Multimodal Opioid-Sparing Postoperative Pain Protocol versus Standard of Care for Patients Undergoing Knee and Shoulder Arthroscopy: A Randomized Controlled Trial

Nolan Stuart Horner, Aaron Gazendam, Seper Ekhtiari, Darren de SA, Moin Khan, Vickas Khanna[1], Anthony Adili, Nicole Simunovic, Devin Peterson, Kim Madden[2], Andrew Duong, Olufemi Rolland Ayeni[2]
[1]St. Josephs Hospital Hamilton, [2]McMaster University

INTRODUCTION:
In arthroscopic knee and shoulder surgery, there is growing evidence that opioid-sparing protocols may reduce postoperative opioid consumption while adequately addressing patients' pain. However, there are a lack of prospective, comparative trials evaluating their effectiveness.
METHODS:
This study was an investigator-initiated, multicenter, parallel, superiority RCT with 1:1 allocation. This multicenter randomized controlled trial included adult patients undergoing arthroscopic shoulder or knee surgery and patients were followed to 6 weeks postoperatively. Two-hundred patients were randomized with 193 included in the analysis. The opioid-sparing group received a prescription of 1) naproxen, acetaminophen, and pantoprazole, 2) a limited "rescue prescription" of hydromorphone, and 3) a patient education infographic. The control group received a standard of care prescription as per the treating surgeon. The primary outcome was oral morphine equivalents (OMEs) consumed at 6 weeks postoperatively. Secondary outcomes included visual analogue score (VAS), patient satisfaction, refills, quantity of OMEs prescribed, patient-reported side effects, and adverse events. Three *a priori* subgroup analyses evaluating sex (male vs. female), joint (knee vs. shoulder), and anesthetic strategy (regional block vs. no regional block). A sensitivity analysis was performed comparing complete cases versus multiple imputation results for the primary outcome.
RESULTS:
There were 98 patients randomized to standard of care and 95 to the opioid-sparing protocol (Figure 1). The mean OMEs consumed at 6 weeks postoperatively in the standard of care group was 72.6mg, compared to 8.4mg in the opioid-sparing group (Mean Difference (MD): 64.2mg; 95% Confidence Interval (CI): 44.4-84.0, p<0.001)(Table 1). The mean amount of OMEs prescribed was 341.17mg; SE: 15.8 in the standard of care group and 40.4mg; SE: 0.4 in the opioid sparing group (MD 300.8mg; 95% CI: 269.4-332.3; p <0.001). No differences in pain, patient satisfaction, adverse events, or opioid refills were found between groups. Significantly more patients reported medication-related side effects in the standard of care group (32% vs. 19%, p=0.043). None of the subgroups (sex, joint, or use of regional block) demonstrated a significant subgroup effect. Sensitivity analyses did not produce any difference in significant results compared to the primary analysis.
DISCUSSION AND CONCLUSION:
A simple to implement opioid-sparing pain management protocol significantly reduced opioid consumption, with a large effect size, in patients undergoing outpatient shoulder and knee arthroscopy compared to a standard opioid prescription. No significant differences in patient-reported pain or patient satisfaction with pain control were found between groups. Significantly less patients experienced medication-related side effects in the opioid-sparing group compared to the standard care group.

Figure 1 - CONSORT Flow Diagram

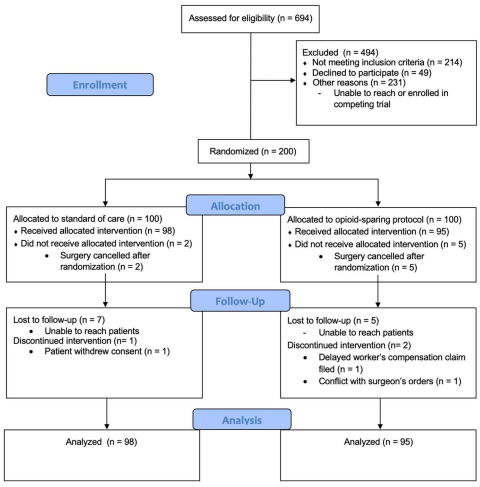

Table 1. Study Outcomes by Treatment Group

	Total N= 193	Standard of Care N = 98	Opioid-Sparing Protocol N = 95	Mean Difference (95% CI)	p-value
PRIMARY OUTCOME					
Total OMEs consumed (mg) Mean (SE) Median (IQR)	40.9 7.5 (0-44.25)	72.6 (9.9) 40.0 (7.5-105.0)	8.4 (1.6) 0.0 (0.0-8.0)	64.2 (44.4-84.0)	< 0.001
SECONDARY OUTCOMES					
Patient-reported pain at 2 weeks (VAS), Mean (SE)	16.6 (1.4)	17.8 (2.0)	15.4 (2.1)	2.7 (-3.0-8.4)	0.419
Patient-reported pain at 6 weeks (VAS), Mean (SE)	13.5 (1.3)	14.8 (1.8)	12.2 (2.0)	2.6 (-2.7-7.9)	0.762
OMEs prescribed at discharge (mg), Mean (SE)	193.1 (13.5)	341.2 (15.8)	40.4 (0.4)	300.8 (269.4-332.3)	<0.001
	n (%)	**n (%)**	**n (%)**	**Odds Ratio S:O (95% CI)**	**p-value**
Patient-reported satisfaction at 6 weeks **Satisfied** ("Always", "Usually") **Unsatisfied** ("Sometimes", "Never")	158 (81.9%) 20 (10.4%)	79 (80.6%) 11 (11.2%)	79 (83.2%) 9 (9.5%)	1.2 (0.5-3.1)	0.896
Opioid Refill Requests Completed	8 (4.2%)	6 (6.2%)	2 (2.1%)	3.07 (0.6-15.6)	0.157
Any Adverse Events	5 (2.6%)	2 (2.1%)[1]	3 (3.2%)[2]	0.65 (0.1-4.0)	0.634

[1]*Adhesive capsulitis, uncontrolled post-operative pain*
[2]*Deep vein thrombosis, calf swelling and leg pain (Baker's cyst)*
S = Standard of Care
O= Opioid-Sparing Protocol