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The effect of scopolamine patch use on post-operative voiding function after transobturator slings

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Abstract

Objectives—The aim of this study was to determine whether the use of a pre-operative transdermal scopolamine patch for post-operative nausea and vomiting prophylaxis affects the success of a voiding trial after a transobturator tape sling procedure.

Methods—This study is a retrospective cohort study of adult women who underwent a transobturator tape sling procedure without concomitant procedures from February 1, 2009 through August 1, 2010. The exposed group included all eligible women who received a pre-operative transdermal scopolamine patch. For each exposed woman, we selected the next two consecutive eligible women who did not receive a transdermal scopolamine patch to be included in the unexposed group. The primary outcome was post-operative voiding trial failure.

Results—We identified 35 women who met eligibility criteria and used a pre-operative transdermal scopolamine patch, and included 70 women who did not use a pre-operative transdermal scopolamine. A significantly higher proportion of women in the transdermal scopolamine patch group (54.3%) failed their voiding trial than in the group that did not receive transdermal scopolamine (7.1%, $P < 0.001$). A history of an incontinence procedure, older age and higher body mass index strengthened the association between transdermal scopolamine patch and voiding trial failure. The adjusted model yielded a risk ratio for voiding trial failure of 13.8 (95% CI: 5.2–36.5) for women who received transdermal scopolamine patch compared to those who did not.

Conclusions—The results of this study demonstrate that use of transdermal scopolamine patches for postoperative nausea and vomiting prophylaxis may negatively affect the success of voiding trials after transobturator tape sling procedures.

Keywords

scopolamine; sling; voiding dysfunction

Introduction

Stress urinary incontinence (SUI) is a common condition affecting 4 to 35% of women. (1) The cumulative lifetime risk of surgery for the treatment of SUI is 13.6%. (2) The most commonly performed procedure for treatment of SUI is the mid-urethral sling. (3) The mid-urethral sling can be performed as an outpatient procedure under local anesthesia (usually with conscious sedation) and has been extensively studied and shown to have excellent long-term results. (4-6) Currently, mid-urethral slings are placed using either a retropubic approach (e.g. tension-free vaginal tape) or a transobturator approach (e.g. transobturator tape). Although serious complications are rare with either type of procedure, there are other potential risks, the most common of which are voiding dysfunction and urinary retention. (5, 7)

Voiding dysfunction can be defined generally as the subjective report of difficulty voiding; although, some authors have applied specific criteria to diagnose this condition. (8) Elevated post-void residuals, greater than 100 mL, or a spontaneous void of less than 75% of the total starting bladder volume are two common criteria for voiding dysfunction. (9) The incidence of voiding dysfunction following a mid-urethral sling can be as high as 34%. (10, 11) Urinary retention is a severe form of voiding dysfunction in which the patient is unable to void spontaneously and requires continuous or intermittent catheterization. Catheterization can increase the risk of urinary tract infection and cause significant discomfort and distress. (12) While both post-operative voiding dysfunction and urinary retention usually resolve spontaneously over a period of days, some cases require revision of the sling to restore normal voiding patterns. (5, 13)

Numerous studies have examined potential risk factors for voiding dysfunction following mid-urethral sling. Pre-operative urodynamic measurements have not been shown to predict post-operative voiding outcomes; however, elevated pre-operative post void residual volumes, diabetes, and older age have been identified as risk factors. (14-18) Multiple medications also have been linked to voiding dysfunction including anticholinergics, sympathomimetics, and β -blockers. (19)

Post-operative nausea and vomiting is another common complication encountered in the immediate post-operative period after mid-urethral sling placement and is a frequent cause of patient dissatisfaction with the procedure. In addition, post-operative nausea and vomiting may cause delays in discharging patients from the post-anesthesia care unit. Scopolamine, also known as levo-duboisine or hyoscine, is a tropane alkaloid drug with antimuscarinic and anticholinergic effects that is used to prevent post-operative nausea and vomiting. While the transdermal scopolamine (TDS) patch has significant benefits over other anti-emetics, adverse effects such as dry mouth, visual disturbances, cognitive effects, and urinary retention, have been reported. (20-22) The aim of this study was to determine whether the use of a pre-operative TDS patch for post-operative nausea and vomiting prophylaxis affects the success of a voiding trial after a transobturator tape sling procedure.

Materials and Methods

This was a retrospective cohort study of adult women who underwent a transobturator sling (TVT-O, Gynecare, Menlo Park, California) procedure without concomitant procedures from February 1, 2009 through August 1, 2010. This time period was chosen due to resource constraints. All women had stress urinary incontinence confirmed via urodynamic testing and all procedures were performed by a urogynecologist with the assistance of a female pelvic medicine and reconstructive surgery fellow. The exposed group included all eligible women who received a pre-operative transdermal scopolamine patch (TDS) patch. For each exposed woman, we selected the next two chronologically consecutive women who met eligibility criteria and did not receive a TDS patch to be included in the unexposed group. The institutional review board at Mount Auburn Hospital approved this study.

All patients at our institution who undergo a surgical procedure are screened in the pre-operative holding area by the anesthesiologist or nurse anesthetist for a history of motion sickness and/or nausea and vomiting associated with anesthesia. Patients with a history of motion sickness or post-operative nausea or vomiting are offered pre-operative TDS. All TVT-O procedures are performed with a local anesthetic (30mL of 0.25% bupivacaine anesthetic injected into the vaginal mucosa and medial thigh, through the medial portion of the obturator foramen) and intravenous administration of midazolam (2mg), fentanyl (100mcg), dexamethasone (4mg), ondansetron (4mg), and a propofol infusion intra-operatively at 50-150mg/kg/min. The TVT-O procedure is performed consistently in the same manner as described by de Leval in 2003 to ensure a standardized method of sling tensioning during each procedure. (23)

Prior to discharge from the post-anesthesia care unit, all patients undergo an active voiding trial. The voiding trial involves backfilling the bladder with 300 mL of normal saline. The 16 French Foley catheter is then removed, and the patient is asked to void within 15 minutes. The voided volume is measured in a urinary collection hat. If 200 mL or more of the fluid (or at least two-thirds of the instilled volume, if the patient was unable to hold the entire 300 mL) is voided, the patient is considered to have passed the voiding trial and discharged home without re-insertion of the catheter. Therefore, the criterion for passing the voiding trial is a post-void residual of one third or less of the total volume instilled into the bladder. This criterion is based on prospective literature demonstrating that a post-void residual of one third or less of the instilled volume did not require reinsertion of the catheter. (24, 25) A patient who fails her voiding trial has the catheter replaced and is instructed to return to the office in two to three days for a repeat voiding trial. A bladder ultrasound (BladderScan, Verathon Medical, Bothell, WA) is performed as needed to confirm the post-void residual.

There was no a priori sample size calculation; this was a sample of convenience that included all women who met the exposure definition. Data are presented as mean $\pm$ standard deviation, median (interquartile range) or proportion, based on data type and distribution. Categorical data were compared using a chi-square or Fisher's exact test; continuous data were compared with the t test of Wilcoxon rank sum test. We used Poisson regression with robust error variance to calculate risk ratios (RR) and 95% confidence intervals (CI). Variables believed to influence both the likelihood that a patient used pre-operative TDS and

the risk of failing the post-operative voiding trial were evaluated as potential confounders. In addition to age and body mass index, this list included variables associated with a prior exposure to anesthesia that would have created the opportunity for a woman to have a known history of post-operative nausea and vomiting, such as parity and prior vaginal or incontinence surgery. Variables that altered the risk ratio by >10% were retained in the final model. While not a potential confounder, given that use of narcotics in the immediate post-operative period is a strong risk factor for postoperative urinary retention, we evaluated whether post-operative narcotics was an effect modifier. (26, 27) A p value <0.05 was considered to be statistically significant.

Results

We identified 275 women who met eligibility criteria during our study period. Of these, 35 (12.7%) used pre-operative TDS. For each of these exposed women, we selected the next two consecutive eligible women who did not receive a TDS patch, yielding 70 unexposed women who did not use pre-operative TDS. Women who used pre-operative TDS were younger, less likely to be post-menopausal and less likely to have prolapse (all P = 0.04). They also had a slightly higher body mass index, though this difference did not reach statistical significance (P=0.06; Table 1).

In the TDS group, the median operative time was 8 minutes shorter (P=0.04) than in the group that did not receive TDS. In addition, women in the TDS group were nearly twice as likely (51.4%) to use narcotics in the immediate post-operative period compared with women who did not receive TDS (28.6%; P=0.02; Table 2).

A significantly higher proportion of women in the TDS group (54.3%) failed their voiding trial than in the group that did not receive TDS (7.1%), yielding a crude risk of voiding trial failure of 7.6 (95% CI: 3.1 - 18.6). Women who used TDS also voided a significantly smaller volume (P<0.001; Table 2). Although age, history of an incontinence procedure and body mass index were not independently associated with post-operative voiding trial failure (all p = 0.57), each of these variables had an appreciable effect on the association between TDS and voiding trial failure and was included in the adjusted model. The fully adjusted model yielded a risk ratio for voiding trial failure of 13.8 (95% CI: 5.2-36.5) for women who received TDS compared to those who did not. In addition, there was no evidence of effect modification as demonstrated by similar adjusted risk ratios for the association between TDS and voiding trial failure among women who did not receive post-operative narcotics (13.9; 95% CI: 3.3-58.8) and those who did (15.2; 95% CI: 2.4-94.3).

Discussion

The results of this study demonstrate that use of TDS pre-operatively for nausea and vomiting prophylaxis may negatively affect the success of voiding trials after transobturator tape sling procedures. Women who received TDS were more likely to fail their voiding trial and void smaller volumes than women who did not receive TDS. This holds true after controlling for potential confounding variables including age, body mass index and prior incontinence procedures.

An unexpected finding of the study was that women who received TDS were significantly younger and consequently also significantly less likely to be menopausal. Anesthesia may have been less likely to offer TDS to an older patient, given that TDS can cause adverse effects such as visual disturbances and cognitive impairment. Given this discrepancy, we controlled for age in the regression model and found that TDS still is associated with patients failing to pass their voiding trials. We also found that a higher proportion of women in the TDS group used narcotics after surgery. The association between TDS use and voiding trial failure was similar in the group that used narcotics and those that did not use narcotics.

Several studies have evaluated the effectiveness of TDS on controlling postoperative nausea and vomiting and have found this medication to be extremely safe and effective. (22) The controlled release of the TDS patch (5 µg/hour over 72 hours) may decrease the risk of plasma concentration-related adverse events. Pharmacologically, there is an initial 140 µg burst of scopolamine transdermally that results in a peak plasma concentration after approximately 8 hours. However, the pharmacokinetics vary among patients. This initial release could be responsible for the saturation of the muscarinic bladder receptors leading to postoperative voiding dysfunction. Another possible mechanism is the relatively slow onset of action of TDS. Although circulating plasma levels can be detected within four hours, plasma levels may not peak until 24 hours after application. This slow onset of action could prolong a patient's inability to mount a detrusor contraction to adequately empty her bladder. (28, 29)

In the anesthesia literature, Keita et al. prospectively collected data to find factors that could predict early postoperative urinary retention in the post-anesthesia care unit. The authors found that intraoperative fluids, age, and bladder volume on entry to the post-anesthesia care unit, independently increased the risk of urinary retention. Interestingly, atropine and atropine-like medications were not associated with urinary retention. (30) The effect of anti-cholinergic medication on postoperative voiding trial results in women undergoing urogynecologic surgery was examined retrospectively by Walter et al. Similar to our results, the authors found the exposure to anticholinergic medications increases the risk of failing a postoperative voiding trial. (29) Our study is unique, however, because we specifically examine the incidence of postoperative voiding dysfunction in conjunction with TDS among patients undergoing one type of anti-incontinence procedure. Walter et al. examined the effect of multiple anti-cholinergic medications on patients undergoing prolapse or anti-incontinence procedures. (31)

Strengths of our study include a standardized perioperative medication regimen by anesthesia, as well as a consistent operative and sling tensioning technique and a standardized voiding trial used by all providers in our practice. All patients underwent the same procedure and did not undergo concomitant prolapse procedures; therefore they were similar in their surgical exposure.

There were several limitations to our study. Due to the retrospective nature of this study, the method by which anesthesia offered TDS to patients was not standardized. While we did not record if patients were on other anti-cholinergic medications or other medications that may have had an anti-cholinergic-like effect, we would expect that these patients would be more

likely to be in the group that did not receive TDS due to the assumption that anesthesia would be less likely to encourage an additional anti-cholinergic medication for patients already taking a medication in that class. If some of the unexposed truly were exposed to other anti-cholinergic medications, then our findings would be an underestimate of the true effect. We also did not record data on co-morbidities, such as diabetes, that could affect the likelihood of passing the voiding trial. It is unclear whether these types of conditions might have influenced whether someone received TDS. Although the generalizability of our findings could be limited by the fact that we restricted to women undergoing TVT-O procedures, we believe that the mechanism of action by which TDS increases the risk of a failed voiding trial would be similar for other urogynecologic procedures.

This study suggests that scopolamine may be associated with increased risk of postoperative voiding dysfunction in patients undergoing transobturator suburethral slings. This finding could potentially be used as a tool for physicians to better counsel patients of their risk of postoperative urinary retention after these procedures. Physicians should question patients about a history of postoperative nausea and vomiting and counsel them appropriately about the potential risks with certain medications and their effects on postoperative voiding function, including the use of TDS. Alternative anti-emetics that do not have anticholinergic properties should be considered in patients with a history of post-operative nausea and vomiting who are undergoing transobturator tape sling procedures.

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Table 1
Pre-operative participant characteristics

Characteristic	Scopolamine		P
	Yes n = 35	No n = 70	
Age (years)	50.5 ± 9.4	57.5 ± 12.4	0.004
Body mass index (kg/m ²)	30.9 ± 6.2	28.3 ± 6.8	0.06
Parity			0.24
Nulliparous	1 (2.9)	7 (10.0)	
1	2 (5.7)	9 (12.9)	
2	32 (91.4)	54 (77.1)	
Post-menopausal	8 (22.9)	33 (47.1)	0.02
Previous incontinence procedure	2 (5.7)	12 (17.1)	0.13
Previous vaginal procedure	10 (28.6)	18 (25.7)	0.76
Prolapse present (any stage)	32 (91.4%)	51 (72.9)	0.04
Stage of prolapse			0.09
None	3 (8.6)	19 (27.1)	
Stage I	18 (51.4)	28 (40.0)	
Stage II	14 (40.0)	21 (30.0)	
Stage III	0 (0.0)	2 (2.9)	

Data are presented as mean ± standard deviation or n (%)

Table 2
Intra-operative and post-operative outcomes

Outcome	Scopolamine		P
	Yes n = 35	No n = 70	
Operative time (min)	41.0 (35.0-53.0)	49.0 (40.0-58.0)	0.04
Estimated blood loss			0.32
20cc	19 (54.3)	45 (64.3)	
> 20cc	16 (45.7)	25 (35.7)	
Post-operative narcotic use			0.02
Yes	18 (51.4)	20 (28.6)	
No	17 (48.6)	50 (71.4)	
Trial of voiding			<0.001
Passed	16 (45.7)	65 (92.9)	
Failed	19 (54.3)	5 (7.1)	
Amount voided in trial of voiding (cc)	170.0 (150.0-300.0)	300.0 (225.0-400.0)	<0.001

Data are presented as median (interquartile range) and n (%).