Antibiotic Prophylaxis for Prevention of Postpartum Perineal Wound Complications

A Randomized Controlled Trial

Neena Duggal, MD, Celia Mercado, MD, Kay Daniels, MD, Alexandra Bujor, MD, Aaron B. Caughey, MD, PhD, and Yasser Y. El-Sayed, MD

OBJECTIVE: To estimate whether prophylactic antibiotics at the time of repair of third- or fourth-degree perineal tears after vaginal delivery prevent wound infection and breakdown.

METHODS: This was a prospective, randomized, placebo-controlled study. Patients who sustained third- or fourth-degree perineal tears after a vaginal delivery were recruited for the study. Each patient was given a single intravenous dose of a second-generation cephalosporin (cefotetan or cefoxitin) or placebo before repair of third- or fourth-degree perineal tears. Obstetricians and patients were blinded to study drug. The perineum was inspected for evidence of infection or breakdown at discharge from the hospital and at 2 weeks postpartum. Primary end points were gross disruption or purulent discharge at site of perineal repair by 2 weeks postpartum.

RESULTS: One hundred forty-seven patients were recruited for the study. Of these, 83 patients received placebo and 64 patients received antibiotics. Forty patients (27.2%) did not return for their 2-week appointment. Of the patients seen at 2 weeks postpartum, 4 of 49 (8.2%) patients who received antibiotics and 14 of 58 (24.1%) patients who received placebo developed a perineal wound complication ($P=0.037$). There were no differences between groups in parity, incidence of diabetes, operative delivery, or third-degree compared with fourth-degree lacerations.

CONCLUSION: By 2 weeks postpartum, patients who received prophylactic antibiotics at the time of third- or fourth-degree laceration repair had a lower rate of perineal wound complications than patients who received placebo.


LEVEL OF EVIDENCE: I

The anal sphincter is susceptible to trauma during a vaginal delivery. Third-degree lacerations extend into the capsule and muscle of the anal sphincter, and fourth-degree lacerations extend through the sphincter and into the rectal mucosa. These lacerations occur in 2.2–19% of vaginal deliveries in the United States. The use of operative vaginal delivery, especially in combination with midline episiotomy, has been associated with a significantly increased risk of anal sphincter trauma in both nulliparous and multiparous women. This risk is significantly higher with forceps deliveries than with vacuum deliveries. Other risk factors include older age, nulliparity, white ethnicity, longer gestation, epidural use, macrosomia, occipitoposterior position, and protracted second stage of labor. The success of an anal sphincter repair is influenced by the surgical technique, the experience of the surgeon, suture material used, and infection at the repair site. Breakdown of a third- or fourth-degree perineal repair can lead to incontinence of stool or flatus, rectovaginal fistula, or sexual dys-
function. Repair breakdown is often associated with infection at the repair site. In one study, the infection rate was 12% after a third-degree perineal laceration repair. Even without apparent breakdown or infection of the perineal wound, 3–6 months after repair, 29–53% of women reported incontinence of flatus, and 5–10% complained of incontinence of stool. This further highlights the importance of preventing perineal wound infections.

The purpose of this study was to estimate whether prophylactic antibiotics given at the time of repair of third- or fourth-degree perineal lacerations would influence the rate of perineal wound infection and breakdown.

MATERIALS AND METHODS

This was a randomized, placebo-controlled trial conducted at Santa Clara Valley Medical Center and Stanford University Medical Center’s Lucile Packard Children’s Hospital from September 2003 to June 2006. The study was approved by the institutional review boards at both centers.

Patients who sustained third- or fourth-degree perineal laceration after vaginal deliveries were candidates for enrollment. Consent was obtained once a third- or fourth-degree laceration was diagnosed. To minimize any delay in health care, we had both English and Spanish consents available on Labor and Delivery, began the consent process as soon as the diagnosis was made, and made sure that the mother was comfortable during the consent process. The delivering obstetrician was encouraged to examine the perineum immediately after the delivery of the infant. The consent was obtained while waiting for the placenta to be delivered. Antibiotics and placebo were immediately available on Labor and Delivery.

Patients were excluded from the trial if they were less than 18 years of age, group B streptococcus–positive, human immunodeficiency virus (HIV)–positive, had chorioamnionitis or a history of inflammatory bowel disease, or were already on antibiotics for any reason. Patients were randomly assigned to a single dose of antibiotic (cefotetan or cefoxitin, 1 g intravenously, or clindamycin, 900 mg intravenously, if allergic to penicillin, in 100 mL of saline) or placebo (100 mL normal saline intravenously). Second- or third-generation cephalosporins are recommended for bowel surgery, while first- or second-generation cephalosporins are recommended for obstetric and gynecologic surgery. We decided to use a second-generation cephalosporin because the laceration involved the bowel in the setting of obstetric practice. The use of two different second-generation cephalosporins was a result of pharmacy formulary constraints at both institutions.

Randomization was done by using a random numbers table. The nurse was instructed to open the randomization envelope and administer the medication or placebo. The log book was kept in a secure location in the medication room. Access to the log book was available only to the registered nurse preparing the study infusion. No physician was involved in preparing the study medications, and obstetricians do not in practice prepare or retrieve medications from the medication room. The registered nurse providing postpartum care was on another floor and did not have access to the log book. Finally, the clinicians evaluating the patient postpartum did not have access to the log book and, thus, would not have a way of determining which arm a patient had been randomized to. The infusion was begun at the time of the repair. The patient and the obstetrician, as well as the nurse taking care of the patient postpartum, but not the Labor and Delivery nurse, were blinded to the medication given.

The repair of the third- or fourth-degree laceration was done by an attending obstetrician or by a resident supervised by an attending member of the staff. The repair was done in a standardized fashion, although variability in suture size to accommodate physician preference was permitted. The perineum was cleansed with povidone-iodine, and the drapes were changed, if soiled. The rectal mucosa was closed with interrupted 3-0 polyglactin 910 or running 4-0 polyglactin 910, followed by a second continuous imbricating layer of 3-0 polyglactin 910. The external anal sphincter capsule was repaired end-to-end with three or four figure-of-eight sutures of 0 polyglactin 910 or 2-0 polyglactin 910. The remainder of the repair was done in the usual fashion for closure of a second-degree laceration with 2-0 or 3-0 polyglactin 910. The postpartum care included sitz baths twice daily and stool softeners (docusate sodium 250 mg twice a day). Patients had daily perineal evaluation to observe for wound complications until day of discharge. All study patients were scheduled for a 2-week follow-up for a perineal examination by one of the investigators. Criteria used to diagnose perineal wound complications were as follows: 1) purulent discharge from the repair site or 2) abscess and breakdown of the repair site. Wound culture and antibiotic treatment were left to the discretion of the attending physician.
A previous review of our institutional data had shown that the infection rate of postpartum third- or fourth-degree perineal tears was approximately 12%. To demonstrate a 75% reduction in this infection rate, with an alpha of 0.05 and a power of 80%, we had planned to recruit 155 patients in each arm of the study. After 3 years of study activity, we had enrolled 147 patients, and it was clear that we could not realistically achieve our originally planned enrollment within an acceptable time frame. We decided to terminate the study and analyze the data. Analysis was based on intent to treat and was performed by using a two-tailed and independent Student \( t \)-test (uncorrected), and Fisher exact tests, as appropriate. Statistical significance was defined as \( P < 0.05 \), and a statistical trend was defined as \( P < 0.10 \).

RESULTS

After 3 years of recruitment, a total of 147 patients had been randomized. Eighty-three patients received placebo and 64 received antibiotics. The study drug was administered at the time of the repair in all patients. Tables 1 and 2 list the baseline maternal and neonatal characteristics of all enrolled patients. There were no significant baseline differences between the groups that received antibiotics or placebo.

All patients received an in-hospital perineal assessment before discharge and no wound complications were noted. Our primary outcome was evidence of a perineal wound complication at the 2-week postpartum visit. Analysis of the data from the 107 patients who returned for their 2-week appointment showed that 4 of 49 (8.2%) patients who received antibiotics and 14 of 58 (24.1%) patients who received placebo developed a perineal wound complication (\( P = 0.037 \), Fig. 1). A significant decrease in purulent discharge from the perineal wound was noted in women who had received antibiotics (4% compared with 17%; \( P = 0.036 \)). All patients who developed a perineal wound complication were treated with antibiotics.

Forty patients did not return for their 2-week postpartum visit. Twenty-one patients missed their 2-week visit but eventually returned for their 6-week postpartum check. A chart review on these patients did not demonstrate any cases of infection at the 6-week postpartum appointment. No details were available regarding any interim complications. Including this group in the analysis, 4 of 55 (7.3%) patients who received antibiotics and 14 of 73 (19.2%) patients who received placebo had perineal wound complications (\( P = 0.07 \)). Nineteen patients missed their study-mandated 2-week appointment as well as their 6-week appointment. If these patients, whose only examination was at hospital discharge, are included in the overall analysis, 4 of 64 (6.3%) patients who received antibiotics and 14 of 83 (16.9%) patients who received placebo developed a perineal wound complications (\( P = 0.07 \)).

DISCUSSION

We conducted this research because we could not find any evidenced-based data in the literature about the benefit of prophylactic antibiotics in preventing perineal wound complications after postpartum third- or fourth-degree perineal tears. A PubMed search using the terms “postpartum perineal tears,” “anal sphincter tears,” and “prophylactic antibiotics” showed no other randomized trials of antibiotic pro-
phylaxis at the time of perineal wound repair. At our institutions, historically we have not routinely given prophylactic antibiotics in this setting. As a result of our findings, the majority of our clinicians now do give prophylactic antibiotics to women with third- or fourth-degree perineal lacerations.

Prophylactic antibiotics are commonly used with both bowel and obstetric–gynecologic surgery. In most clean-contaminated and contaminated surgery where antibiotic prophylaxis has been found to be most effective, the etiology of the infection is often mixed aerobic and anaerobic flora, with a predominance of gram-negative microorganisms. Cephalosporins (first to third generation) have often been advocated as the drug of choice for prophylaxis because of their broad-spectrum action, minimal risk of allergic reaction, and convenience.

A major strength of the current study was that this was a randomized trial, and the patient and the physician doing the repair were blinded to the medication given. The patients were followed and examined during their hospital stay and at 2 weeks postpartum to rule out any infection. All examinations were performed by physicians blinded to the study drug. As much as possible, we used standardized repair techniques and postpartum perineal care. We limited our diagnosis of a wound complication to obviously purulent discharge from the repair site or gross disruption of the repair site. Induration or tenderness in and of themselves did not qualify as wound complications.

Our study had several limitations and weaknesses. We terminated our study early because it became clear that we could not realistically hope to achieve our desired enrollment number within a reasonable time period. Although we attempted to enroll all patients with third- and fourth-degree lacerations, we speculated that our study recruitment was negatively impacted by patients refusing study participation, as well as missed opportunities for enrollment on very busy Labor and Delivery wards. We did not keep a log of the number of patients in either of these categories. The study was taking place in two centers already and, after 3 years, we did not feel it was realistic at such a late stage to initiate the study in additional centers. The study was stopped before any data analysis was performed. The biggest problems this would introduce would be lack of statistical power and type 2 error. However, because we did find a statistically significant difference in the rate of perineal wound complications, this problem is limited. As noted in the Results section, our perineal wound complication rate was higher than we had predicted, although the large reduction in these complications was approximately what we had predicted. This increase in the baseline risk of complications gave us the increased power to find a statistically significant difference in the outcomes of interest. It is possible that the higher rate of complications we found is related to careful attention given to these patients, resulting in fewer missed complications than might occur in routine clinical practice.

Fig. 1. Perineal wound complication rates (%) for patients receiving antibiotics or placebo. The total wound complication rate is less than the two components because some women had both suboutcomes. Wound disruption $P = .162$; purulent discharge $P = .036$; any complication $P = .037$.

The perineal repairs were done by varying providers. Repair was done by an attending physician or a resident with attending supervision. Furthermore, due to the presence of multiple surgeons and the concomitant need to accommodate established surgical technique and suture predispositions, we permitted some variation in the suture size and repair technique. The fact that the study was randomized should help alleviate any confounding introduced by multiple surgeons participating in the study. Although the physician, patient, and postpartum floor nurse were all blinded to the study drug, the labor and delivery nurse administering the drug was not blinded. However, because these nurses were not involved in the eventual evaluation of the patients, we doubt that much bias could be introduced into the study. We used two different second-generation cephalosporins due to pharmacy constraints across institutions. However, the similar coverage provided by these two drugs should limit any confounding effect.

Finally, we had a high no-show rate at 2 weeks postpartum. Forty of the 147 patients did not return for their scheduled 2-week postpartum visit. Our primary outcome was based on evidence of perineal wound complication by the second postpartum week. Analysis of the data from the 107 patients who returned for their 2-week appointment, revealed that 4 of 49 (8.2%) patients who received placebo developed perineal wound complications (P= .037). Analysis of the data including patients with only a 6-week postpartum visit or only an evaluation before discharge continues to show a large clinical difference and strong statistical trend favoring antibiotic therapy (7.3% compared with 19.2%, P= .07, and 6.3% compared with 16.9%, P= .07, respectively). Most patients in our study population were receiving public assistance, and financial and social hardships may have contributed to the poor compliance with outpatient follow-up, despite multiple efforts made to contact patients by phone. Our patients receive prenatal and postpartum care from one of several outlying clinics, and unfortunately, we were limited to a retrospective chart review of the 21 patients who were seen at 6 weeks postpartum at one of these clinics. As such, details of any interim complications that may have occurred are not available.

In conclusion, the findings of our study suggest that prophylactic antibiotics given at the time of third- or fourth-degree perineal laceration repair decrease the perineal wound complication rate. Our high failed-appointment rate and specific patient population may limit the generalizability of our conclusions. We await verification of our findings from future studies, which could also evaluate outcomes in lower-risk populations, as well as longer-term outcomes, such as fecal and flatal incontinence and sexual function and satisfaction.

REFERENCES


