Effect of pre-operative tizanidine on postoperative urinary retention after sacrospinous vaginal vault suspension: a pilot study

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Purpose

The purpose of this study is to evaluate the effect of tizanidine on postoperative urinary retention after sacrospinous vaginal vault suspension compared with baseline data.

Background

Postoperative urinary retention has been defined as the inability to void despite having fluid in the bladder during the postoperative period (1). Urinary retention after pelvic reconstructive surgery requiring indwelling catheter or self-catheterization usage occurs in approximately 30-60% of patients postoperatively (1,2,3). Our prior retrospective chart review reviewing postoperative urinary retention rates after pelvic reconstructive surgery demonstrated postoperative urinary retention after a sacrospinous vaginal vault suspension to be approximately 78.9%.

Each patient after surgery undergoes a "voiding trial" where their voided volume is compared to their post-void residual volume. "Passing" a voiding trial has traditionally been defined as voiding a greater volume than the post-void residual volume (4). If the patient does not "pass" the voiding trial, the patient is characterized as having postoperative urinary retention and is discharged home with an indwelling catheter to prevent detrusor injury from bladder overdistention, pain and urinary tract infection (5).

Many women consider being discharged home with a Foley catheter to be a surgical complication and describe catheter use as the worst aspect of their surgery (1,6). Indwelling catheters are the leading cause of hospital-acquired urinary tract infections (UTIs), are often a source of embarrassment and inconvenience for patients, and often require additional office visits and healthcare utilization (7).

The leading hypotheses regarding the incidence of postoperative urinary retention after sacrospinous ligament suspension includes postoperative pain and pelvic floor muscle spasm leading to retention. The sacrospinous suspension includes a suture that is passed through the sacrospinous ligament and, therefore, through the coccygeus muscle with irritation of the pudendal nerve (8). The pelvic floor is a synergistic team of muscles that work together to support the pelvic organs and spasm of the coccygeus muscle, rather than an isolated muscle, can cause spasm of the entirety of the pelvic floor leading to retention. Tizanidine is a muscle relaxant which can work to alleviate this spasm and, theoretically, prevent postoperative urinary retention (9). Tizanidine also works as an alpha-adrenergic receptor blocker which can increase smooth muscle relaxation around the urethra specifically and, theoretically, improve urine flow (9).

Tizanidine is also frequently given for postoperative pain after sacrospinous ligament suspension and may act as an adjunct to a non-narcotic pain regimen to improve postoperative pain while reducing narcotic use after surgery. Postoperative buttock and posterior thigh pain are common symptoms after SSLF, with immediate pain reported in 6–84% of patients and persistent pain at 6 weeks occurring in 1–15% (7). Untreated acute postoperative pain has been shown to lead to increased morbidity and mortality (10). Pain is the most common reason for a postoperative unplanned hospital admission and poor postoperative pain control can lead to decreased ambulation, increased incidence of thromboembolism, and decreased inspiratory effort leading to postoperative pneumonia, therefore postoperative pain control is critical (11,12). In a country with rising narcotic-use and dependence, it is critical that we continue to explore non-narcotic alternatives for patients after surgery.

Postoperative urinary retention is extremely common after pelvic reconstructive surgery involving a sacrospinous vaginal vault suspension and is extremely bothersome to patients. Tizanidine is a low-risk,

well tolerated, cost-effective medication (9). No study to date has evaluated preoperative administration of tizanidine for postoperative urinary retention.

Hypothesis

We hypothesize that providing tizanidine preoperatively will improve postoperative urinary retention rates compared with our previously defined baseline data.

Objectives

The **primary objective** of this study is to evaluate whether preoperative administration of tizanidine will decrease the rate of postoperative urinary retention sacrospinous vaginal vault suspension compared with previously defined data. The **secondary objective** of this study is to evaluate for any differences in postoperative pain after administration of tizanidine compared to previously defined data.

Specific Aims

1. Evaluate the postoperative urinary retention rate in patients undergoing sacrospinous ligament suspension after postoperative administration of tizanidine.
2. Evaluate the postoperative pain scores after postoperative administration of tizanidine in patients undergoing sacrospinous vaginal vault suspension (postoperative nursing documentation performed in the recovery area based on a Likert scale of 0-10) and compare the differences in postoperative pain with previously collected data.
3. Evaluate the difference in unplanned admission the day or surgery or unplanned admission within 30 days after surgery, unplanned office visits within 30 days after surgery or Northshore encounters within 30 days after surgery after postoperative administration of tizanidine. These medical encounters will include any need for additional medical treatment, phone calls, complications or patient concerns within 30 days postoperatively. This data will be collected via chart review.

Outcome measures

1. Primary outcome measure:

a. Determine the postoperative urinary retention rates in patients undergoing a sacrospinous ligament suspension after postoperative administration of tizanidine. This will be determined immediately postoperative in the postoperative recovery room based on whether patients pass or fail their voiding trial described above. The result will be documented in electronic medical records and obtained from chart review.

2. Secondary outcome measures:

a. Determine differences in postoperative pain after postoperative administration of tizanidine. This data will be obtained by electronic data pull and chart review.

b. Determine the difference in unplanned admissions, office visits or Northshore encounters within 30 days after surgery after postoperative administration of tizanidine. This data will be collected via chart review.

Methods

This is a prospective trial of patients who are undergoing sacrospinous ligament suspension with or without concomitant incontinence or pelvic reconstructive surgery with the Center for Pelvic Health at the Northshore University Health System.

Women presenting to our tertiary urogynecology clinic with pelvic organ prolapse who decide to proceed with surgical treatment via a sacrospinous ligament suspension will be invited to participate in this study. This study will be discussed with the patient by their surgeon during their clinic initial screening visit or preoperative visit based on inclusion and exclusion criteria listed below. This study will involve no additional pre-operative tests or questionnaires, beyond our routine clinical pathway for women presenting with stress urinary incontinence. Written consent will be obtained.

During the initial clinic visit or at a subsequent encounter prior to their surgery, patients will be provided information on the research study by their care provider and given the opportunity to ask any questions. Patients will then be given a consent form to take home and review, discuss with others and consider participation. At the second preoperative encounter, patients will have another opportunity to discuss the study and ask any questions to their care provider. At that point, patients will be given the opportunity to sign the consent form if they would like to participate in the study. Participation is voluntary. For patients who will not have a second preoperative clinic visit prior to surgery, during the initial clinic visit, the care provider will discuss the research study, provide a consent form to the patient to review and ask for permission from the patient to be contacted by a study team member. If permission is granted, a study team member will contact the patient via telephone to discuss the study further and allow for the patient to consider participation in the study and ask any questions. If at that time the patient decides to participate in the study, written consent will be obtained the morning of surgery. All consent documentation and research participation will be documented in the patient's chart.

Patients who are undergoing a sacrospinous ligament suspension will be enrolled (after the previously described informed consent discussion) to receive a single preoperative dose of tizanidine 2mg or in the preoperative holding area on the day of their scheduled surgery as well as continued tizanidine postoperatively as needed every 6 hours.

After surgery, patients will then undergo a voiding trial in the recovery area. As described in prior studies, the patient will fail the voiding trial if voided volume is less than the PVR volume. Upon failing the voiding trial, the patient will be discharged home with a Foley catheter with plan for outpatient Foley catheter removal, consistent with our current protocol. According to our current protocol, patients discharged with a Foley catheter can either remove the catheter at home in 48-72 hours after surgery or call our office to have it removed at the next available appointment within 2-5 days postoperatively.

We will then evaluate the rate of postoperative urinary retention after administration of tizanidine compared with our previously studied and documented postoperative urinary retention incidence after sacrospinous ligament. Any collected information will be de-identified.

The current rate of postoperative urinary retention at our institution based on chart review after sacrospinous ligament suspension is 78.9%. Based on a sample size calculation to achieve 80% power, to evaluate for a 50% decrease in our urinary retention rate (from 78.9% to approximately 39.5%) we will need 23 subjects total. We aim to complete 23 subjects and expect to enroll 30 subjects to account for participant dropout.

Postoperative pain data will be evaluated by reviewing postoperative pain scales documented by the nursing staff in the postoperative area on a Likert scale 0-10. We will also evaluate narcotic administration in the postoperative area as a proxy for pain.

Inclusion criteria

Sacrospinous ligament suspension (CPT 57282)

Exclusion criteria

Age <18

Planned combined cases with colorectal surgery, general surgery, or gynecology-oncology

Known history of urinary retention

Known contraindication to tizanidine

Concomitant use of the following:

- Fluvoxamine, Ciprofloxacin (Patients are eligible if 3-5 half-lives have passed since they have taken Fluvoxamine, Ciprofloxacin)
- Potent CYP1A2 inhibitors
- Oral contraceptive
- Alpha-adrenergic agonists

Stage 4 Chronic Kidney Disease (eGFR <30), or worse

Breastfeeding

Hypersensitivity to tizanidine

Pre-existing psychiatric illness

Hypotension and chronic hypotension (<90/50 mmHg)

Variables

MRN

Age (at time of surgery)

Gravity and para

Race/ethnicity

Smoking status

Menopausal status

BMI

Comorbid conditions

- Diabetes
- Hypertension
- Other cardiovascular disease
- Respiratory disease
- Obstructive sleep apnea
- Chronic pain conditions

Prior hysterectomy

Prior abdominal surgery

History of prior prolapse surgery

History of prior incontinence surgery

Continence status

Prolapse stage

Location of surgery (Highland Park Hospital, Evanston)

Type of anesthesia

ASA grade

Incontinence procedure

Mid-urethral sling placement: CPT 57228

Concomitant prolapse procedures

- Anterior colporrhaphy: CPT 57240

- Posterior colporrhaphy: CPT 57250
- Combined anterior and posterior colporrhaphy: CPT 57265
- Hysterectomy
- Rectopexy

Intraoperative complications
Additional procedures (ie. lysis of adhesions)
Intraoperative consultations
Length of procedure
Estimated blood loss
Surgeon
Surgeon experience (< 5 years, > 5 years)
Total time in PACU
Time of day in ASU
Total time in ASU
Immediate postoperative complications
Uncontrolled pain
Postoperative pain scores upon admission to the ASU
Postoperative pain scores at discharge
Reason for postoperative admission (surgeon choice, comorbid conditions, nausea/vomiting, etc.)
Time from voiding trial to void
Postoperative urinary retention
Postoperative urinary tract infection (UTI)
Unanticipated healthcare encounters

- Urogynecology office visit (excluding voiding trial(s))
- ED visit
- Readmission within 30 days of discharge
- Unplanned phone calls

Complications 30 days after discharge

- Urinary tract infection
- Reoperation
- Venous thrombotic event

Statistical Methodology

A statistician from the NorthShore Research Institute will assist with statistical analysis. Data will be analyzed using SAS 9.4 (SAS Inc., Cary, NC). Demographic and clinical characteristics between groups will be compared using Student t-test (parametric) or Mann-Whitney U test (nonparametric) for continuous variables and Chi-squared test or Fisher exact test for categorical variables. Multivariable logistic regression models will be constructed to examine the relationship of an outcome with demographic and clinical covariates. Statistical significance will be defined at p-value < 0.05.

Literature review

1. Wang, Rui, et al. “Voiding Trial Outcome Following Pelvic Floor Repair without Incontinence Procedures.” *International Urogynecology Journal*, vol. 27, no. 8, Aug. 2016, pp. 1215–20. *Springer Link*, https://doi.org/10.1007/s00192-016-2975-y.1.

2. Geller, Elizabeth J., et al. “Diagnostic Accuracy of Retrograde and Spontaneous Voiding Trials for Postoperative Voiding Dysfunction: A Randomized Controlled Trial.” *Obstetrics &*

Gynecology, vol. 118, no. 3, Sept. 2011, pp. 637–42. *DOI.org (Crossref)*, https://doi.org/10.1097/AOG.0b013e318229e8dd.
3. Willis-Gray, Marcella G., et al. "Is a Postvoid Residual Necessary? A Randomized Trial of Two Postoperative Voiding Protocols." *Female Pelvic Medicine & Reconstructive Surgery*, vol. 27, no. 2, Feb. 2021, pp. e256–60. *DOI.org (Crossref)*, https://doi.org/10.1097/SPV.0000000000000743.
4. Pulvino, James Q., et al. "Comparison of 2 Techniques to Predict Voiding Efficiency after Inpatient Urogynecologic Surgery." *The Journal of Urology*, vol. 184, no. 4, Oct. 2010, pp. 1408–12. *PubMed*, https://doi.org/10.1016/j.juro.2010.05.096.
5. Pomajzl, A. J., and Larry E. Siref. "Post-Op Urinary Retention." *StatPearls*, StatPearls Publishing, 2022. *PubMed*, http://www.ncbi.nlm.nih.gov/books/NBK549844/
6. Elkadry, Eman A., et al. "Patient-Selected Goals: A New Perspective on Surgical Outcome." *American Journal of Obstetrics and Gynecology*, vol. 189, no. 6, Dec. 2003, pp. 1551–57. *DOI.org (Crossref)*, https://doi.org/10.1016/S0002-9378(03)00932-3.
7. Lovatsis D, Drutz HP. Safety and efficacy of sacrospinous vault suspension. Int Urogynecol J Pelvic Floor Dysfunct. 2002;13(5):308–13.
Unger CA, Walters MD. Gluteal and posterior thigh pain in the postoperative period and the need for intervention after sacrospinous ligament colpopexy. Female Pelvic Med Reconstr Surg. 2014;20(4):208–11.
8. *Kondo W, Corrêa Leite GK, Fernandes R, Kamergorodsky G, Fin FR, Cordeiro Fernandes LF et al. Useful pelvic retroperitoneal neuroanatomy for benign gynecologic surgery: a cadaveric dissection. J Minim Invasive Gynecol 2020;22:S1553–4650(20)30245–4.*
Roshanravan SM, Wieslander CK, Schaffer JI, Corton MM. Neurovascular anatomy of the sacrospinous ligament region in female cadavers: Implications in sacrospinous ligament fixation. Am J Obstet Gynecol. 2007 Dec;197(6):660.e1-6. doi: 10.1016/j.ajog.2007.08.061. PMID: 18060971.
9. Ghanavatian S, Derian A. Tizanidine. [Updated 2023 Aug 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519505/
10. Lovich-sapola J, Smith CE, Brandt CP. Postoperative pain control. Surg Clin North Am. 2015;95(2):301-18.
11. Schug SA, Chong C. Pain management after ambulatory surgery. Curr Opin Anaesthesiol. 2009;22(6):738-43.
12. Collins SA, Joshi G, Quiroz LH, Steinberg AC, Nihira MA. Pain management strategies for urogynecologic surgery: a review. Female Pelvic Med Reconstr Surg. 2014;20(6):310-5.