TME (163.4 vs. 225.2; $p = 0.006$) than those in the Pre-MMPP group (Table 2).

With the MMPP, patients had a significantly shorter LOS (1.5 days vs. 1.8 days; $p < 0.001$). Despite the use of celecoxib in the MMPP, these patients had no increase in bleeding complications (1.2 vs. 2.3%; $p = 0.38$) or marginal ulcers (1.6 vs. 1.6%; $p = 1.00$) when compared to Pre-MMPP patients. MMPP patients were more likely to have minor complications (14.7% vs. 7.3%; $p = 0.003$) and pulmonary complications (2% vs. 0.3%; $p = 0.036$) and to present to the emergency room (18.4% vs. 11.5%; $p = 0.015$) than the Pre-MMPP cohort (Table 3).

We obtained Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey scores for a subset

Table 1 Patient demographics

Total eligible	Pre-MMPP $n = 481$	MMPP $n = 347$	
Excluded patients	*n = 97*	*n = 102*	
GFR < 60	*n = 49*	*n = 90*	
Unknown pain scores	*n = 48*	*n = 12*	
Unreliable implementation period			*n = 57*
Variable	Pre-MMPP $n = 384$	MMPP $n = 245$	*p* value
Age [mean(SD)]	44.2 (10.9)	44.3 (11.2)	0.866
Gender			0.851
Female	289 (75.3%)	186 (75.9%)	
Male	95 (24.7%)	59 (24.1%)	
BMI at baseline* [mean (SD)]	48.1 (7.7)	47.8 (7.8)	0.691
BMI at surgery [mean (SD)]	45.6 (7.0)	45.5 (6.9)	0.928
Charlson Comorbidity Score [mean (SD)]	0.69 (1.1)	0.75 (0.94)	0.483
Surgery duration [mean (SD)]	169 (50.7)	157.1 (45.0)	0.001

*Baseline is upon entry to our bariatric surgery program. Patients are seen at least 6 months prior to surgery

Table 2 Pain scores

Variable	Pre-MMPP $n = 384$ mean (95% CI)	MMPP $n = 245$ mean (95% CI)	p value
TME (total oral morphine equivalent)	225 (195–256)	163 (135–191)	0.0059
Pain scores (postop inpatient)			
Mean pain score	3.7 (3.6–4.0)	3.7 (3.5–4.0)	0.5967
Max pain score	7.7 (7.5–7.9)	7.1 (6.8–7.4)	0.0011

of 111 patients. There were no significant differences between groups across all HCAHPS questions related to pain management. (Table 4).

Discussion

In June 2016, The American Medical Association dropped pain as "the fifth vital sign". AMA President Andrew Gurman, MD has stated that physicians played a key role in starting the so-called opioid epidemic by overprescribing pain medication, and now must do their part to end it: "We have taken ownership of that, and physicians have taken ownership of being part of the solution." [23] The US Centers for Disease Control and Prevention has defined prescription drug abuse an epidemic [24]. Healthcare problems associated with the opioid epidemic include drug diversion, abuse, and death secondary to overdose [25]. Despite the increasing adoption of MMPPs and enhanced recovery pathways, opioids remain the primary pharmacotherapy for intraoperative and postoperative pain management [26]. Up to 9% of opioid-naïve patients undergoing bariatric surgery continue to use opioids a year after their surgical care is complete [4–6]. While opioids are effective in controlling postoperative pain, they are frequently associated with nausea which can lead to both vomiting and dehydration after bariatric surgery [7, 8]. These symptoms are the most frequent cause for hospital readmission in bariatric surgery patients [10–15].

In 2013, our institution implemented an opioid-sparing MMPP for patients undergoing bariatric surgery. The MMPP included preoperative analgesia which has been shown to be useful to minimize intraoperative central sensitization that may begin with the first incision as well as postoperative hyperalgesia which can increase threshold for control of postoperative pain [27]. Acetaminophen and celecoxib were utilized as the mainstay for pain control since nonsteroidal anti-inflammatory drugs (NSAIDS) may have a synergistic effect when used with acetaminophen to control the inflammatory pain common in patients after surgery [27]. This combination has been shown to result in a reduction in

Table 3 A 30-day surgical outcome

Variable	Pre-MMPP $n = 384$	MMPP $n = 245$	p value
Length of stay	1.8 (1.0)	1.5 (0.71)	< 0.001
ER visit	44 (11.5%)	45 (18.4%)	0.015
Any readmissions	28 (7.3%)	23 (9.4%)	0.348
30-day mortality	0 (0.0%)	1 (0.4%)	0.390
90-day mortality	0 (0.0%)	1 (0.4%)	0.390
Any complications	49 (12.8%)	40 (16.3%)	0.211
Any major complications	21 (5.5%)	6 (2.5%)	0.068
Any minor complications	28 (7.3%)	36 (14.7%)	0.003
Placed on ventilator	2 (0.5%)	2 (0.8%)	0.645
Return to OR	13 (3.4%)	11 (4.5%)	0.485
Bleeding complications	9 (2.3%)	3 (1.2%)	0.384
Leak complications	2 (0.5%)	0	0.522
Pulmonary complications	1 (0.3%)	5 (2.0%)	0.036
Wound complications	1 (0.3%)	3 (1.2%)	0.305
Cardiac complications	3 (0.8%)	1 (0.4%)	1.000
Acute kidney injury	4 (1.0%)	2 (0.8%)	1.000
Admitted to ICU	5 (1.3%)	0	0.162
Marginal ulcer	6 (1.6%)	4 (1.6%)	1.000
Percent excess weight Loss within 6 months (95% CI)	68.6 (66.7–70.4)	70.8 (68.2–73.3)	0.1558

Table 4 HCAHPS responses

Question	Pre-MMPP $n = 13$	MMPP $n = 98$	p value
During this hospital stay, did you need medicine for pain?			1.000
No	0	6 (6%)	
Yes	13 (100%)	91 (93%)	
Unreported	0	1 (1%)	
During this hospital stay, how often was your pain well controlled?			0.7348
Never	0	0	
Sometimes	1 (8%)	4 (4%)	
Usually	4 (31%)	25 (26%)	
Always	8 (62%)	63 (64%)	
Unreported	0	6 (6%)	
During this hospital stay, how often did the hospital staff do everything they could to help you with your pain?			0.1338
Never	0	1 (1%)	
Sometimes	0	3 (3%)	
Usually	4 (31%)	7 (7%)	
Always	9 (69%)	79 (81%)	
Unreported	0	8 (8%)	
Would you recommend this hospital to your friends and family?			0.3658
Never	1 (8%)	2 (2%)	
Sometimes	0	4 (4%)	
Usually	3 (23%)	12 (12%)	
Always	9 (69%)	79 (81%)	
Unreported	0	1 (1%)	
How well your pain was controlled?			0.7208
Very poor	0	1 (1%)	
Poor	0	0	
Fair	1 (8%)	3 (3%)	
Good	3 (23%)	24 (24%)	
Very good	9 (69%)	68 (69%)	
Unreported	0	2 (2%)	

postoperative opioid use [27]. Ziemann-Gimmel et al. examined the impact of intravenous acetaminophen and intravenous ketorolac compared to hydromorphone PCA among patients undergoing LRYGB [28]. They found that patients receiving the non-opioid based regimen had a 74% reduction opioid use after discharge from the recovery room. This study also reported that these patients were less likely to require antiemetic medications compared to those receiving hydromorphone PCA (20.2% vs. 34.8%) [28]. Song et al. added 1 g of intravenous acetaminophen every 6 h for the first 24 h after bariatric surgery, to their prior opioid-based pain regimen [29]. With this addition, they found a 45% reduction in TME among patients undergoing either LRYGB or laparoscopic sleeve gastrectomy. Our MMPP study of oral acetaminophen and oral celecoxib found that mean pain scores were similar to Pre-MMPP patients utilizing opioid-based PCAs yet TME after LRYGB significantly decreased (28%) and also resulted in a significant reduction in maximum pain scores after surgery. Our study is also unique in that we permitted patients to use PCA postoperatively as needed with no basal rate. This permitted for accurate measurement of TME use after surgery while hospitalized. TME use has been rarely reported in association with bariatric surgery. While not significant, all pain-related HCAHPS scores were as good or improved in the MMPP patients.

The impact of MMPPs on LOS has been mixed in previous studies. Song et al. in their study of intravenous acetaminophen found a reduced LOS compared with prior opioid-based regimens [29]. Wang et al. [30] compared bariatric surgery patients receiving intravenous acetaminophen to supplement an opioid-based regimen and found a no change in TME as well as no difference in LOS. There was a highly significant reduction in LOS in our study. We did not collect data on nausea, but the reduced need for narcotics and lower maximum pain scores may be one important factor contributing to the reduced LOS. We made no other significant changes to our

care pathway during the study period, but our understanding of the opportunities presented by enhanced recovery pathways did lead to a programmatic focus on earlier discharge.

NSAIDS are associated with increased risk of bleeding as well as gastroduodenal ulcers. Unlike other NSAIDS, celecoxib does not impair platelets and therefore has a potentially lower risk of causing perioperative bleeding. [27] Another advantage is a long half-life requiring only once daily dosing making it an optimal agent for pain control in postsurgical patients. While not significant, our study found a lower incidence of bleeding in patients on the MMPP with a nearly identical incidence of marginal ulcers.

Despite these benefits, the MMPP was associated with greater rates of minor complications and emergency room visits with no increased risk of cardiovascular events, acute kidney injury, or anastomotic leaks. There was an increased rate of pulmonary complications noted in the MMPP group, though the study was underpowered to detect a difference (total of 6 events), the finding was unexpected given the diminished use of opioids in the MMPP group. Both groups were provided with the same preoperative instruction regarding use of incentive spirometry and early ambulation. There was a statistically significant difference in the operative time in the MMPP group. We attribute this temporal effect reflecting the increasing experience of the surgeons. While this was statistically significant, it is unlikely that a mean 12-min reduction in length of surgery resulted in a clinically significant change in postoperative pain especially given a standard deviation of 50 and 45 min, respectively, between the two groups. Our study has several limitations. A retrospective comparison against historical control is subject to observer bias, unrecognized confounders, and temporal effects, and these could have impacted our LOS and complication results. Other than the primary outcome, the study was underpowered, and adjusted analyses could have controlled for some measured confounders. For the measurement of patient satisfaction were limited in that not every patient is surveyed and the data available to us overrepresented patients receiving the MMPP.

Conclusions

We believe this is the first study to report the effects of an MMPP based on oral acetaminophen and celecoxib in bariatric surgery patients. We found that this regimen provided similar baseline pain control (reflected by mean pain scores) when compared to an opioid-based IV PCA regimen. Analgesia was achieved with significantly better maximal pain scores and significantly lower morphine equivalent use. This regimen appears to be safe with no observed increase in bleeding or marginal ulcer rates, and the reduction in opioid use has the potential to improve postoperative nausea, which may be a factor in earlier discharge.

Since analyzing these results, our current pain management protocol for bariatric surgery patients has evolved significantly. We now utilize a transverse abdominus plane block with 0.25% bupivacaine routinely and dedicated anesthesia team that limits inhalational agents and favors total IV anesthesia with no opioids. Intravenous fluids are limited to < 2500 ml. We have eliminated PCAs from our MMPP and reduced patient's discharge oxycodone prescription dosing by 75%.

Compliance with Ethical Standards

Conflict of Interest Horsley, Vogels, McField, Parker, Dove, Fluck, Gabrielsen, Gionfriddo, and Petrick have no conflicts of interest. Medico has a relevant financial activity outside of the submitted work.

Ethical Approval Statement For this type of study formal consent is not required.

Informed Consent Statement Does not apply.

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