Original Study

Multi-modal pain control regimen for anterior lumbar fusion drastically reduces in-hospital opioid consumption

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Background: The opioid epidemic is at epic proportions currently in the United States. Exposure to opioids for surgery and subsequent postoperative pain management is a known risk factor for opioid dependence. In addition, opioids can have a negative impact on multiple aspects including clinical outcomes, length of hospital stay, and overall cost of care. Thus, the greatest effort to reduce perioperative opioid use is necessary and a multimodal pain control (MMPC) has been gaining popularity. However, its efficacy in spine surgery is not well known. We aimed to evaluate the efficacy of a MMPC protocol in patients undergoing lumbar single-level anterior lumbar interbody fusion (ALIF).

Methods: This is a retrospective comparative study. From a prospective, single-surgeon, surgical database, consecutive patients undergoing single-level ALIF with or without subsequent posterior fusion for degenerative lumbar conditions were identified before and after initiation of the MMPC protocol. The MMPC protocol consisted of a preoperative oral regimen of cyclobenzaprine (10 mg), gabapentin (600 mg), acetaminophen (1 g), and methadone (10 mg). Postoperatively they received a bilateral transverse abdominis plane block with 0.5% Ropivacaine prior to extubation. We compared in-hospital opioid consumption between the MMPC and non-MMPC cohorts as well as baseline demographic, the length of hospital stay, cost, and rate of postoperative ileus. Opioid consumption was calculated and normalized to the morphine milligram equivalents (MMEs).

Results: In total, 68 patients in the MMPC cohort and 39 in the non-MMPC cohort were identified. There was no difference in baseline demographics including sex, body mass index, smoking status, or preoperative opioid use between the two groups. Although there was no difference in the MMEs on the day of surgery (58.5 *vs.* 66.9, P=0.387), cumulative MMEs each day after surgery was significantly lower in the MMPC cohort, with final cumulative MMEs being reduced by 62% (120.2 *vs.* 314.8, P<0.001). There was no difference in postoperative ileus, length of stay, and hospital costs.

Conclusions: The use of a MMPC protocol in patients undergoing single-level ALIF for degenerative conditions reduced opioid consumption starting on the first day after surgery, resulting in a cumulative reduction of 62%.

Keywords: Postoperative pain; multimodal pain control (MMPC); opioid; spine surgery; anterior interbody fusion

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Introduction

The United States is in the midst of an unprecedented opioid epidemic. More than 2 million people are addicted to prescription opioids (1). The rate of deaths involving opioid overdose has increased over 200% since 2000 (2). Recent studies have shown that surgery is a risk factor for developing opioid dependence (3-5). In opioid-naive patients, 3% continued to use opioids for more than 90 days after major elective surgery (3). A greater amount of initial opioid use is associated with greater risks of long-term use, misuse, and overdose (6,7).

Opioids have numerous dose-dependent adverse effects, including nausea, ileus, urinary retention, respiratory depression, hyperalgesia, and delirium, which can impair postoperative recovery. Additionally, opioids are associated with worse clinical outcomes including higher complication rate, longer hospital stay, higher costs, and need for early revision surgery (8-11). Thus, perioperative opioid use should be limited to the lowest effective dose and the shortest duration.

The multimodal pain control (MMPC) approach was developed to decrease perioperative opioid consumption (12). The principle of MMPC is to use multiple agents in a combination of both systemic and regional anesthesia in efforts to reduce overall opioid consumption. MMPC targets several different pathways and mediators involved in nociception to improve analgesic effect, reduce the doses of each agent to minimize the side-effects (12,13). MMPC has been reported to be associated with less postoperative pain and opioid consumption, shorter hospital stay, and increased patient satisfaction in other elective orthopedic procedures (14-16).

In spine surgery, several studies have examined the efficacy of MMPC. Intravenous lidocaine, ketamine, postoperative intramuscular local anesthetic infiltration, and oral pregabalin have been reported to reduce postoperative pain and opioid consumption (17-20). The number of patients undergoing spine surgery is increasing (21) and patients with spine pathology have a high incidence of preoperative opioid use, ranging from 20% to 55% (22,23). Alarmingly, as much as 38% of patients undergoing spine surgery were still on opioids one year after surgery (24). Given these reports, developing a protocol to minimize opioid consumption following elective spine surgery is of paramount importance. Here, we established the perioperative pain management protocol using MMPC approach. The purpose of this study was to evaluate the efficacy of the protocol on patients undergoing single-level anterior lumbar interbody fusions (ALIF).

We present the following article/case in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/jss-20-629).

Methods

Subject

This is a retrospective comparative study. A retrospective review of a prospective, single-surgeon, surgical database was utilized for consistency in surgical technique. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of University of Louisville (#18.1197) and individual consent for this retrospective analysis was waived. Consecutive patients undergoing single-level ALIF with subsequent posterior fixation/fusion for degenerative lumbar conditions were identified before and after initiation of the MMPC protocol.

Sample size calculation

The sample size calculation is based on the parameters α=0.05 (two-sided) and power: 1-β=0.8. With MMPC having a medium effect size of 0.5 on reducing postoperative opioid consumption the sample size was calculated to be 102.

Outcome

Our primary outcome was total, in-hospital opioid consumption, which was calculated and normalized to the morphine milligram equivalents (MMEs). Postoperative opioids were administered based on doctors' pro re nata order and pain severity. Total daily opioid consumption was calculated and converted to the MMEs as follows:

$$\text{MMEs} = \text{total dose (mg)} \times \text{MME conversion factor}$$

MME conversion factor is 0.1 for tramadol, 1 for morphine and hydrocodone, 1.5 for oxycodone, and 4 for hydromorphone. Then, MMEs of used opioids were added.

We compared baseline demographic, surgical data [estimated blood loss (EBL), surgical time, level fused, and primary *vs.* revision], and preoperative opioid use as all of these could affect postoperative pain and opioid use. We defined revision surgery as history of spine surgery involving the same level, such as pseudoarthrosis and

Table 1 Background and surgical characteristics in each group

Parameters	Non-MMPC (n=39)	MMPC (n=68)	P value
Age (years)	51.6±11.6	56.8±10.4	0.026
Male (%)	44	54	0.534
BMI, kg/m^2	31.5±6.4	30.2±5.1	0.283
Current smoker (%)	31	34	0.895
Operative time (minutes)	125±64	78±38	0.071
EBL (mL)	57±35	46±29	0.436
Number of fused levels* (%)			0.578
1	82	87	
2	18	13	
Revision (%)	39	44	0.685
Preop MME	4.3±13.4	7.3±34.5	0.546

*, posterior fusion. MMPC, multi-modal pain control; BMI, body mass index; EBL, estimated blood loss; MME, morphine milligram equivalent.

adjacent segment disease. As well as baseline demographic, the length of hospital stay (LOS), cost, rate of postoperative ileus were assessed.

Surgical procedure

Patients were placed in the supine position. The approach was transperitoneal for L5–S1 and retroperitoneal for the proximal levels. For the transperitoneal approach, a transverse incision was made between the umbilicus and the symphysis pubis. The exposed linea alba was vertically divided using monopolar diathermy. Peritoneum was bluntly perforated, and colon was retracted superiorly and laterally. The retroperitoneum was divided in the middle line, and the iliac arteries and veins are then retracted laterally, with the median sacral vessels double clipped and divided. The anterior disc space dissection is performed with a Kittner to avoid injury to the sympathetic nerves to reduce the risk of retrograde ejaculation.

Retroperitoneal approach was done using a left paramedian incision. The anterior rectus sheath was opened, and the rectus mobilized laterally. A retroperitoneal pocket was created bluntly to place a spinal Thompson retractor and blunt dissection carried out between the iliac vessels and psoas muscles.

Once the disc of interest was exposed, the disc was excised using a knife followed by Cobb elevator and endplate preparation tools. It was then dilated to accommodate a cage. The endplates were cleaned off all disc, and the posterior annulus was exposed. A cage was packed with an allograft and bone graft substitutes or extenders. It was impacted into the disc space with good fit and fixation. Patients were then positioned in the prone position and posterior fusion were performed in standard fashion.

Regimen

The MMPC protocol consisted of a preoperative oral regimen of cyclobenzaprine (10 mg), gabapentin (600 mg), acetaminophen (1 g), and methadone (10 mg). Postoperatively patients received a bilateral transverse abdominis plane (TAP) block with 0.5% Ropivacaine prior to extubation. This regimen is based on the fact that patients undergoing combined procedure typically complain of abdominal pain as well as back pain and spasm postoperatively. Therefore, we included TAP block in addition to standard pain medications such as cyclobenzaprine, gabapentin, and acetaminophen.

Statistical analysis

Difference between groups were analyzed using Fisher exact test for categorical variables or Mann-Whitney U test for continuous variables. All statistical analyses were performed using SPSS Statistics 25 (IBM Corp., Armonk, NY, USA). A statistical significance was defined as P value <0.05.

Results

Patient demographics

In total, 68 patients in the MMPC cohort and 39 in the non-MMPC cohort were identified. There was no difference in baseline demographics including sex, body mass index (BMI), smoking status, or preoperative opioid use between the two groups. The MMPC cohort was older (56.8 *vs.* 51.6 years, P=0.026). There was no difference in surgical data including operative time, EBL, number of fused levels, and rate of revision surgery (*Table 1*).

In-hospital opioid consumption

Although there was no difference in the MMEs on the day

Table 2 Comparison of in-hospital opioid consumption between the two groups

Parameters	Non-MMPC (n=39)	MMPC (n=68)	P value
MME on the day of surgery	66.9±45.5	58.5±51.0	0.387
Cumulative POD 1 MME	153.3±80.7	107.0±79.7	0.006*
Cumulative POD 2 MME	224.1±119.3	111.9±84.5	<0.001*
Cumulative POD 3 MME	263.1±145.2	114.9±92.0	<0.001*
Cumulative POD 4 MME	282.0±157.9	117.8±117.8	<0.001*
Cumulative POD 5 MME	293.1±171.7	118.4±97.8	<0.001*
Cumulative POD 6 MME	305.8±193.3	119.9±100.0	<0.001*
Cumulative POD 7 MME	314.8±212.3	120.2±100.7	<0.001*

*, statistically significant difference. MMPC, multi-modal pain control; MME, morphine milligram equivalent; POD, postoperative day.

of surgery (58.5 *vs.* 66.9, P=0.387), cumulative MMEs each day after surgery was significantly lower in the MMPC cohort, with final cumulative MMEs being reduced by 62% (120.2 *vs.* 314.8, P<0.001) (*Table 2*).

Secondary outcomes

Postoperative ileus was identified more in the non-MMPC cohort (6 patients; 15%) compared to the MMPC cohort (4 patients; 6%) although there was no statistical difference (P=0.102). Similarly, there was no difference in LOS (4.5 days in the non-MMPC; 3.8 days in the MMPC, P=0.246) and index hospital costs ($24,627 in the non-MMPC; $25,755 in the MMPC, P=0.824).

Discussion

MMPC was initially introduced in abdominal surgery and is currently used in orthopedic and spine procedures. Although some studies have shown that MMPC reduced opioid consumption (16,25-27) other studies have not (28). A variety of agents are available for MMPC and have been studied to reduce postoperative opioid consumption. There are numerous reports detailing the efficacy of acetaminophen for postoperative pain management, showing reduced LOS, opioid consumption, and complication rate (29-31). Gabapentin also has been studied regarding its efficacy in the reduction of postoperative pain and opioid consumption (16,32,33). TAP block has been considered an effective analgesia for abdominal surgery (34,35). These studies examined the efficacy of a single modality, with each medication having a significant benefit in reducing postoperative opioid consumption. Since our patients underwent ALIF and subsequent posterior fusion surgery, our regimen included a combination of oral agents and a TAP block. In our cohort and regimen, MMPC significantly decreased in-hospital opioid consumption (62%). In our cohort and regimen, MMPC significantly decreased in-hospital opioid consumption (62%). Soffin *et al.* examined the efficacy of MMPC including pre-incisional TAP block, regularly scheduled non-opioid analgesics (gabapentin, acetaminophen, ketorolac) for ALIF and lateral lumbar interbody fusion (LLIF) (36), which is similar to our study. They showed median MME was 57.5. The MMEs are much lower than those of our patients, which may be due to the difference in procedure. They evaluated patients undergoing ALIF/LLIF without posterior procedures whereas our patients all underwent posterior fusion. Also, their study did not have a control group, and sample size was small (n=32). In our study, we compared opioid consumption between MMPC and non-MMPC (control group) with relatively large size. Our finding provided a concrete evidence in the efficacy of MMPC regimen including TAP block.

There was no significant difference in the LOS in the present study. Meta-analysis of 11 prospective randomized clinical trials examining the efficacy of intramuscular local anesthetic infiltration prior to wound closure has shown that it significantly reduced postoperative opiate requirements, but did not reduce LOS after lumbar surgery (19). Brown *et al.* evaluated local infiltration of liposomal bupivacaine after lumbar fusion surgery and also found no reduction in LOS (28). On the contrary, Gianesello *et al.* reported that perioperative pregabalin administration after major spine surgery reduced LOS with less postoperative opioid consumption (32). It appears that a gastrointestinal complication due to opioids may affect the LOS; postoperative nausea, vomiting, and constipation were significantly less in the pregabalin group in their cohort, resulting in earlier postoperative up-site position, oral intake, and subsequent discharge. In our cohort, gastrointestinal complication was more common in the non-MMPC group, but the difference was not statistically significant, which may be related to the equivalent LOS in our study. Further evaluation with a larger sample size might be necessary to truly differentiate this as we feel clinically we have noticed a reduced number of these complications since we initiated the protocol.

Debate exists regarding the impact of MMPC on the hospital cost. Surgery-related materials such as implant and bone graft choices may influence cost more than MMPC (37). However, several studies reported that MMPC has a positive impact on the cost. Carr *et al.* compared the LOS and cost in major elective spine surgeries between traditional perioperative care and enhanced perioperative care including MMPC (38). They found that enhanced perioperative care decreased LOS and cost in major elective spine surgeries. A large part of difference in the cost was attributed to shorter hospital and intensive care unit stay. Similarly, in pediatric scoliosis surgery, preoperative patient education and MMPC have led to a decrease in LOS of 1.3 to 2 days and a 22% decrease in hospital cost (39,40). Another study revealed that postoperative intravenous acetaminophen is associated with shorter LOS, lower doses of opioids, and lower cost (31). In the present study, there was no difference in the cost, which may be due to less opioid-related complications in our cohort.

There are several limitations in this study. First, this is a retrospective study with a relatively small sample size. This is because we limited inclusion to patients undergoing single-level ALIF performed by a single surgeon. This type of study also limits the generalizability of these results. Conversely, a single-surgeon study can minimize the impact of difference in procedure and surgical skill. Second, some bias may be present. MMPC group was not blinded to surgeons, which might lead to less narcotics prescription in the group. Thirdly, we evaluated not chronic opioid dependence after discharge but in-hospital opioid consumption. Further research is necessary to see the downstream effects. Nonetheless, our findings are valuable as the amount of in-hospital opioid may have strong impact on the transition to chronic opioid use, especially in opioid naïve patients (6,7). Lastly, we only evaluated patients undergoing single-level ALIF. There are numerous spine surgery procedures and majority is posterior only approach. TAP block is not applicable for posterior only approach. Modification of protocol is necessary for posterior only procedures.

Conclusions

We examined the effect of an MMPC regimen in patients undergoing single-level ALIF for degenerative conditions. Our regimen significantly reduced in-hospital opioid consumption. An MMPC may reduce risk of opioid dependence as a greater amount of initial opioid exposure is associated with greater risks of long-term use.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/jss-20-629

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of Norton Healthcare (#18.1197) and individual consent for this retrospective analysis was waived.

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