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RAPID COMMUNICATION

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Six-week postoperative opioid use and pain following a randomized controlled trial evaluating multimodal analgesia for head and neck free flap patients

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Abstract

Introduction: Head and neck malignancy treatment often involves invasive surgeries, necessitating effective postoperative pain control. However, chronic reliance on opioid medications remains a challenge for many patients after surgery. Multimodal analgesia (MMA) within enhanced recovery after surgery protocols has shown success in limiting narcotic pain medications for other cancer types. In a prior study, MMA comprising acetaminophen, ketorolac, gabapentin, and a neurogenic block reduced opioid use in the 7-day postoperative period for major head and neck reconstructive surgery. This study investigates the impact of multimodal analgesia on opioid prescription and pain during the 6-week postoperative period for patients undergoing major head and neck oncologic surgeries, aiming to understand the longer-term effects of narcotic use.

Methods: The study retrospectively examined participants in a [hybrid type 1 effectiveness-implementation pragmatic trial to assess multimodal analgesia's long-term effectiveness in head and neck free flap surgery. Arm A received scheduled acetaminophen and as-needed opioids, while Arm B received scheduled gabapentin, ketorolac, a regional nerve block at the donor site, scheduled acetaminophen, and as-needed opioids. Retrospective data collection included opioid prescription use and pain scores up to 6 weeks after surgery, gathered from the Kansas prescription drug monitoring program, K-TRACS.

Results: Thirty patients participated, 14 in Arm A and 16 in Arm B. The average morphine milligram equivalents per day of filled prescriptions were not significantly different between Arm A and Arm B (7.23 vs. 7.88, $p = .845$). Additionally, average pain

This project was presented at the 11th Annual International Meeting of the American Head and Neck Society in Montreal, Quebec, Canada, July 10, 2023.

scores at 6 weeks showed no significant difference between the two groups (1.4 vs. 1.9, $p = .612$).

Conclusion: Patients with head and neck cancer treated with multimodal analgesia during the perioperative period did not exhibit significant differences in opioid use and pain within 6 weeks after discharge. To confirm these findings, a re-examination with strict measures of opioid use and scheduled pain assessments in a prospective manner is warranted.

Level of Evidence: 4.

KEYWORDS

enhanced recovery after surgery, free flap surgery, head and neck cancer, head and neck surgery, multimodal analgesia, opioid use

1 | INTRODUCTION

The US opioid epidemic has been exacerbated by increasing opioid prescriptions, especially in post-surgical patients, highlighting a need for improved postoperative pain management strategies.[1] Inclusion of multimodal analgesia (MMA) in enhanced recovery after surgery (ERAS) protocols is supported by a high level of evidence.[2] However, long-term opioid consumption and pain after discharge have not been studied.[3] This study builds on a previously published randomized controlled trial (RCT) demonstrating that an MMA regimen reduced opioid use in the 7-day postoperative period with similar pain scores during hospitalization compared with usual care; however, this trial did not examine long-term outcomes.[4] Thus, the aim of this study is to evaluate whether this in-hospital MMA regimen may reduce 6-week opioid prescription use and postoperative pain in patients undergoing head and neck free flap surgery.

This retrospective cohort study was IRB approved and consisted of RCT participants undergoing free flap surgery for head and neck cancer (HNC) or osteoradionecrosis in 2022. Patients were included if they were at least 18 years old; patients with a preoperative history of opioid use for over 6 months were excluded. The RCT included two arms: Arm A (standard of care regimen of scheduled acetaminophen with as-needed opioids) and Arm B (scheduled gabapentin, ketorolac, and acetaminophen, a peripheral nerve block of the reconstructive donor site, and as-needed opioids).[4] As the original scope of the RCT protocol was limited to in-hospital perioperative medication regimens, patients were discharged on pain control regimens determined by their treating physician's individualized evaluation. Data collected included pain scores within 6 weeks of follow up, as well as discharge pain regimen and opioid prescriptions filled from the Kansas prescription monitoring program, K-TRACS, calculated in average Morphine Milligram Equivalents (MME) per day.[5] Pain scores were measured using the visual analog pain scale (VAS).

A total of 30 patients were included, 14 in arm A and 16 in arm B. After the first 30 patients were enrolled, an interim analysis for safety and futility resulted in study termination at this point. As previously published, there were no significant differences between the arms in demographics or clinical variables.[4] At discharge, most patients were prescribed either oxycodone and acetaminophen ($N = 14$) or oxycodone, acetaminophen, and gabapentin ($N = 11$), followed by other regimens (combinations of hydrocodone-acetaminophen or tramadol with/without gabapentin; one patient did not receive any opioids). There were no significant differences in discharge pain regimen type or MME prescribed at discharge between arms (Table 1). At 6-week follow-up, there was no significant difference between arms in mean MME per day of opioid prescriptions filled and neither arm was more likely to fill opioid prescriptions in excess of the discharge regimen. However, patients in the multimodal arm were more likely to fill an opioid prescription (100.0% vs. 64.3%, $p = .014$). At post-operative follow-up, there was no difference in mean pain scores, the proportion of patients off narcotics, or the proportion of patients who returned for additional surgery between intervention arms (Table 1).

2 | DISCUSSION

This retrospective, pragmatic study of an RCT's participants[4] did not demonstrate a difference at 6-week follow-up in opioid use or pain scores between treatment arms in the setting of similar discharge regimens. However, patients in the MMA arm were more likely to fill an opioid prescription after discharge.

Although the current study did not utilize a standardized discharge regimen, it does offer a window into how MMA regimens may impact opioid use in a real-world setting, where patients may not strictly follow discharge regimens. Our findings agree with research demonstrating that patients undergoing a pulmonary resection treated with a regional block and MMA utilized decreased MME compared to the pre-MMA cohort during admission and at discharge, but similar opioid use at 14–90 and 90–180 days postoperatively.[5] This data combined with the current study raises concerns that MMA protocols may not modify opioid use long-term. Future studies should prospectively evaluate direct measures of opioid use, further investigate the finding that MMA patients were more likely to fill an opioid prescription, and prioritize patients with

TABLE 1 Comparison of discharge regimen and outcomes between control (or could say standard) (Arm A) and multimodal (Arm B) treatment groups at 6 weeks post-surgery.

	Total ($N = 30$)	Arm A (standard care) ($N = 14$)	Arm B (multimodal analgesia) ($N = 16$)	*p*-value	Effect size[a]
Discharge pain regimen, *N* (%)					
Oxycodone, Acetaminophen, Gabapentin	11 (36.7)	3 (21.4)	8 (50.0)	.174	0.062
Oxycodone, Acetaminophen	14 (46.7)	9 (64.3)	5 (31.3)		
Other	5 (16.7)	2 (14.3)	3 (18.8)		
Opioid prescription sent at discharge (MME/day), mean (SD)	43.7 (9.5)	43.6 (4.2)	43.7 (12.7)	.960	0.018
Opioid prescription filled (MME/day), mean (SD)	47.7 (58.7)	48.6 (78.3)	47.1 (36.8)	.377	0.025
Filled an opioid prescription after discharge					
Yes, *N*, (%)	25 (83.3)	9 (64.3)	16 (100.0)	**.014**	**0.478**
No, *N*, (%)	5 (16.7)	5 (35.7)	0 (0.0)		
Filled opioid prescriptions in excess of discharge regimen					
Yes, *N*, (%)	7 (23.3)	4 (28.6)	3 (18.8)	.675	0.116
No, *N*, (%)	23 (76.7)	10 (71.4)	13 (81.3)		
VAS pain at 6-weeks, mean (SD)	2.0 (2.6)	1.4 (2.6)	1.9 (2.7)	.612	0.196
Off narcotics by 6-weeks, *N* (%)	13/18 (72.2%)	6/8 (80.0%)	7/10 (70.0%)	.814	0.043
Return to OR, *N* (%)	7 (23.3%)	3 (21.4%)	4 (25.0%)	.818	0.042

Note: Bolded values indicate statistical significance.
[a]Cohen's D, Cohen's W.

known risk factors for chronic opioid use such as tobacco use and advanced pathologic T-stage.[5,6]

Limitations of the current study include its small sample size and retrospective nature; it was only able to measure opioid prescriptions filled and could not account for actual use.[5] Additionally, discharge pain regimens were not standardized in the current study, which could present a limitation, although any attempt to standardize discharge regimens could prove challenging. Finally, pain was assessed only at postoperative visits rather than throughout recovery, which may limit generalizability.

3 | CONCLUSION

HNC patients treated with MMA perioperatively show similar opioid use and pain levels at 6 weeks, despite reduced immediate postoperative opioid use. This highlights the real-world impact of in-hospital MMA interventions; additional prospective studies are needed to definitively assess the influence of MMA protocols on long-term opioid use in HNC patients.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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