

A randomized-controlled trial of post-operative narcotic quantities after urogynecologic surgery

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BACKGROUND

The opiate abuse epidemic in the United States is a costly and deadly issue. Opiate overdose leads to 78 deaths each day, and half of these deaths involve prescription opiates¹. Heroin overdose is also relevant given that three out of four heroin users reported abusing prescribed opiates prior to using heroin². Recent government-led initiatives have attempted to reduce opiate prescriptions for patients with chronic pain^{1,3}, but there are currently no guidelines regarding quantities of prescribed opioid medications for post-operative pain management. Balancing pain control with limiting opiate exposure may be a difficult task, especially in patients at risk for adverse events with narcotic use or potential diversion of prescribed opiate into abuse or addiction. Older patients may be at increased risk of development of chronic opiate abuse; a retrospective analysis of over 390,000 patients found that in opiate-naïve patients 66 years old and older who underwent a short-stay surgery and received post-operative opiates, these patients were 44% more likely to become a long-term opiate user by post-operative year one than those who did not receive post-operative opiate medications.⁴

In routine post-operative practice, many surgeons likely provide a standardized amount of pain medication after a procedure for all patients in anticipation of expected pain, potentially more than necessary in order to avoid patient phone calls. In Bates et al's survey of post-operative urology patients, there was an excess of prescribed opiates for over two thirds of patients⁵. Most surveyed patients did not know how to safely dispose of unused pills, and the majority of patients kept the excess at home. The median number of pills used was less than ten for minimally invasive procedures and less than twenty for the more invasive procedures despite prescribed numbers around twenty and thirty respectively. This meant that over 40% of prescribed medication was going unused and potentially available for diversion. Recent results from a similar survey in a urogynecology patient population showed that patients are using approximately one third of prescribed opiate medications after minimally invasive urogynecology surgery⁶. This study also showed that patients given a large quantity of medication used more of the medication. Given these findings that physicians are not appropriately prescribing opiate medications which may be potentially contributing to the opiate abuse epidemic, it is important to determine an appropriate amount of pills to prescribe after surgery so that surgeons can be better stewards of these potentially dangerous prescriptions. The aim of this study is to provide information to inform future guidelines for prescription opiates after urogynecologic surgery.

HYPOTHESIS

Patients prescribed fewer or no opiates will have no difference in satisfaction with pain control.

STUDY DESIGN

Randomized controlled non-inferiority clinical trial

Primary Outcome:

Patient satisfaction with pain control

Secondary Outcomes:

1. Number of opiate tablets used by patients
2. Number of patient requests for narcotic medication
3. Number of unscheduled visits for pain control
4. Time of return to baseline activities
5. Side effects of medications (such as constipation, dizziness)
6. Patient use of other analgesics (such as ibuprofen, acetaminophen)
7. Patient willingness to dispose of excess pills

Study Population: Study subjects will be recruited from patients that present to the Center of Urogynecology and Pelvic Floor Disorders in the Department of Obstetrics and Gynecology at their preoperative visit at Main Campus.

Inclusion Criteria:

1. Women 18 years or older
2. Women scheduled to undergo minimally invasive surgery within the urogynecology division at Cleveland Clinic with a plan to stay one night in the hospital afterwards for a benign indication which includes:
 - Vaginal hysterectomies with prolapse repair
 - Sacrospinous ligament fixations
 - Hysteropexy
 - Sacrocolpopexy
3. Women able to provide consent for research participation and to sign an informed consent

Exclusion Criteria:

- Women with chronic pain or chronic pain syndrome
- Women undergoing concurrent bowel surgery
- Women with pre-operative chronic opiate use
- Inability to comprehend written and/or spoken English
- Inability to provide informed consent
- Inability to take oxycodone
- Inability to take acetaminophen due to allergy or liver disease
- Women will be excluded if they undergo an unplanned laparotomy

- Pain catastrophization score
 - This is a previously published instrument to assess how patient's handle pain; those who score high on this instrument have increased rumination over pain, increased sense of helplessness, and magnification of pain. Those who score 30 or more (75%ile) will be excluded as they have a higher post-operative pain rating.⁷

Safety/Data Monitoring:

Any adverse event or unanticipated events will be reported immediately to the IRB using IRB WebKit. All events will be recorded and kept in a research binder assigned to this study in a locked office. Monthly reviews during the study period will be done by all involved study staff members to ensure that events are not occurring, and if they are, that they are being handled and reported properly. The study will be terminated if over 50% of patients in the decreased opiate group request more or stronger medication during interim analysis or have >20% decreased satisfaction to the control group; this will be assessed monthly at the reviews mentioned above.

STUDY PROCEDURES

Study Identification and Recruitment

Potential subjects will be identified by members of the Center for Urogynecology and Pelvic Reconstructive Surgery at the Cleveland Clinic Main Campus. At the time of decision for surgery, attending staff who have been counseled about how to discuss the study will bring up the study. Fliers will be available to give to patients. Patients will be offered a visit with research staff at this time. They also will have the opportunity to meet research staff at their preop visit which is when consent forms would be signed and prescriptions given. Phone calls from research staff will also be made to interested patients or potential subjects. Eligible patients who agree to participate will be provided written informed consent administered by the collaborators listed on the IRB. Consents can be obtained at the Cleveland Clinic Main Campus or Fairview hospital.

Randomization

All subjects will be scheduled for surgery by their surgeon. Consenting patients who meet inclusion criteria will be randomized into one of two arms: "routine opiate prescription" or "decreased opiate prescription" according to a computer-generated randomization schedule with random block sizes with the use of the JMP statistical software. The routine arm will receive twenty-eight tabs of oxycodone at discharge - thirty was the usual number prescribed for these surgeries, but new opiate prescribing guidelines limit the amount prescribed as 28 tablets based on morphine equivalent doses and a 7 day prescription limit. The decreased prescription arm will receive five tabs of oxycodone. All subjects will be instructed to use the opiate pills only as a back-up pain plan after the NSAID and acetaminophen. All subjects will be instructed to use the same schedule: schedule ibuprofen and acetaminophen for 3 days followed by these as needed. Subjects will have their prescriptions filled on day of discharge at the Cleveland Clinic pharmacy based on the randomization in addition to the following medications that per protocol all patients will receive unless contraindicated due to allergy/medication interaction: Colace (100mg tablets to take PO BID, #60), Miralax (17gm packets to take PO daily, #30), and ibuprofen (600mg tablets to take PO every 6 hours for 3 days postoperatively then as needed, #60). The use of scheduled NSAIDs is based on benefit of multimodal therapy in an effort to minimize opiate use. Despite these medications' potential effect to decrease effect seen between the study groups, their use in the trial provides increased clinical applicability.

Dispensing Medication

If the patient approves to participate in the study, they will receive the allotted post-operative medication at time of discharge prescriptions for their postoperative medications as above at their preoperative visit. In addition, patients will also receive a sealed envelope with a prescription for a back-up supply of pain medication (10 pills of oxycodone 5mg). They will be instructed to fill these only if they run out of the previous supply and are still requiring stronger pain medication. Because of the way the prescription will be written (with instructions to the pharmacy not to fill before the date of post-operative day 2), they cannot automatically fill the same day as discharge (post-operative day 1) and this prescription is only valid for two weeks after this date. They will be instructed that if they require more pain medication than this, they will need to be seen. Patients will be provided with a daily pain and activity diary and medication log. At their 6-week postoperative visit, patients will bring in this diary as well as any remaining opiate medication and/or the sealed envelope containing the back-up prescription.

Data Collection & Management:

Other than the study forms (see attached), the electronic medical record (EPIC) will be used to obtain basic medical information including medical problems, height & weight/BMI, past surgeries, current medications, and allergies.

Preoperative data will include the following:

- Patient age, race and ethnicity, menopausal state, tobacco use, BMI, education level, patient income level

Peri-operative data will include the following:

- Surgery performed
- Surgical complications
- EBL
- Hospital complications
- Delayed complications
- Prescribed medications (with detail given to agreement with randomization arm and if multimodal agents were not prescribed and for what reason)
- Post-operative pain scores at last RN assessment on day of discharge
- Medication records of quantity of narcotics used perioperatively (to be standardized to morphine equivalents)

Postoperative data will include the following:

- Patient's daily pain diaries including medications used which can be completed on paper diaries to be turned in at their post-operative visit OR entered electronically using REDCap (see below)
- Patient satisfaction with post-discharge pain control
- Patient's daily activities
- Whether patient received additional narcotic prescription through the following:
 - Study protocol through a phone call
 - Study protocol through an outpatient visit
 - Other (e.g. emergency room, urgent care)
- Patient satisfaction with bowel symptoms and constipation treatment as needed
- Number of pills used (as calculated by pill count or pain diary if pills not returned)
- Number of remaining pills (as calculated by pill count or pain diary if pills not returned)
- Patient's willingness to destroy remaining pills

Protection of each subject's personal health information will be a priority in this study. One master excel file containing subject personal information including name and medical record number will be kept in a password-protected file, on a designated protected research drive on a password-protected computer in a locked office at the Cleveland Clinic. In that file, each subject will be assigned a subject identification number that will be used for the purposes of data collection in order to de-identify subjects.

All paper forms used for data collection will be kept in a research cabinet dedicated to this project which will be locked at all times, in a locked office at the Cleveland Clinic. All forms will contain de-identified information – identification numbers will correspond to the subjects listed in the master excel file.

All study data will be transferred and managed electronically using REDCap (Research Electronic Data Capture). Each subject will be entered into REDCap using the assigned identification number from the master excel file. REDCap is a secure, web-based application designed to support data capture for research studies, providing user-friendly web-based case report forms, real-time data entry validation, audit trails, and a de-identified data export mechanism to common statistical packages. The system was developed by a multi-institutional consortium which was initiated at Vanderbilt University and includes the Cleveland Clinic. The database is hosted at the Cleveland Clinic Research Datacenter in the JJN basement and is managed by the Quantitative Health Sciences Department. The system is protected by a login and Secure Sockets Layers (SSL) encryption. Data collection is customized for each study based on a study-specific data dictionary defined by the research team with guidance from the REDCap administrator in Quantitative Health Sciences at the Cleveland Clinic. The REDCap database will include potential identifiers to enable online surveys. The collected potential patient identifiers include:

Date of Birth

Surgery Date

Subject Email (that they provide for the study)

Analysis Plan:

Sample size calculation was based on data suggesting a 92% satisfaction with a regimen of pain control similar to the study's control group. With a power of 90% at an alpha of 5%, we would require 57 subjects per arm. With a drop-out rate of 3% (based on 2016 post-operative visit "no-show" rates for the Urogynecology division – the timepoint when the primary outcome is collected), 59 subjects per arm will be recruited for a total goal recruitment of 118.

Continuous data will be analyzed using Student's *t* test or the Mann-Whitney U test, and proportions will be compared using a χ^2 or Fisher's exact test, as appropriate. P values ≤ 0.05 will be considered statistically significant, and we will use JMP as our statistical package to perform these analyses.

STUDY COST/BUDGET

The study budget is estimated at \$10,000. Estimated sample size is 59 patients per arm in each group for a total of 118 subjects.

Patient reimbursement:

- \$10 for parking at post-op visit x 118 subjects = \$1180
- \$25 for diary completion x 118 subjects = \$2950

Research Nurse Support:

- Salary: \$4586
- Fringe: \$1284

Summary of tasks for study:

	Preop	Day of Surgery	Post-operative: Daily Basis	Post-operative: As Needed Basis	Post-operative: Post-op visit
Informed consent	X				
Demographic data	X				
Randomization and scripts	X				
Patients fill prescription		X			
Patients receive backup written prescription in sealed envelope		X			
Pain diary and medication use			X		
Return to baseline function assessment			X		
Post-operative satisfaction survey					X
Remaining medication count					X
Patient reimbursement (parking and incentive – total \$35)					X

References:

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7. Sullivan M, Biship S, Pivik J. The pain catastrophizing scale: development and validation. *Psychol Assess*. 1995;7(4):524-532.