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# A Comparison of Multimodal Analgesic Regimens for Opioid Reduction in Elective Plastic Surgery: A Randomized Study

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**Background:** This trial aimed to compare the efficacy of a multimodal analgesic regimen with gabapentin to a multimodal nonsteroidal anti-inflammatory drug (NSAID) regimen following cosmetic surgery. This was a prospective randomized study of 106 patients undergoing elective outpatient cosmetic surgery.

**Methods:** Patients were randomly assigned to a multimodal regimen of postoperative acetaminophen, gabapentin, and oxycodone with an acetaminophen and gabapentin preload or postoperative ibuprofen and oxycodone-acetaminophen protocol without a preload. Data on compliance, number of narcotic pills consumed, duration of analgesic use, pain levels, patient satisfaction, time from incision close to postanesthesia care unit (PACU) admission, and incidence of bleeding-related complications were collected and analyzed.

**Results:** Patients from both regimens reported equivalent postoperative pain control with the exception of pain in PACU. NSAID patients exhibited a 9.3% higher rate of compliance ($P = 0.01$), a 6.0% higher rate of satisfaction with pain control ($P = 0.04$), a 25.2% shorter interval between closure and PACU (=0.01), and an 8.2% lower rate of bleeding-related complications, all of which were statistically significant ($P < 0.05$).

**Conclusions:** Both regimens are viable tools in combating opioid overprescription as they both effectively reduce postoperative pain. However, the NSAID protocol resulted in greater satisfaction related to pain management and was more cost-effective by reducing emergence time from anesthesia. As there were no hematomas associated with the use of NSAIDs and a significantly higher rate of compliance, the use of NSAIDs in enhanced recovery after surgery protocols is supported. *(Plast Reconstr Surg Glob Open 2023; 11:e5181; doi: 10.1097/GOX.0000000000005181; Published online 9 August 2023.)*

## INTRODUCTION

Opioid misuse is a ubiquitous societal problem in the United States, and plastic surgery is a significant contributor to this problem. A population-based cohort study assessing 466,677 patients undergoing cosmetic or reconstructive surgery found that over 30,000 patients (~7%) became chronic opioid users. More than 10,000 patients (~2.3%) became long-term opioid users who remained on narcotics more than 6 months after surgery.[1] Overprescription in plastic surgery also plays a significant role in the national reservoir of unused narcotic medications. A study of 170 plastic surgery patients found that "plastic surgeons are prescribing almost double the amount of opioids consumed by patients after outpatient plastic surgery procedures," whereas another study of elective surgery patients found that 67% of patients who received an average of 30 doses of opioids for pain management had 19 doses left over after their pain was controlled.[2,3] Furthermore, over 90% of elective surgery patients have reported keeping leftover narcotics.[4]

In an effort to reduce plastic surgery's role in the nation's opioid crisis, we previously conducted a

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randomized prospective study comparing a standard postoperative pain regimen versus a multimodal analgesic protocol using gabapentin and acetaminophen with oxycodone. We included gabapentin in the multimodal protocol as the nerve pain medication has been adopted in enhanced recovery after surgery (ERAS) protocols due to recent findings that when used for pain management, it results in reduced postoperative narcotic needs in plastic surgery patients, with no increased risk of adverse effects.[5,6] The results of the previous trial demonstrated a 35% reduction in opioid use and an 18.4% reduction in the duration of consumption with the multimodal analgesic approach.[7] However, critical review of our study design focused on its failure to implement a 24- or 12-hour preload/preoperative dose of gabapentin and acetaminophen, as advocated for in the literature.[8,9] Additionally, our previous study solely examined a multimodal approach with acetaminophen, not recognizing the role nonsteroidal anti-inflammatory drugs (NSAIDs) play in postoperative pain management. Although NSAIDs are key instruments in pain management, surgeons have historically shied away from NSAID-based pain medications due to a theoretical risk of bleeding.[10] However, current literature rejects this hypothesis, indicating no increased risk of bleeding when utilizing ibuprofen as a postoperative analgesic.[11] As such, this study aims to prospectively evaluate if a multimodal NSAID/oxycodone-acetaminophen regimen is equivalent in pain control to a multimodal gabapentin/acetaminophen/oxycodone regimen, without increasing bleeding complications. The gabapentin-based protocol incorporates the use of a preload of gabapentin with acetaminophen, as current literature indicates premedication and combination of acetaminophen with gabapentin is best practice to reduce postoperative pain scores and analgesic demands when prescribing gabapentin.[9]

### Null Hypothesis

A multimodal gabapentin/acetaminophen/oxycodone regimen with a gabapentin preload is equivalent to a multimodal NSAID/oxycodone-acetaminophen regimen in controlling postoperative pain.

### Experimental Hypothesis

A multimodal gabapentin/acetaminophen/oxycodone regimen with a gabapentin preload is superior to a multimodal NSAID/oxycodone-acetaminophen regimen without a gabapentin preload in controlling postoperative pain, with decreased bleeding complications.

## METHODS

We prospectively studied 106 participants between the ages of 18 and 65 who scored an average American Society of Anesthesia Physical Status (ASA-PS) of 1.5. This randomized study evaluated a postoperative gabapentin/acetaminophen/oxycodone ERAS protocol with a gabapentin/acetaminophen preload versus a postoperative NSAID/oxycodone-acetaminophen protocol to manage postoperative pain in patients undergoing elective cosmetic surgery under general anesthesia on an outpatient basis.

### Takeaways

**Question:** What is the efficacy of a multimodal analgesic approach which includes a gabapentin preload regimen compared to a multimodal nonsteroidal anti-inflammatory drug (NSAID) approach in cosmetic surgery.

**Findings:** Both pain protocols effectively reduce postoperative pain. Neither protocol proved statistically more efficacious with regards to controlling postoperative pain.

**Meaning:** Although neither protocol was statistically superior in pain management, patients in the NSAID protocol had greater patient satisfaction, and the protocol was more cost-effective. Additionally, no hematomas were associated with NSAID use, and a significantly higher rate of compliance was observed, which supports the use of NSAIDs in enhanced recovery after surgery protocols.

Inclusion criteria were defined as having an age between 18 and 65, undergoing outpatient cosmetic surgery, not receiving a long-acting nerve block, and not having a contraindication to either proposed protocol. Patients were also not included if the procedure they were undergoing required use of a tailored pain management regimen (ie, abdominoplasty patients were not included, as the procedure often involves muscle disruption that would indicate use of a muscle relaxant). The outpatient cosmetic procedures included were augmentations (using chin, calf, or breast implants), implant exchanges, breast reductions, mastopexies, gynecomastias, brachioplasties, liposuction, upper eyelid and lower lid blepharoplasties, fat grafting to body, facelifts, rhinoplasties, browlifts, facial fat grafting, and revisions of the aforementioned procedures (Fig. 1). Combination procedures were included, and upper eyelid blepharoplasties were only included in combination with other procedures, as upper eyelid blepharoplasties alone do not indicate the need for stronger narcotics such as oxycodone or oxycodone-acetaminophen. The NSAID/oxycodone-acetaminophen combination was selected for ease of compliance, cost, anti-inflammatory benefits, and availability. Study variables include pain scores, narcotic use, compliance, time of emergence, and incidence of bleeding complications in the postoperative period.

At the preoperative appointment, patients were assigned to one of two postoperative pain regimens based on the parity of their record number. In the preload group (Table 1), each patient was prescribed an ERAS protocol of 300 mg of gabapentin and 650 mg of acetaminophen and instructed to take them together PO TID (by mouth, three times a day) to manage postoperative pain. Patients in this group were also instructed to take 650 g of Acetaminophen with 300 mg of gabapentin PO the night before surgery. The same dose of gabapentin with 1 g of acetaminophen was provided by clinical staff in the preoperative suite, 1 hour before the start of surgery. Patients in this protocol were also prescribed 5 mg of oxycodone and instructed to use it PO q4–6 hours, as needed for breakthrough pain. In the NSAID group (Table 1), each patient was prescribed a standard postoperative protocol of 600 mg ibuprofen PO q6 hours with no preload.

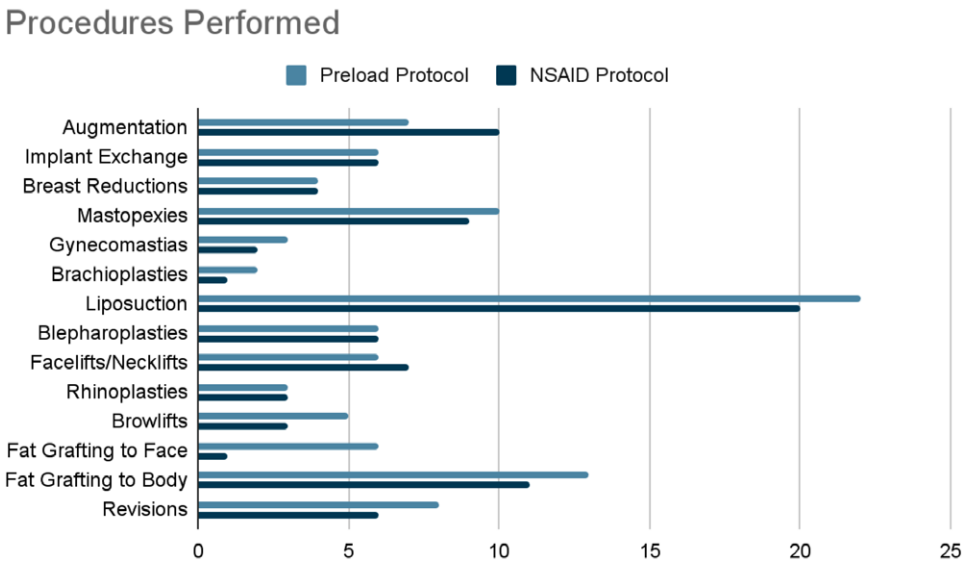


**Fig. 1.** Chart of all procedures included in study.

**Table 1. Multimodal Pain Management Protocols**

| | Preoperative Medications | Postoperative Medications |
|---|---|---|
| Multimodal analgesic protocol with a preload | 650 mg of acetaminophen with 300 mg of gabapentin by mouth the night before surgery | 650 mg of acetaminophen with 300 mg of gabapentin by mouth every 8 h |
| | 1 g of acetaminophen with 300 mg of gabapentin by mouth 1 h before surgery | 5 mg of oxycodone by mouth every 4–6 h for breakthrough pain only |
| Multimodal NSAID protocol | None | 600 mg of ibuprofen every 6 hours |
| | | 5–325 mg of oxycodone-acetaminophen by mouth every 4–6 h for breakthrough pain only |

They were also prescribed a 5- to 325-mg formulation of oxycodone-acetaminophen and instructed to use it PO q6 hours, as needed for breakthrough pain. All patients were counseled on study protocols and instructed to record the day they stopped taking narcotics and how many narcotics they had remaining at the time they stopped.

Standard anesthesia medications were administered across both groups in an AAAHC office-based operating suite, at the discretion of two consistent anesthesiologists who used the same anesthesia techniques. Each patient received 100–200 µg of fentanyl intraoperatively, based on the length of their case. No other intravenous pain medications were administered intraoperatively. Before incision, all patients were also injected at their surgical sites with short-acting local anesthetic (1% lidocaine with 1:100,000 epinephrine). In the postanesthesia care unit (PACU), patients were given pain medications of Valium, Vicodin, oxycodone IR, fentanyl, Percocet, or Dilaudid by a dedicated, single PACU nurse, according to PACU protocol, based on the patient's reported pain levels. Upon entry to PACU, patients were asked to rate their pain on the 0–10 numerical verified Likert pain scale (0 = no pain, 10 = most pain ever felt).[12] Patients were then asked 5 minutes before discharge to rate their pain again. As gabapentin has sedative properties, and preload could impact recovery time, a measurement of emergence time from general anesthesia to PACU admission was recorded and then computed as a time–cost ratio. The PACU experience was controlled by the use of a single consistent recovery room nurse for the entire study period. The surgeons, anesthesiologists, and recovery room nurse remained blinded throughout the study.

During a 1-day postoperative call, patients were counseled on their medication protocol again and asked to record the day they stopped taking narcotics and how many narcotics they had remaining. Patients were asked to record these data rather than bring in their pain medications due to compliance issues noticed in our last study. At the 1-week postoperative visit, patients were asked to complete a survey reporting their pain level at that visit, their average pain level in the first week, the number of days needing narcotics, the number of narcotics used, and their satisfaction with their pain management, all on a Likert scale of 0–10. Additional metrics include incidence of bleeding-related complications, as identified by the physician, and compliance with pain protocols. All data were analyzed using an independent two-sample *t* test with the statistical level of significance set at 0.05 ($P < 0.05$).

## RESULTS

There were no significant differences in patient demographics or length of surgery between the preload group and NSAID group (Table 2), with similar procedure distribution across groups (Fig. 1). As the preload group required a preoperative dose, any patient who did not take this preoperative dose was considered noncompliant for the purpose of our study. Any patient who used medication that was not prescribed to manage postoperative

**Table 2. Patient Demographics**

| | Preload Group | NSAID Group | *P* |
|---|---|---|---|
| Mean age ± SD, y | 42.5±12.7 | 39.1±13.4 | 0.20 |
| Mean body mass index ± SD, kg/m$^2$ | 24.1±3.7 | 24.1±3.8 | 0.98 |
| Mean length of surgery ± SD, min | 143.1±71.5 | 163.1±157.3 | 0.46 |

pain was considered noncompliant as well. There was a 9.3% noncompliance rate in the preload group compared to a 0% noncompliance rate in the NSAID group, which proved to be statistically significant ($P$= 0.01) and resulted in the exclusion of five noncompliant preload patients. Three patients were excluded for the addition of long-acting bupivacaine (Exparel) to their surgery, leaving 49 participants in the preload group and 49 in the NSAID group. The groups were equivalent with regard to various demographic indices, including age, body mass index, and length of surgery (Table 2).

The time from incision closure to PACU was recorded, with the preload group taking 15.4±7.2 minutes and the NSAID group taking 12.3±5.4 minutes, exhibiting a 25.2% reduced time of emergence ($P$= 0.01). This indicates that the preload protocol results in longer emergence times, a finding that was clinically evident, as the preload patients were more somnolent both pre- and postprocedure. Upon arrival to PACU, initial pain scores were recorded on a scale of 1–10, with the preload group averaging pain levels of 4.1±3.4 and the NSAID group averaging 5.2±2.9 (Table 3). There was a statistical significance between groups that we attribute to the preload ($P$ = 0.04). However, this significance does not persist to the time of discharge from the PACU. Patients then reported their pain level at their initial postoperative appointment and estimated their average pain level the first postoperative week, with no statistically significant difference between groups (Table 3). There was no significant difference between groups in the number of days requiring narcotics or the number of pills taken postoperatively to manage pain (Table 3). Bleeding-related complications were only observed in preload protocol patients, at a rate of 8.2% (one blood clot and three hematomas). The findings indicate a statistical difference between groups ($P$ = 0.02), with the NSAID group resulting in no bleeding-related complications. Additionally, data of self-reported satisfaction with pain management show a significant difference between groups ($P$ = 0.04), with the NSAID group participants all reporting satisfaction with their pain management, whereas the preload group reported a 6.0% dissatisfaction rate with their pain management (Table 3), potentially pointing to complexity of protocol as the main cause.

**Table 3. Postoperative Pain Scores and Narcotic Use**

| Postoperative Period | Preload Group | NSAID Group | *P* |
|---|---|---|---|
| Time from close to PACU admission (min) | 15.4±7.2 | 12.3±5.4 | 0.01* |
| Initial pain level at PACU | 4.1±3.4 | 5.2±2.9 | 0.04* |
| Pain level at discharge from PACU | 3.1±1.6 | 3.3±1.9 | 0.28 |
| Pain level at initial PO | 3.9±2.3 | 3.9±2.1 | 0.48 |
| Average pain level in first week | 5.1±2.1 | 5.6±2.3 | 0.73 |
| No. days needing narcotics | 4.1±1.9 | 4.0±2.0 | 0.95 |
| No. pills needed in first week | 10.6±6.5 | 10.9±6.9 | 0.79 |
| Satisfied with pain control | 0.9±0.2 | 1.0±0.0 | 0.04* |

*Statistical significance ($P$ value <0.05).

## DISCUSSION

As a practice, we are actively investigating the most effective pain regimen while reducing narcotic use. To be adopted, an ERAS protocol must show improved efficacy, be easy for patients to follow, and reduce complications. Earlier work by our group had shown that our ERAS protocol, which included postoperative gabapentin and acetaminophen with oxycodone for breakthrough pain only, had reduced narcotic use by a statistically significant 35.0%.[7] This in turn led to a reduction in the number of narcotics prescribed in our practice from 40 to 24 tablets, which was two times the average number of tablets used per patient. During this study, we found prescribing 20 narcotic tablets per cosmetic surgery patient would be sufficient coverage, as an average of 10.6±6.54 pills were used in the preload group and 10.9±6.92 pills were used in the NSAID group. The goal of the examined protocols was to reduce postoperative narcotic reliance, which they did in comparison to 11.9 tablets in our previous study group of similar design. However, this study did not find a significant difference between the protocols in the number of pain pills needed, the duration pain pills were needed, or the pain scores assessed except upon arrival to PACU. As most patients have some retroactive amnesia in the PACU, the pain score on entering is the least important. It does, however, support an ERAS regimen that includes a preload.

To maintain benefit, an ERAS protocol has to have a simple enough implementation and have no untoward effects. In the case of the preload, we found difficulty with compliance. A total of five patients (~9%) in the preload group were excluded from the study due to preloading noncompliance, despite a preoperative education appointment and written instructions. The higher patient satisfaction for equivalent pain control most likely reflects ease and familiarity with use, which are consistent with compliance data. Additionally, the preload anecdotally made patients more somnolent during the presurgical check-in. This somnolence has implications for practices which do not consent patients at their preoperative visit like we do. Importantly, the preload statistically increased the time of emergence from anesthesia and entrance into PACU by 3.14 minutes or by 25.2% compared to the NSAID group. With anesthesia and facility fees costing roughly $27.08 per minute at our center, the additional practice expense in care was $85.03 per case or $4166.53 in additional costs for 49 preload patients. According to the American Society of Plastic Surgeons, in the year 2019, about 2,678,302 cosmetic surgical procedures were performed, resulting

in a potential national expense of $227,739,233.00 for as little as 3.14 minutes per case in additional recovery time.[13]

Paradoxically, the anecdotal risk of NSAIDs influencing bleeding was not realized. In fact, all the bleeding-related complications were in the preload group. There was a 8.2% rate of bleeding complications in the preload group but a 0% rate in the NSAID group. The difference between the groups was statistically significant, again discrediting the widely held belief that NSAID-based protocols increase bleeding-related complications and should therefore be avoided. The only significant benefit from the preload group was a decrease in initial PACU pain score, as to be expected from the regimen with a preload pain management versus none; however, this benefit was short-lived, as pain levels by discharge from PACU were equal to the non-preload group. As an extrapolation from this study and other clinical studies indicating the efficacy of preoperative acetaminophen administration in reducing postoperative pain, we will add a preload of acetaminophen the morning of surgery to decrease this initial PACU score.[14]

## CONCLUSIONS

This study showed that an NSAID/oxycodone-acetaminophen protocol is equal in efficacy for pain control after initial PACU score to a gabapentin/acetaminophen/oxycodone protocol with a preload. The NSAID protocol had better patient compliance and satisfaction with fewer bleeding-related complications. These findings support current literature that despite physician's concerns about NSAIDs increasing risk of bleeding, NSAIDs do not affect postoperative bleeding or increase hematomas in plastic surgery patients.[10,11] Additionally, the gabapentin preload caused more preoperative somnolence and delayed emergence, prolonging operating room time, and was considered more complicated, affecting compliance. For these reasons, our surgery center adopted the multimodal NSAID protocol for ERAS, with a limit of 20 postoperative narcotic tablets prescribed per case. However, to maintain the reduced pain levels at PACU, clinical staff administer patients 1 g of acetaminophen in the preoperative suite, without gabapentin, to avoid compliance issues and stave off emergence delays.

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### DISCLOSURE

*The authors have no financial interest to declare in relation to the content of this article.*

### PATIENT CONSENT

*The patients/participants provided their written informed consent to participate in this study and for results to be published.*

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