Published in final edited form as:

Eur J Obstet Gynecol Reprod Biol. 2014 October ; 181: 37–40. doi:10.1016/j.ejogrb.2014.07.016.

SINGLE VERSUS MULTI-DOSE ANTIBIOTIC PROPHYLAXIS FOR PELVIC ORGAN PROLAPSE SURGERY WITH GRAFT/MESH

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Abstract

Objective—To compare the risk of postoperative infections in women who receive single-dose versus multi-dose prophylactic antibiotic regimen during prolapse surgery with mesh/graft.

Study Design—Retrospective cohort study of 460 women who underwent prolapse surgery with mesh/graft. We compared women who received a single-dose prophylactic antibiotic regimen to those who received a multi-dose regimen. The primary outcome was the presence of any post-operative infection, defined as the presence of any of the following infections: urinary tract infection (UTI), fever, wound or trocar site infection, mesh infection or pelvic abscess. Associations between prophylactic antibiotic regimen and post-operative infections were estimated using univariable and multivariable analysis.

Results—Rate of any postoperative infection was similar between the single-dose and multi-dose groups (19% vs. 16%, $p=0.50$). Rate of UTI was significantly higher in the single-dose compared to the multi-dose group (13% vs. 7%, $p=0.03$). On multivariable analysis, after controlling for vaginal route of surgery, the odds of UTI was not significantly different between groups (OR 0.59, 95% CI 0.27, 1.26).

Conclusion—A single dose antibiotic regimen is sufficient for prophylaxis against post-operative infections in women undergoing prolapse surgery with graft/mesh.

Keywords

pelvic organ prolapse; mesh; graft; infection; antibiotic prophylaxis

INTRODUCTION

Approximately one-third of surgeries performed for pelvic organ prolapse are augmented with graft or mesh material. [1] The United States Food and Drug Administration (FDA)

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Conflict of Interest: The authors report no conflict of interest

lists infections as one of the most frequent adverse events reported after mesh-augmented prolapse surgery.[2] Infections reported after prolapse repair using mesh or graft include urinary tract infection (UTI) with reported rates of 3.5% to 31%[3–6], wound infections (3–6%) [3, 6], vaginal infections (0–18.4%) [4, 7], mesh infections (1%) [8], and pelvic infections and abscess (1–2%) [9, 10].

Antibiotic prophylaxis is widely accepted as a means of decreasing postoperative infectious morbidity and is recommended for surgery in women undergoing prolapse surgery with mesh. Based on data from the vaginal hysterectomy and orthopedic literature [11, 12], the American Urologic Association(AUA) recommends antimicrobial prophylaxis for 24hours or less at the time of “vaginal urologic surgery” and “surgery involving implanted prosthesis”. [13] The American College of Obstetrics and Gynecology(ACOG) recommends a single dose of perioperative antibiotic for “urogynecology procedures, including those involving mesh”. [14] However, the optimal duration of antibiotics prophylaxis for women undergoing prolapse surgery is not known. Studies comparing single dose to multi-dose antibiotic prophylaxis regimens in women undergoing prolapse surgery with mesh are lacking and it is unclear if these women have any additional benefit from multi-dose as compared to single-dose regimens.

The aim of this study was to compare the risk of postoperative infections in women who receive single-dose versus multi-dose prophylactic antibiotic regimens during prolapse surgery augmented with mesh/graft.

MATERIAL AND METHODS

Following approval by the institutional review board at the University of Pennsylvania, we conducted a retrospective cohort study of women who had undergone prolapse surgery between January 2008 and March 2012 in the University of Pennsylvania Health System. Eligible subjects were identified by Current Procedural Terminology codes for prolapse surgeries in which mesh or graft could have been used (anterior colporrhaphy, posterior colporrhaphy, combined anterior-posterior colporrhaphy, combined anterior-posterior colporrhaphy with enterocele repair, insertion of mesh for repair of pelvic floor defect, vaginal repair of enterocele, extra-peritoneal vaginal colpopexy, intra-peritoneal vaginal colpopexy, abdominal sacrocolpopexy, laparoscopic sacrocolpopexy). We were purposefully broad in our search to minimize missing any cases. Inclusion criteria were surgical repair of prolapse with mesh or graft as documented on the operative report, administration of perioperative antibiotics, and follow up of at least 6 weeks after surgery. We excluded women with prolapse surgery in which mesh was only used for anti-incontinence procedure such as sling, incomplete documentation regarding antibiotic administration, women with less than 6 weeks post operative follow up, and women who underwent concomitant non-gynecologic surgery.

Preoperative data recorded included age, body mass index, race, parity, smoking status, hormone use, medical co-morbidities, preoperative prolapse stage, and preoperative post void residual volume. Surgical and perioperative data including surgical approach, procedures performed, length of surgery, antibiotic choice and regimen, were also recorded.

Surgical approach was classified as abdominal (robotic or open) or vaginal. A co-incidental vaginal procedure was defined as a vaginal procedure (such as sling or posterior repair) in a patient who had undergone abdominal prolapse surgery. Postoperative information on duration of indwelling catheter, number of voiding trials, prescription of antibiotic prophylaxis for prolonged indwelling catheter, and postoperative complications were extracted.

Women received either a single-dose or multi-dose perioperative antibiotic regimen at the time of surgery based on the surgeon's usual practice. A single-dose regimen was defined as the administration of a dose of antibiotics within one hour of incision and no other antibiotic given in the postoperative period except in the presence of a diagnosed infection. Patients who received one additional dose of antibiotics in cases that exceed four hours in length were included within the single-dose group. A multi-dose regimen was defined as administration of a dose of antibiotics within one hour of incision followed by additional doses in the postoperative period in the absence of a clinically diagnosed infection.

Our primary outcome was the presence of any postoperative infection, defined as the presence of any one of the following: UTI, fever, wound or trocar site infection, mesh infection, or pelvic abscess. A UTI was defined as the documentation of irritative voiding symptoms such as dysuria, worsening urgency, frequency, or nocturia requiring antibiotics treatment in the six-week period following surgery. Urinalysis and urine culture data were collected when available. Postoperative fever was defined as documentation of a temperature greater than 101F OR a temperature greater than 100.4 on two occasions at least four hours apart, excluding the first 24h postoperative, within six weeks of surgery. [15] The diagnosis of a wound or trocar site infection was based on documentation of examination findings by a physician or nurse and antibiotic treatment for wound infection within the six week postoperative period. The diagnosis of mesh infection was based on the documentation of signs of local tenderness at the site of mesh insertion with or without the presence of redness or purulent discharge within the six week postoperative period. [16]

We compared demographic data between the single-dose and multi-dose groups using Pearson chi-squared tests for categorical variables and student's t-tests or Wilcoxon Rank Sum test as appropriate for continuous variables. The odds ratio of postoperative infections in the two groups was estimated using univariable and multivariable logistic regression analysis. Baseline characteristics that were significantly different between the two groups were included in our multivariable model as potential confounders. All reported p-values were two-sided and p-values < 0.05 were considered statistically significant. All data analysis was performed in STATA 10.1(Stata Corp., College Station, TX). Prior studies have reported that UTI is the commonest infection in women undergoing prolapse surgery with mesh. The rate of UTI in women undergoing prolapse surgery and who had received a single dose of antibiotics is approximately 10% [6, 7, 18]. Our retrospective sample would allow us to detect a three-fold reduction in the rate of UTI between the single dose and multi-dose groups with power of 80% at a significance level of 0.05.

RESULTS

During the study period, 489 women underwent graft/mesh-augmented prolapse surgery by one of four attending surgeons and met our eligibility criteria. We excluded 4 women due to missing data on antibiotic regimen, 6 were excluded due to less than six weeks follow up, and 19 women underwent concomitant non-gynecologic surgery, resulting in 460 records for analysis. Of these, 306(67%) received a multi-dose regimen and 154(33%) received a single-dose regimen.

Antibiotics administered included cefazolin alone(77%) or cefazolin plus gentamicin or metronidazole (5%). Women allergic to penicillin or cephalosporins received gentamicin and/or clindamycin(11%), vancomycin(3%), levofloxacin(1%), or doxycycline(<1%). The median number of doses in the multidose group was 3 administered during the first 24 hours after surgery (range 2–4). Antibiotic dosing regimens (single or multidose) administered were based on the surgeon's usual practice and preference. Surgeons 1 and 2 preferred a multidose regimen and 88% and 87%, respectively, of their cases received a multidose regimen. A hospital-wide policy resulted in a change of practice in December 2011 when they switched uniformly to a single dose regimen. Surgeons 3 and 4 preferred a single-dose regimen and 90% cases of surgeon 3 and 100% cases of surgeon 4 received a single dose regimen. In both groups, all patients who were discharged with indwelling foley catheters received prophylactic antibiotics.

Baseline demographic data is presented in table 1. Age, body mass index, tobacco use, baseline post-void residual and co-morbid conditions were not significantly different between the two groups. The differences in route of surgery and duration of indwelling catheter reflect individual surgeon practice patterns. Women in the single-dose group had a higher overall prolapse stage, were more likely to have undergone a vaginal or co-incidental vaginal procedure for prolapse or incontinence (82% vs. 26%, $p < .001$) and had an indwelling catheter for a significantly longer duration (4.2 ± 4.1 vs. 2.7 ± 2.4 days, $p < .001$) than the multi-dose group. However, the number of voiding trials was similar between the two groups.

Any post-operative infection

Overall, 79/460(17%) of women were diagnosed with any postoperative infection. The rate of any postoperative infection was similar in women who underwent vaginal and coincidental vaginal procedures compared to those who underwent abdominal procedures alone (20% v, 15%, $p=0.18$). The risk of post operative infection was not associated with preoperative prolapse stage or duration of indwelling catheter. The rate of any postoperative infection was similar in the single dose and the multi-dose group (19% vs.16%, $p=0.50$) (Table 2). The odds of any postoperative infection were not significantly lower than for the multi-dose compared to the single-dose groups (Odds ratio 0.84, 95% CI (0.51, 1.39)).

Urinary tract infection

The commonest reported infection was a UTI (41/460, 9%). Positive urinalysis and urine cultures were documented in 29/41(71%) women. Univariable analysis showed no

association between development of UTI and preoperative prolapse stage, duration of indwelling catheter, or choice of antibiotic used in patients with indwelling catheter. The rate of UTI was higher in women who underwent vaginal and co-incidental vaginal procedures compared to those who underwent abdominal procedures alone (24/207, 12% v. 17/253, 7%); however, this difference did not reach statistical significance ($p=0.07$). The rate of UTI was similar in women who had a concomitant sling and women who did not (19/177, 10.7% v. 22/283, 7.8% $p=0.28$).

The rate of UTI was significantly lower for the multi-dose than the single-dose group (7% vs. 13%, $p=0.03$). In the subgroup of women who underwent vaginal or coincidental vaginal procedures, the rate of UTI was similar in the single dose and multi-dose groups (17/126, 13% v. 7/81, 9% $p=0.29$). On univariable analysis, women in the multi-dose group were at significantly lower odds for UTI than women in the single-dose group (OR 0.49, 95% CI (0.26, 0.94)). On multivariable logistic regression analysis, after controlling for vaginal and co-incidental vaginal procedures, the odds of UTI for women in the multi-dose group and the single-dose group was similar (OR 0.59, 95% CI 0.27, 1.26, $p=0.08$).

Other infections

Postoperative fever was reported in 7% (32/460) women; the duration of fever ranged from 1 to 3 days (median 1 day). Reported causes of fever were: atelectasis (7/32, 22%), UTI/pyelonephritis (6/32, 19%), wound infection (3/32, 9%), pneumonia (3/32, 9%), and unknown (13/32, 41%). The rate of wound/trocar site infection was low. There were no documented cases of mesh infection or pelvic abscess. The rates of post-operative fever and wound/trocar site infections were not significantly different between the two groups (Table 2).

COMMENT

We report the rate of post-operative infection in a cohort of 460 women who underwent graft/mesh-augmented prolapse repair. In this cohort of women, all of whom received prophylactic antibiotic, either single dose or multi-dose, the rate of any post-operative infection was 17%. The commonest postoperative infection was UTI (9%) followed by transient fevers (7%). No case of mesh infection or pelvic abscess was documented. Our findings should reassure patients and surgeons that when prophylactic antibiotics are used, the rate of serious pelvic infections in women who undergo prolapse surgery with mesh is low.

The optimal regimen of prophylactic antibiotics for women undergoing prolapse surgery with mesh is not known. Ensuring that adequate concentration of antibiotics are available in the tissue to kill bacteria that inoculate the wound must be balanced with overprophylaxis which may lead to introduction of resistant bacteria, increased costs, and increased incidence of adverse reactions. In this study, the rate of any postoperative infection was similar between women who received a single dose (19%) or a multidose antibiotic prophylaxis regimen (16%). The rate of UTI was significantly higher in the single dose than the multi-dose group (13% v. 7%, $p=0.03$), however, women in the single-dose group were more likely to have undergone vaginal or coincidental vaginal surgery than women in the multi-

dose group (82% vs. 26%, $p < .001$). Vaginal surgery is a known risk factor for UTI [17]. After controlling for the confounding effect of vaginal surgery, women in the single dose group were no longer at increased odds for UTI than the multi-dose group. These findings suggest that a single dose of antibiotics is likely sufficient for preventing infection in women who undergo prolapse surgery with mesh.

Similar to a prior study [17], we found a higher rate of UTI in the vaginal and coincidental vaginal group compared to the abdominal group; however, this difference was not statistically significant. In the subgroup of women who underwent vaginal or coincidental vaginal procedures, the rate of UTI in the single dose (13%) and multi-dose group (9%) was not significantly different. Thus, a single dose of prophylactic antibiotics is likely sufficient for preventing infections even in women undergoing vaginal prolapse surgery with mesh.

Prior studies in women undergoing vaginal hysterectomy with native tissue repairs did not find a difference in the rates of postoperative infections in those who received a single versus multi-dose antibiotic prophylaxis regimen.[18, 19] Similarly, in a study of single versus multi-dose antibiotic regimens in women undergoing anti-incontinence surgery with mesh slings, Swartz et al found that a single dose of antibiotics was adequate for preventing infections. [20] Our findings suggest that similar to native tissue and anti-incontinence mesh slings, a single dose of preoperative antibiotic is effective in preventing postoperative infections in mesh augmented prolapse repairs.

Strengths of our study include a large sample size of women all whom underwent prolapse repair using mesh. Our study was adequately powered to detect a difference in the primary outcome, the rate of post operative infection. We performed a detailed examination of inpatient and outpatient records to minimize the rate of missing data for all outcomes treated within six weeks of surgery. We also examined the relationship of several preoperative and peri-operative variables that could potentially confound the association between antibiotic regimen and post-operative infections. Our study also has some limitations. The choice of antibiotic regimen was based on physician preference and could have been influenced by patient and operative characteristics that could potentially influence the rate of postoperative infections. However, only 6 of 112 patients of the two surgeons who preferred single-dose antibiotics received multi-dose antibiotics and prior to the change in the hospital policy, no patient of the two surgeons who preferred multi-dose regimen, received single-dose regimen. This consistent practice pattern of antibiotic administration across surgeons makes our data in the single-dose and the multi-dose groups comparable with low risk of bias. A retrospective study design is often perceived as a limitation. However, given the large sample size and expense of conducting a prospective randomized clinical trial of antibiotics regimens, our study population and antibiotic prescribing practices provided us with a unique opportunity to study an important clinical question and provide valid results.

CONCLUSION

The rate of postoperative infections in women who undergo prolapse surgery with mesh/graft is low and our findings support current recommendations for administration of a single dose of perioperative prophylactic antibiotics.

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Table 1

Demographics

	Single dose Regimen N = 154	Multi dose Regimen N = 306	p value ^a
Age(years)	58.4 ± 9.6	60.3 ± 10.1	0.06
Body Mass Index(kg/m2)	26.9 ± 5.0	26.7 ± 4.8	0.88
Parity	2(2–3)	3(2–3)	0.42
Current tobacco use	12(7.8)	15(4.9)	0.21
Postmenopausal	119(77.3)	259(84.6)	0.05
Current hormone replacement therapy use	10(6.5)	16(5.2)	0.58
Current Vaginal Estrogen use	9(5.8)	33(10.8)	0.08
Preoperative Prolapse Stage			
2	7(4.5)	58(19)	<0.001
3	143(92.8)	237(77.4)	
4	4(2.6)	11(3.6)	
Preoperative Post Void Residual(median)	20(5–20)	20(5–50)	0.41
Presence of comorbid condition			
Diabetes mellitus	7(4.5)	20(6.6)	0.190.78
Recurrent UTI	2(1.3)	5(1.6)	0.15
Renal disease	0(0)	4(1.3)	0.69
Hypertension	53(34.4)	111(3.6)	0.39
Any of above	57(37)	126(41.2)	
Surgical approach			
1. Open	53 (34.4)	213 (69.6)	<.001
2. Robotic/Laparoscopic	49 (31.8)	60 (19.6)	
3. Vaginal	52 (33.8)	33(10.8)	
Vaginal procedures coincidental with abdominal surgery	73/102(71.6)	49/273(17.9)	< .001
Length of surgery (minutes)	240.9 ± 114	217 ± 73	0.20
Duration of indwelling catheter (days)	4.5 ± 4.4	2.9 ± 2.5	<0.001
Number of void trials	1(1–4)	1(1–4)	0.75

Data are mean standard deviation, n(%), or median(interquartile range)

^a p value from Student's t, chi-square, equality of median, or Wilcoxon rank sum test as appropriate

Table 2

Postoperative Outcomes

	Single-dose Regimen N = 154	Multi-dose Regimen N = 306	p value^a
Any Postoperative Infection	29(18.8)	50(16.3)	0.50
Postoperative UTI	20(13)	21(6.9)	0.03
Postop Fever	8(5.2)	24(7.8)	0.29
Postop Wound/Trocar site Infection	5(3.2)	9(2.9)	0.86
Mesh infection	0(0)	0(0)	-
Pelvic abscess	0(0)	0(0)	-

Data are mean standard deviation, n(%), or median(interquartile range)

^a p value from chi-square test.