Ambulatory Gynecologic Surgery: Finding the Optimal Opioid Prescription

Introduction:

Currently there is a nationwide epidemic in opioid abuse and overdose deaths. While the opioid epidemic is multi-factorial, one major source of excess opioids may be over-prescribing in the post-operative period. There is wide variation in the prescribing practices for post-operative pain control and there is no standard of care for pain control after minor laparoscopic surgery in general or after laparoscopic gynecologic surgery. There is also evidence to show that less than half of the opioids prescribed are used by the patient (Hill 2017, As-Sanie 2017) and that many patients feel they are prescribed too many opioids (Hota 2017). We are aiming to examine how the number of narcotic pills prescribed post operatively may affect the patient experience in the recovery period.

Study Design:

This will be a randomized controlled study enrolling patients scheduled for outpatient minor laparoscopic gynecologic surgery. Enrollment will start after IRB approval. We aim to enroll 120 patients to be able to evaluate outcomes for 100 patients with an anticipated 10-20% dropout rate. This is a two arm study consisting of 60 subjects in each arm. The patients will be randomized at the time of enrollment. We will use computer generated blocks of four patients. Both arms of patients will receive the same non-narcotic pain medication prescriptions which will include 50 tablets of acetaminophen 500mg (1-2 tablets every 6 hours as needed) and 25 tablets ibuprofen 600mg (1tablet every 6 hours as needed). The standard arm will receive a prescription for 10 tablets of 5 mg oxycodone (1 tablet every 6 hours as needed). The intervention arm will be prescribed 5 tablets of 5mg oxycodone. Both of these prescription regimens are within the range of normal clinical practice for post-operative pain control.

Patient demographics to be studied will include age, race, parity, body mass index, insurance status, smoking status, medical co-morbidities and ASA classification. Other variables of interest include patient surgical history (number of previous abdominopelvic surgeries- total, laparoscopic, and open), surgeon characteristics, procedure performed and surgical findings.

The patients will receive a telephone call by administrative staff, who is not directly involved in the patient care or data collection for the study subjects, on postoperative day 1 and 7. The subjects will all be scheduled for a 2- week post-operative follow up with the surgeon in the office. The primary outcome to be assessed will be number of opioids used by the patient at 24 hours and 7 days post-operative. Our hypothesis is that patients prescribed only 5 tabs of oxycodone will not require more medication. Our secondary hypothesis is that the pain scores between the two groups will not be different. The other variables being studied include the following: having had a post-operative bowel movement, presence of nausea, number of ibuprofen, acetaminophen tablets remaining, calls to the office prior to their follow up visit for

pain issues, and urgent or emergency department visits for pain issues. These assessments will be asked during the brief telephone calls and also at the postoperative visit.

All patients will be given the clinic phone number and advised to call with any questions or clinical concerns. They will be advised if possible to return to a Montefiore ER or GYN provider in case of an urgent issue prior to their 2 week postoperative visit, as opposed to an outside facility. They will be counseled to bring their medical records with them to their postoperative visit or notify us of any such outside visit.

Study Population:

All patients presenting for outpatient laparoscopic gynecologic surgery will be assessed for inclusion. Exclusion criteria include: recent opioid use as determined by use in the past 3 weeks, and those with contraindications to receiving the study medications. These include: hypersensitivity or allergy to any NSAID, aspirin, ibuprofen, acetaminophen, oxycodone, a history of coronary artery bypass graft, any active gastrointestinal bleeding, active gastrointestinal ulcer disease, advanced hepatic disease, alcoholic liver disease, coagulopathy, heart failure, impaired renal function (Creatinine >1.2), G6PD deficiency, respiratory depression, or hypotension.

Clinicians will identify patients during pre-operative evaluation and will approach to inquire if patients are interested. The study team will consent patients pre-operatively for enrollment. There will be no exclusion of non-English language speakers; the Montefiore telephonic interpreter services will be utilized for translation services.

Risks:

This study will use post-operative pain control regimens that are within the standard of care, therefore the intervention itself does not pose additional risk to the patient. Medications will be prescribed as clinically necessary and will not be withheld from the patient as needed. As is routinely done for all post surgical patients, patients will be counseled to take the pain medications as prescribed and not take additional over the counter pain medications without speaking to their provider first. Patients will be asked during the phone surveys and at the follow up visit if additional medications were taken for pain control. All appropriate measures will be taken to prevent any breach in confidentiality of protected health information. Some physicians typically call their patients on the first post-operative day as well; hence this is not a significant change in clinical practice.

Benefits:

Study benefits are to future patients undergoing ambulatory laparoscopic surgery to find the best modalities to treat post-operative pain. The benefits are also to society at large if we are able to decrease the excess opioids contributing to the opioid epidemic.

Sample Size Calculation:

The primary outcome will be the number of opioids used by the patients. With N=50 sample size for each group after dropout, standardize effect sizes (i.e., mean difference in SD units between groups) of the primary outcome greater than 0.6 will be detected with >80% power at a two-sided significance level of 0.05 with application of a Mann-Whitney test.

Data Analysis:

Software use for analysis will be based on the discretion of the statistician. A p-value of <0.5 will be considered to be significant. The chi-squared test and the Fisher's exact test will be used to compare categorical variables. The Mann-Whitney U test will be used to analyze continuous variables. The treatment arms will be compared to assess for any significant differences in baseline characteristics including demographic variables, surgical data, and surgeon characteristics. These differences will be controlled for in a secondary analysis.

Data Safety and Monitoring Plan:

Data quality control and database management:

Data collected for study use will be maintained in a locked office on a password protected computer and accessible only to study investigators. Patient identifiers will be kept separate from the data collection sheet on a password protected computer and accessible only to study investigators.

Patient cases will be continually reviewed on a bi-weekly basis by the PI. If any safety issues arise they will be addressed by the study team. The patients will be in continuous care of the physicians for the weeks after surgery should any issues arise.

References:

Thomazeau J, Rouquette A, Martinez V, Rabuel C, Prince N, Laplanche JL, Nizard R, Bergmann JF, Perrot S, Lloret-Linares C. Acute pain factors predictive of post-operative pain and opioid requirement in multimodal analgesia following knee replacement. Eur J Pain. 2016 May;20(5):822-32. doi: 10.1002/ejp.808. Epub 2015 Oct 30. PubMed ID: 26517014

De Oliveira GS Jr, Ahmad S, Fitzgerald PC, Marcus RJ, Altman CS, Panjwani AS, McCarthy RJ. Dose ranging study on the effect of preoperative dexamethasone on postoperative quality of recovery and opioid consumption after ambulatory gynaecological surgery. Br J Anaesth. 2011 Sep;107(3):362-71. doi: 10.1093/bja/aer156. Epub 2011 Jun 13. PubMed ID: 21669954

As-Sanie S, Till SR, Mowers EL, Lim CS, Skinner BD, Fritsch L, Tsodikov A, Dalton VK, Clauw DJ, Brummett CM. Opioid Prescribing Patterns, Patient Use, and Postoperative Pain After Hysterectomy for Benign Indications. Obstet Gynecol. 2017 Dec;130(6):1261-1268. doi: 10.1097/AOG.0000000000002344. PubMed ID: 29112660

Baruch AD, Morgan DM, Dalton VK, Swenson C. Opioid Prescribing Patterns by Obstetrics and Gynecology Residents in the United States. Subst Use Misuse. 2018 Jan 2;53(1):70-76. doi: 10.1080/10826084.2017.1323928. Epub 2017 Sep 1. PubMed ID: 28862884

Darnall B, Li H. Hysterectomy and predictors for opioid prescription in a chronic pain clinic sample. Pain Med. 2011 Feb;12(2):196-203. doi: 10.1111/j.1526-4637.2010.01038.x. Epub 2011 Jan 11. PubMed ID: 21223499

Hill MV, McMahon ML, Stucke RS, Barth RJ Jr. Wide Variation and Excessive Dosage of Opioid Prescriptions for Common General Surgical Procedures. Ann Surg. 2017 Apr;265(4):709-714. doi: 10.1097/SLA.0000000000001993. PubMed ID: 27631771

Hota LS, Warda HA, Haviland MJ, Searle FM, Hacker MR. Opioid use following gynecologic and pelvic reconstructive surgery. Int Urogynecol J. 2017 Sep 9. PubMed PMID: 28889218

https://www.cdc.gov/drugoverdose/data/index.html