Transition to Nonopioid Analgesia Does Not Impair Pain Control After Major Aesthetic Plastic Surgery

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Abstract

Background: Multimodal analgesic protocols are increasingly favored over traditional opioid regimens due to decreased adverse side effects and reduced opioid consumption. Concomitant use of selective cyclooxygenase (COX)-2 inhibitor celecoxib and anticonvulsant gabapentin have been proposed to adequately control acute postoperative pain.

Objectives: To determine efficacy of postoperative pain control using nonopioid pain regimen vs traditional opioids for all aesthetic plastic surgery procedures.

Methods: A retrospective chart review was performed on 462 consecutive outpatient plastic surgery procedures by a single surgeon between November 2015 and July 2017. Procedures in the historical control group (n = 275) received traditional postoperative narcotic, hydrocodone-acetaminophen. Patients in the more recent nonopioid study group (n = 187) received a pre-, peri-, and postoperative regimen of celecoxib and gabapentin.

Results: Similar demographic characteristics between the control and study groups were observed: mean age, 39.7 vs 39.5 years; BMI, 24.6 vs 24.4 kg/m^2; and ratio of female patients 92.7% vs 92.4%. A significant reduction in rescue analgesia (meperidine 44.6% vs 14.9%, $P < 0.001$) and antiemetic use (ondansetron 24.2% vs 16.3%, $P < 0.05$; promethazine 17.0% vs 4.7%, $P < 0.001$) in postanesthesia recovery unit (PACU) was noted in the nonopioid group compared to the control. The average stay in PACU also decreased in the study group (82 ± 39 min vs 70 ± 22 min, $P < 0.001$). Both groups reported low numbers of adverse events and need for additional pain prescriptions. These findings were reproducible in the breast subgroup.

Conclusions: This nonopioid regimen is as effective as traditional opioid use for acute postoperative pain control and decreased recovery time for outpatient aesthetic plastic breast surgeries.

Level of Evidence: 3

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The use of multimodal analgesia, defined as the administration of at least two drugs that act by different mechanisms, has been increasingly recommended in the management of acute postsurgical pain to improve pain control as well as decrease adverse effects associated with standard opioid treatment.[1] Recent practice guidelines addressing acute pain management in the perioperative setting recommend the scheduled use of nonsteroidal anti-inflammatory drugs (NSAIDs), selective cyclooxygenase (COX)-2 NSAIDs, or acetaminophen unless contraindicated.[2] The COX-2 inhibitors

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are comparable to nonselective NSAIDs, but are associated with less adverse gastrointestinal side effects and risks of perioperative bleeding.[3,4] Specific COX-2 inhibitors, such as valdecoxib and rofecoxib, were linked with increased risk of myocardial infarction and hypertension resulting in their withdrawal from the market, but use of celecoxib did not demonstrate an increased cardiovascular risk compared to other nonselective and selective NSAIDs.[5] Gabapentin, an anticonvulsant often used to treat neuropathic pain, has also been considered an adjunct for improving analgesia and reducing opioid consumption.[6] As such, both COX-2 inhibitors such as celecoxib and gabapentinoids such as gabapentin and pregabalin have been studied in regard to postoperative analgesia either alone or concomitantly. Celecoxib and gabapentin have been shown to independently improve postoperative pain management and significantly reduce opioid consumption.[6-8] Preemptive oral celecoxib decreased acute postoperative pain in patients undergoing facelifts[9] while perioperative pregabalin was shown to have similar results in septoplasty.[10] Their combined use in multimodal pain management has been shown effective in some laparoscopic[8,11] procedures as well as in cosmetic and reconstructive breast surgery.[12,13] However, there is a paucity of literature regarding the efficacy of postoperative celecoxib and gabapentin for all plastic surgery procedures.

Based on concerns of adverse side effects and inadequate postoperative pain control in patient using opioids, the senior author (C.L.M) adopted a nonopioid multimodal pain regimen consisting of celecoxib and gabapentin for all surgical patients in his cosmetic plastic surgery practice starting in October 2016. The purpose of this study is to evaluate patient outcomes between those following the new nonopioid protocol vs those prescribed traditional postoperative narcotics.

METHODS

Patients

A retrospective chart review was performed in accordance with the Declaration of Helsinki and its revisions on patients who underwent any plastic surgery procedure with the senior author (C.L.M.) between November 2015 and July 2017. Informed consent was given by all patients involved in this study. Inclusion criteria were all consecutive patients who underwent a surgical procedure under general anesthesia during the study timeline, received postoperative pain medications, and had postoperative follow up. Exclusion criteria consisted of patients who were not prescribed postprocedure pain medications, those with allergy to opioids, celecoxib, gabapentin, or local anesthetics, a history of alcoholism, or drug addiction.

Patients undergoing surgery between November 2015 to September 2016 were prescribed an opioid analgesic for postoperative pain control (opioid control group) while patients undergoing surgery between October 2016 to July 2017 received the new protocol of pre-, peri-, and postoperative celecoxib and gabapentin for pain management (nonopioid study group). The latter patients were provided explicit instruction to take 400 mg Celecoxib and 600 mg Gabapentin the day before surgery and four hours prior to surgery, followed by 200 mg Celecoxib twice daily and 300 mg Gabapentin three times daily for one week. Additional over the counter acetaminophen was used for breakthrough analgesia postoperatively. Both groups of patients underwent general anesthesia with adjunct use of opioids, meperidine, or hydromorphone, intraoperatively. All patients undergoing breast surgery received a postoperative muscle relaxant, cyclobenzaprine or methocarbamol. Antiemetics were provided in the postanesthesia care unit as needed for both groups.

Age, medical history including tobacco use, body mass index (BMI), operation type, procedure length, time spent in postanesthesia recovery unit (PACU) before discharge, use of additional opioid or antiemetics in PACU were recorded for both cohorts. Primary outcomes of interest were PACU time, total opioid use, and the need for additional (rescue) analgesics. Secondary outcomes included pain referral, nausea, or vomiting requiring antiemetics, surgical as well as pharmacological complications of our medications.

Statistics

Descriptive statistics and profiles were calculated and reviewed for all patients included in this study. Univariate analysis compared the two cohorts for demographics, surgical details, and their perioperative medicinal management. The statistical level of significance was set at 5% ($P < 0.05$) for all analyses using the independent sample *t* test for continuous and the chi-square test for categorical variables. Analyses were conducted using SPSS version 25.0 (IBM Corp., Armonk, NY).

RESULTS

Initially, a total of 538 plastic surgery procedures were identified within the study period. Due to the aforementioned exclusion criteria, 76 cases were removed, leaving 462 cases to be analyzed. Of those, 275 (59.5%) were performed with postoperative opioids and formed the control group. The other 187 cases (40.5%) in the study group followed the newer nonopioid protocol. Average follow up for all patients was 112 days (range, 14-295 days).

With regards to demographic characteristics, there were no significant discrepancies between the two cohorts. The control group consisted of 255 females (92.7%) and 20 males aged 18 to 75 years (average, 39.7 years) with a

BMI ranging from 17.0 to 37.0 kg/m^2 (average, 24.6 kg/m^2). Similarly, the nonopioid study group consisted of 171 females (92.4%) and 16 males aged 18 to 71 years (average, 39.5 years) with a BMI ranging from 17.2 to 44.1 kg/m^2 (average, 24.4 kg/m^2). The patients presented with similar frequencies of comorbidities such as hypertension, diabetes mellitus, or hyperlipidemia. The majority of patients reported prior childbirth (65.5% vs 75.1%, $P = 0.034$) and certain nondrug allergies (25.7% vs 26.6%, $P = 0.836$). The ethnic distribution between both groups was statistically similar. These findings are shown in Table 1.

From a surgical standpoint, the patients in both groups underwent a similar mix of aesthetic and reconstructive procedures with comparable operative times. Patients undergoing breast surgery accounted for over 50% of all cases in both control and study cohort followed by combined procedures, face, liposuction, trunk, and extremities (Table 2).

Although all patients were given a single dose of their prescribed postoperative pain medication prior to discharge, significantly fewer patients were given meperidine for rescue analgesia in PACU using the new nonopioid protocol: 45.1% in the control group vs 12.3% in the study group ($P < 0.001$). Analog to the reduction of opioid use in the PACU, decreased need for antiemetic medications, such as ondansetron (24.7% vs 15.5%, $P = 0.017$) and promethazine (16.7% vs 2.7%, $P < 0.001$) was observed in the nonopioid group. In addition, the average stay in the PACU was shorter for patients in the study group (82 ± 39 min vs 70 ± 21 min, $P < 0.001$). Please see Table 3 for PACU management.

After surgery, patients included in the study group received significantly less opioid medications than controls (100.0% vs 0.0%, $P < 0.001$). The combination drug of acetaminophen and hydrocodone (Norco or Lortab) was the predominant opioid of choice. On the other hand, gabapentin (0.4% vs 98.4%, $P < 0.001$) and celecoxib (0.4% vs 100.0%, $P < 0.001$) was more frequently prescribed in the new protocol. The number of patients who, after discharge, necessitated additional medications was low and indifferent in both our cohorts: 6.2% vs 3.2%, $P = 0.149$ (Table 4).

No single adverse reaction was noted during postoperative follow-up visits, which could be attributed to short-term prescription of medications. Surgical complications were infrequent in both groups: 1.5% vs 1.0%, $P = 0.719$ (Table 5).

Table 1. Demographics and Preoperative Characteristics

Variable	Control (N = 275)	Study (N = 187)	*P* value
Gender, female (% of total)	255 (92.7)	171 (92.4)	0.906
Age, years (mean ± SD)	39.7 ± 12.4	39.5 ± 11.0	0.836
BMI (mean ± SD)	24.6 ± 3.8	24.4 ± 3.8	0.532
Comorbidities (% of total)			
Hypertension	23 (8.4)	19 (10.2)	0.518
Diabetes	3 (1.1)	1 (0.5)	0.522
Hyperlipidemia	5 (1.8)	2 (1.1)	0.512
Cardiac disease	2 (0.8)	1 (0.5)	0.769
Thyroid disease	27 (10.3)	26 (13.9)	0.250
Smoking	41 (15.0)	21 (11.5)	0.286
Prior childbirth (% of total)	175 (65.5%)	127 (75.1)	0.034*
History of allergies (% of total)**	61 (25.7)	49 (26.6)	0.836
Ethnicity (% of total)			0.063
White	189 (68.7)	152 (81.3)	
Hispanic	58 (21.1)	25 (13.4)	
Black	14 (5.1)	7 (3.7)	
Asian	12 (4.4)	3 (1.6)	
Other	2 (0.7)	0 (0.0)	

BMI, body mass index. * Significant with $P < 0.05$. ** Excludes allergies to medications used in the study.

DISCUSSION

In response to the growing opioid epidemic and common adverse effects of narcotics, recent literature and clinical practice have slowly adopted various iterations of multimodal nonopioid pain regiments for pre-, peri-, and postoperative pain control in lieu of opioid therapy. Research on use of these therapies has concentrated on laparoscopic surgery[8,11] and few cosmetic surgeries, in addition to being studied as adjuncts for enhanced recovery after surgery (ERAS) protocols.[14,15] As such, this study aimed to broaden the literature by analyzing pain control using a pre-, peri-, and postoperative nonopioid vs traditional opioid therapy for all outpatient plastic surgery procedures.

Our results suggest that the newer nonopioid analgesia protocol was superior to traditional opioids in the majority of measured outcomes. The study group required significantly less rescue analgesia and antiemetics in the PACU, had a shorter PACU stay, and overall received less opioid medication. Looking at the cohorts by procedure type, the aforementioned results apply only to the "breast" subcategory, which accounted for over 50% of the surgical cases. Although celecoxib has been shown to decrease acute postoperative pain and opioid use in patients undergoing facelift,[9] the surgical categories of face, trunk, extremities, liposuction, and

Table 2. Operative Details

Variable	Control (N = 275)	Study (N = 187)	*P* value
Procedure category (% of total)			0.597
Face	34 (12.4)	24 (12.8)	
Breast(s)	166 (60.4)	103 (55.1)	
Trunk	13 (4.7)	7 (3.7)	
Extremity(ies)	4 (1.5)	3 (1.6)	
Liposuction	21 (7.6)	13 (7.0)	
Combined procedures	37 (13.5)	37 (19.8)	
Operative time, minutes (mean ± SD)	115 ± 67	109 ± 64	0.398

Table 3. Postanesthesia Care Unit (PACU) Management

Variable	Control (N = 275)	Study (N = 187)	*P* value
Opioids (% of total)			
Meperidine	124 (45.1)	23 (12.3)	<0.001*
Total opioid doses (mean ± SD)**	1.6 ± 0.8	1.5 ± 0.7	0.426
Antiemetics (% of total)			
Ondansetron	68 (24.7)	29 (15.5)	0.017*
Promethazine	46 (16.7)	5 (2.7)	<0.001*
Total antiemetic doses (mean ± SD)**	1.4 ± 0.8	1.3 ± 0.5	0.203
PACU stay, minutes (mean ± SD)	82 ± 39	70 ± 21	<0.001*

* Significant with $P < 0.05$. ** Includes only patients who were given medications.

Table 4. Postoperative Management

Variable (% of total)	Control (N = 275)	Study (N = 187)	*P* value
Opioids	275 (100.0)	0 (0.0)	<0.001*
Acetaminophen/hydrocodone	272 (98.9)	0 (0.0)	
Hydromorphone	1 (0.4)	0 (0.0)	
Tramadol	4 (1.8)	0 (0.0)	
Gabapentin	1 (0.4)	184 (98.4)	<0.001*
Cyclobenzaprine	119 (43.8)	74 (39.6)	0.373
Celecoxib	1 (0.4)	187 (100.0)	<0.001*
Need for extra medication	17 (6.2)	6 (3.2)	0.149

* Significant with $P < 0.05$.

Table 5. Adverse Events

Variable (% of total)	Control (N = 275)	Study (N = 187)	*P* value
Medication-related	0 (0.0)	0 (0.0)	—
Nausea	0 (0.0)	0 (0.0)	
Rash	0 (0.0)	0 (0.0)	
Pruritus	0 (0.0)	0 (0.0)	
Surgical site	4 (1.5)[a]	2 (1.0)[b]	0.719

[a]2× seromas, 1× hematoma, 1× nerve pain breast. [b]1× recurring fluid collection, 1x residual eyelid discoloration.

combined procedures in this study did not produce similar findings as calculations were likely underpowered. Of note, the number of people necessitating additional medications postoperatively and the number of surgical complications were low and statistically indifferent in both groups. Although the various adverse effects of opioid use are well documented in literature, our patients curiously did not experience many side effects during postoperative follow up. We attribute this finding to the short prescription patterns of all of our medications. Our results demonstrate that the use of a nonopioid protocol works just as well as opioid narcotics for acute postoperative pain control and may have preferable postoperative outcomes, such as shorter recovery time in outpatient aesthetic and reconstructive breast surgery. These findings contribute significantly to the growing body of literature that supports the use of nonopioid analgesics over opioid narcotics for pain control.

Despite the increase in medications used in a multimodal pain regimen, nonopioid analgesics may be more cost effective as less resources are necessary to ensure a positive patient outcome. As our study among others suggests a trend toward decreased need for opioids, there would subsequently be less opioid-related side effects and potential for addiction. In 2014, Kane-Gill et al reviewed 20 articles to examine the excess economic burden that results from adverse effects of opioids. Those who experienced adverse effects of opioids spent between 7.4% and 47% more than their counterparts who did not experience adverse effects. The economic burden is further compounded when one considers the high hospital costs and prolonged hospital stays that result from opioid side effects.[16]

The switch from an opioid-based to a nonopioid pain management protocol could also have wide-reaching implications due to the social impact of opioids in regard to addiction and mortality. Patients who may be prone to an opioid addiction or have a worrisome history of analgesia use are spared from the risks of opioids in the first place.

According to investigations by Canfield et al, the majority of opioid dependencies begin with legitimate prescriptions by physicians and only later transition to illicit purchases.[17] Although the amount of fatal opioid drug overdoses has increased in all age groups, Hedegaard et al found that the highest rates of fatal opioid overdose occurred in adults aged 25 to 34, 35 to 44, and 45 to 54.[18] Furthermore, the rate of illicit opioid overdose jumped by 73% between 2014 and 2015, while the rate of prescription-opioid overdose only rose by 4%.[19] These studies suggest that while physicians have been contributing to the fight against the opioid epidemic, more can still be done. This is especially important in the context of cosmetic surgery as the average age of patients at our practice is 40 years; one of the most at-risk age groups for fatal drug overdose.

As demonstrated by Kane-Gill et al, opioid adverse effects account for higher hospital and patient costs and prolonged hospital stays.[16] According to Weiss et al, between 2005 and 2014, the rate of opioid-related emergency department admissions rose by 99.4% and the rate of opioid-related inpatient admissions rose by 64.1%.[20] The increase in opioid-related hospital visits further emphasizes the need for a nonopioid analgesic protocol to combat the rising amount of opioid related hospital admissions and costs. As physicians, the simplest measure to stall the opioid epidemic is to decrease the number of opioid medications prescribed and duration of use. With growing evidence that certain nonopioid medications are equally effective for postoperative pain control, the need to change physician prescription practices is clear.

As is common in retrospective studies, the two arms of this study are similar but not identical, let alone matched. Both groups received the same preventive analgesia in the form of general inhalational anesthesia with intraoperative opioids by the same anesthesia team during induction and had similar anesthesia requirements intraoperatively. The amount of local anesthetic was also consistent among patients undergoing breast augmentation. However, the study group received additional preemptive and preventive analgesia in the form of celecoxib and gabapentin the night prior and four hours before surgery. Preemptive analgesia refers to the administration of analgesics before, but not after, initial operative incision to prevent central nervous system sensitization.[1,21] Thus, the lack of preemptive analgesia could be a confounder resulting in the increased use of PACU pain medications in the control group while decreased rescue analgesia may have been influenced by its use in the study arm. The nonstandardized use of liposomal bupivacaine in patients undergoing abdominal procedures in both control and study groups could also be a confounding factor towards PACU rescue analgesia requirements.

Although the many adverse effects of opioids ranging from itchiness to respiratory depression are well documented,[1,16] few side effects were observed in both the control and study groups. As this is a cosmetic practice, the follow-up period was generally shorter with an average of 3 months depending on the procedure performed than what it would be at major institutions where there are typically more complex surgical procedures. However, as our study has a pharmacological focus, we feel this follow-up period is an appropriate length to monitor short-term drug effects. Patients in the control group were typically prescribed forty 10-325 mg hydrocodone-acetaminophen pills to be taken every six hours as needed. This prescription was generally the same for those who needed additional pain control at follow up, excepting a lesser number of pills. It could be that patients did not need to take all the pills prescribed or that this amount was not enough to induce adverse effects. Due to the negligible amount of data on adverse effects, we could not accurately assess any difference in adverse effects between the two groups. In addition, opioid utilization per individual patient was not recorded during follow up visits for the control groups. Therefore, although the study arm received less opioid prescriptions, there are no conclusive data on consumption between the two groups. However, it should be noted that our practice experienced a sharp decrease in telephone calls and patient complaints about constipation and skin reactions when opioids were no longer prescribed postoperatively. Both effects ranged in severity, but more often than not, medications had to be discontinued and new therapies started at additional cost to the patient. To address these limitations, further research could focus on detailed patient reports of pain medication use in the acute postoperative period days 0 to 5, akin to a study by Parsa et al where patients were asked to document any use of opioid analgesics following surgery after receiving preoperative celecoxib and gabapentin.[12]

Overall, the patients in the nonopioid protocol arm of our study required less rescue analgesia, less PACU time, less PACU antiemetics, and less opioid medications. Due to the strong statistical significance of our results and our large sample size, we can say that the nonopioid protocol is at least as effective as opioids for postoperative pain control in all aesthetic and reconstructive breast surgeries and may improve patient care and morbidity.

CONCLUSION

The use of multimodal analgesia as described in this study proved as effective as traditional narcotics in the control of acute postoperative pain and may be associated with better patient outcomes for all outpatient plastic surgery breast procedures. Significantly less rescue analgesia and antiemetics in the PACU, a shorter PACU stay, and less overall narcotic use was observed with the nonopioid regimen. Our results support proponents of nonopioid multimodal

pain control and hopefully impact the prescribing habits of plastic surgeons in the battle against the rising opioid epidemic.

Disclosures

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