

Do Prophylactic Antibiotics After Manual Exploration of the Uterus Decrease the Incidence of Postpartum Endometritis?

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OBJECTIVE: To evaluate whether antibiotics decrease the incidence of postpartum endometritis after manual exploration of the uterus.

STUDY DESIGN: All patients who underwent uterine exploration after vaginal delivery at a single tertiary medical center from December 2012–November 2015 were retrospectively analyzed to determine whether they were then treated for postpartum endometritis.

RESULTS: The study group included 242 women, who were 30.3 (5.4) years old with a BMI of 31.5 (6.6) kg/m²; most were white (88.8%), nonsmokers (92.8%), and multiparous (47.9%). Antibiotics were given at the time of exploration in 121 (50%) cases. Postpartum endometritis occurred in 9/242 (3.7%) patients, 6 of whom required inpatient admission for treatment. Among patients who had not previously received intrapartum antibiotics, the incidence of postpartum endometritis was significantly lower in women who received prophylactic antibiotics (0/85, 0%) as compared with those who did not (5/75, 6.7%) ($p=0.022$). The number needed to treat to prevent 1 case of endometritis among women who were not taking concurrent

antibiotics for other conditions was estimated as 15 (95% confidence interval 8.1–97.9).

CONCLUSION: Prophylactic antibiotic use after uterine exploration was associated with a significantly decreased incidence of postpartum endometritis in women who had not received prior intrapartum antibiotics. (J Reprod Med 2019; 64:3–7)

...we recommend ... a single prophylactic dose of broad-spectrum antibiotics in patients undergoing manual uterine exploration who have not previously received antibiotics during their labor.

Keywords: antibiotic prophylaxis; antibiotics; D&C; dilatation and curettage; endometritis; endomyo-

metritis; extraction, obstetric; manual extraction; manual sweep; obstetric delivery; postpartum period; vaginal delivery.

There is a 1–2% incidence of endometritis after vaginal delivery.¹ Some of the factors shown to increase this risk include maternal age <17 years, postpartum hemoglobin <10 g/dL, and ruptured membranes >24 hours.² While manual placental extraction during cesarean deliveries has been shown to increase the risk of postpartum endometritis,^{3–5} there is disagreement over whether the

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same is true of manual extraction during vaginal deliveries.^{2,6} In a large retrospective cohort study, Ely et al² reported an odds ratio of 2.9 for endometritis after manual extraction. Conversely, Tandberg et al⁶ reported that postpartum endometritis was rare after manual placental extraction and similar to the overall population incidence (3/165, 1.8%).

This conflicting evidence is reflected in inconsistencies among practice guidelines that address the use of prophylactic antibiotics after manual extraction. The American College of Obstetricians and Gynecologists' practice bulletin states that "no data exist to support the practice of antibiotics."⁷ The Society of Obstetricians and Gynaecologists of Canada (SOGC) reports insufficient evidence to guide either way.⁸ In 2009 the World Health Organization recommended a single dose of antibiotics after manual removal, though they admitted that the quality of evidence is "very low."⁹ No randomized controlled trials have evaluated this issue.¹⁰

We have addressed the lack of information in the literature by performing a retrospective study to evaluate whether the incidence of postpartum endometritis is increased after manual exploration of the uterus and to determine whether prophylactic antibiotic treatment decreases the incidence of endometritis.

Materials and Methods

This was a retrospective cohort study of women who underwent manual exploration of the uterus after vaginal delivery at a tertiary center between December 2012 and November 2015. Potential study subjects were identified in the electronic medical record system using a keyword search that included the terms "manual" or "sweep" or "extract" or "explore." Each chart was then reviewed manually by one of the authors (P.H.). Inclusion criteria included vaginal deliveries occurring at Maine Medical Center which required manual extraction of the placenta or manual sweep of the uterus within 24 hours of delivery, patients aged ≥ 18 years, gestational age ≥ 28 weeks, and complete 6-week follow-up either from the electronic medical record or by follow-up with individual physician practices. All study records were de-identified prior to analysis; the study was reviewed as exempt by our Institutional Review Board.

Manual exploration was defined as manual uterine sweep, manual placental extraction, or both; prolonged rupture was defined as time ≥ 18 hours since rupture of membranes. Body mass index (BMI)

was measured at the time of admission. The primary outcome measure was endometritis diagnosed by the provider within 6 weeks of delivery, based on temperature $>38^{\circ}\text{C}$ and/or inappropriate fundal tenderness.

Statistical analyses were performed using IBM SPSS v.9.1 (IBM Corp., Armonk, New York). Continuous data were summarized as mean (SD), and categorical data were expressed as frequencies (n, %). Comparisons of clinical and demographic data between endometritis subgroups were performed by independent *t* test (continuous data) or by Fisher's exact test (categorical data), as appropriate.

Results

The logistics of study group selection are illustrated in Figure 1. We identified 294 women who had undergone manual exploration of the uterus during the study period; after applying demographic inclusion criteria, 276 women remained eligible, and of those, 242 (87.7%) had complete follow-up. Of those, 63 (26.0%) underwent manual placental extraction only, 121 (50.0%) underwent manual uterine sweep only, and 58 (24.0%) underwent both maneuvers. The most frequent reasons for uterine exploration included retained placenta or products of conception (128, 52.9%); increased bleeding, uterine atony, or postpartum hemorrhage (74, 30.6%); and cord avulsion (22, 9.1%). Prophylactic antibiotics were given after time of exploration in 121 (50.0%) cases, and most of those women (106, 87.6%) received a single-dose regimen. The antibiotics used most frequently were ampicillin-sulbactam (80, 65.6%) and cefazolin (30, 24.6%).

Table I shows the demographic and pregnancy characteristics of the study group, stratified by the use of prophylactic antibiotic after uterine exploration. Overall, the women in this cohort were 30.4 (5.4) years old and had a BMI of 31.5 (6.6) kg/m²; 116 (47.9%) were multiparous, 214/241 (88.8%) were white, and 225/233 (92.7%) were nonsmokers. None of these variables differed significantly between prophylactic antibiotic use subgroups.

Table II shows the association of selected clinical factors associated with delivery and postpartum, stratified by the use of prophylactic antibiotics. Gestational age at delivery was 39.1 (2.1) weeks, overall. Women receiving prophylactic antibiotics were significantly more likely to have had a preterm delivery (gestational age <37 weeks), prolonged rupture, or postpartum dilation and cu-

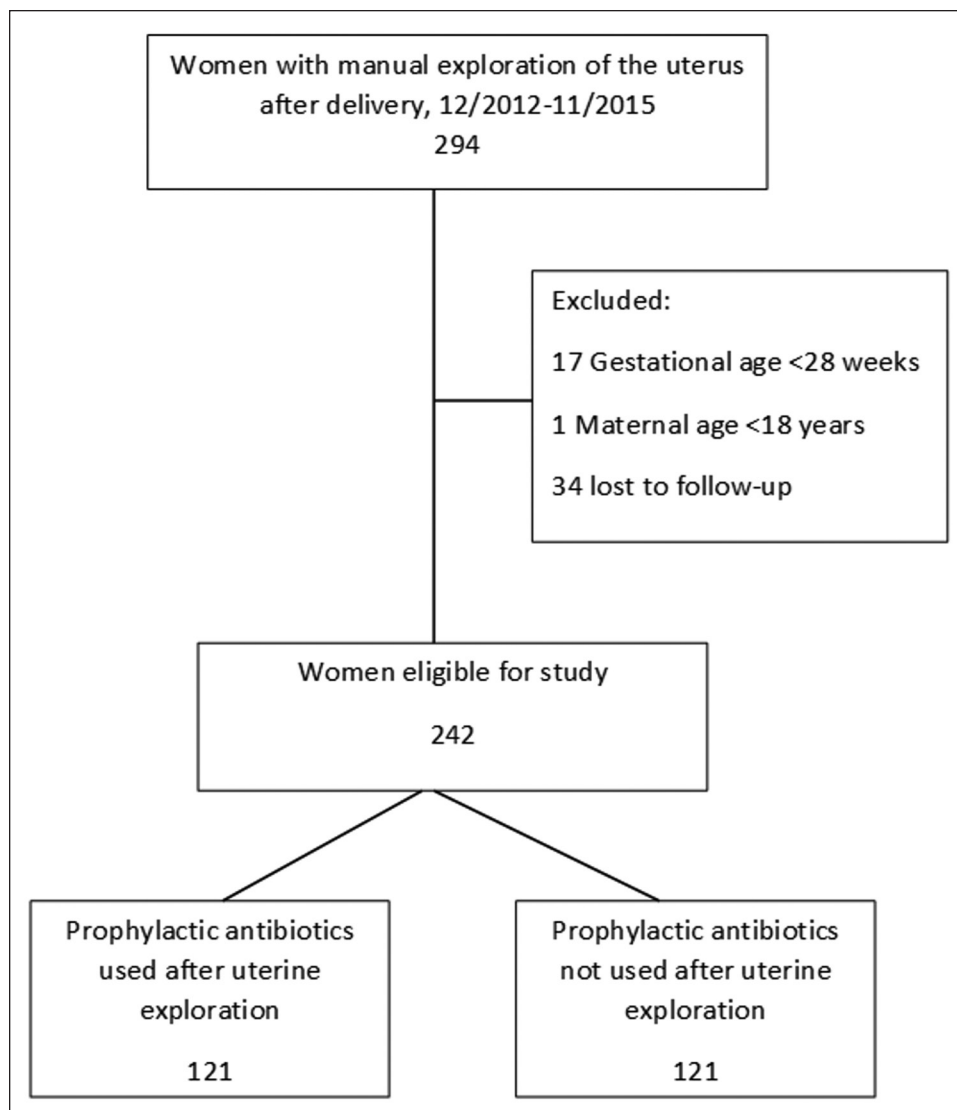


Figure 1
Identification of the study cohort.

retage; none of the other variables listed differed between prophylactic antibiotic use groups. Of the 121 women who received antibiotics at the time of exploration, 37 (30.6%) had received antibiotics prior to delivery.

Table III shows the incidence of endometritis stratified by prophylactic antibiotic use and by the use of antibiotics prior to delivery. Clinical findings that prompted the diagnosis of endometritis were temperature $>38^{\circ}\text{C}$ (3/9), inappropriate fundal tenderness (5/9), or both (1/9). The most common reason for receiving antibiotics prior to delivery was Group B streptococcal status (79/83, 95.2%). Postpartum endometritis occurred in 9/242

(3.7%) women, 6 of whom required inpatient admission for treatment. Those receiving prophylactic antibiotics had a decreased incidence of endometritis (5.8% vs. 1.7%), but the difference was not significant. When the analysis was limited to women who were not using antibiotics predelivery, prophylactic antibiotic use was associated with a significantly lower incidence of endometritis during the 6 weeks postpartum (0% vs. 6.7%, $p=0.022$). Among women not treated with antibiotics predelivery who underwent manual exploration of the uterus, the number needed to treat with prophylactic antibiotics to prevent 1 case of endometritis was 15 (95% confidence interval 8.1–97.9).

Table I Demographic Characteristics of the Study Group

| Variable | Prophylactic antibiotics | | p Value |
|---|--------------------------|-------------|---------|
| | Yes N=121 | No N=121 | |
| Age (years) ^a | 30.7 (5.4) | 30.1 (5.3) | 0.33 |
| BMI (kg/m ²) ^{a,c} | 31.3 (5.5) | 31.8 (7.5) | 0.63 |
| Race ^{b,d} | | | 0.58 |
| White | 107 (88.4) | 107 (88.4) | |
| Black | 7 (5.8) | 8 (6.6) | |
| Other | 6 (5.0) | 6 (5.0) | |
| Current smoker ^{b,e} | 7 (6.0) | 10 (8.5) | 0.46 |
| Multiparous ^b | 56 (46.3) | 60 (49.6) | 0.61 |

^aData shown as mean (SD) and analyzed by *t* test.

^bCategorical data were analyzed by χ^2 test.

^cBMI was measured at admission for labor and delivery. Data were available for 179 women; 91 were given prophylactic antibiotics after manual exploration and 88 were not.

^dData were available for 241 women and were analyzed by χ^2 test after stratification as white versus black/other. The "other" category includes 6 Asian, 1 Middle Eastern, 1 Hawaiian, 1 Native American, and 3 other, unspecified.

^eData were available for 233 women; 116 were given prophylactic antibiotics after manual exploration and 117 were not.

We examined factors potentially associated with endometritis that could confound the observed relationship with prophylactic antibiotic use. Prolonged membrane rupture (3 [33.3%] vs. 36 [15.5%], $p=0.16$), antepartum maternal fever (1 [11.1%] vs. 8 [3.4%], $p=0.29$), postpartum D&C (2 [22.2%] vs. 29 [12.4%], $p=0.32$), or predelivery antibiotic use (4 [44.4%] vs. 79 [33.9%], $p=0.51$) did not differ significantly between women who developed endometritis and those who did not.

Discussion

To the best of our knowledge, this study provides the first evidence that, among women who were not taking intrapartum antibiotics for other indications, prophylactic antibiotic use at the time of manual uterine exploration is associated with a decreased incidence of postpartum endometritis. The lack of effect among women who were taking intrapartum antibiotics may suggest confounding, or may be related to the small study size. The majority of women in our study received a single dose of a broad-spectrum antibiotic for prophylaxis, a clinical practice that was supported indirectly by previous findings in similar clinical populations. For example, Edwards and Duff¹¹ reported that a single postpartum dose of a broad-spectrum antibiotic or combination of antibiotics is sufficient to treat chorioamnionitis. Additional work will be needed, both to confirm the effect of prophylactic

antibiotics and to establish the optimal type and dose of antibiotic for postpartum endometritis prophylaxis.

The overall incidence of endometritis was 3.7% overall and 6.7% among women who had no antibiotic exposure, intrapartum or prophylactic, during delivery; although formal statistical comparisons were not possible, both of these rates exceed the reported population incidence (1–2%).¹ Thus, our findings are consistent with those of Ely et al,² who reported a higher incidence of endometritis after manual placental extraction. As our study group included women with either manual sweep and/or manual extraction of the placenta, any interpretation of these data must acknowledge the possibility of risk heterogeneity within the group. There were too few subjects to stratify the analysis by type of exploration, and further study will be needed to determine whether manual sweep and extraction procedures confer different levels of risk for endometritis.

The strengths to this study were its high follow-up rate at a single tertiary medical center and the similar demographic characteristics of the 2 retrospective treatment groups. Limitations are the low number of endometritis cases and the retrospective study design, which meant that we were unable to collect data for all variables potentially associated with infection risk, such as the number of cervical examinations during labor, the length of the labor itself, and whether the operator's gloves were changed prior to uterine exploration. The

Table II Delivery Characteristics of the Study Group

| Variable | Prophylactic antibiotics | | p Value |
|---|--------------------------|-------------|---------|
| | Yes N=121 | No N=121 | |
| GA at delivery (weeks) ^a | 38.7 (1.7) | 38.6 (2.2) | 0.89 |
| Delivery <37 weeks ^b | 19 (15.7) | 6 (5.0) | 0.006 |
| Singleton gestation ^b | 117 (96.7) | 119 (98.3) | 0.68 |
| Prolonged rupture ^{b,c} | 27 (22.1) | 12 (9.9) | 0.009 |
| Intrapartum maternal fever ^b | 7 (5.8) | 2 (1.7) | 0.17 |
| Postpartum D&C ^b | 26 (21.5) | 5 (4.1) | <0.001 |
| Antibiotic use predelivery ^b | 37 (30.6) | 46 (38.0) | 0.22 |

D&C = dilation and curettage, GA = gestational age.

^aData shown as mean (SD) and analyzed by *t* test.

^bCategorical data were analyzed by Fisher's exact test if $n \leq 5$ in 1 or more cells; otherwise, χ^2 test was used.

^cProlonged rupture was defined as rupture of membranes ≥ 18 hours prior to delivery.

Table III Effect of Predelivery Antibiotic Use and Prophylactic Antibiotic Use After Manual Exploration of the Uterus on the Incidence of Endometritis Up to 6 Weeks Postpartum

| Prophylactic antibiotics | Incidence of endometritis, n/n (%) | | | p Value ¹ |
|-------------------------------|------------------------------------|-------------|-------------|----------------------|
| | Yes | No | Total | |
| Antibiotics prior to delivery | | | | |
| Yes | 2/37 (5.4) | 2/46 (4.3) | 4/83 (4.8) | 1.0 |
| No | 0/84 (0.0) | 5/75 (6.7) | 5/159 (3.1) | 0.022 |
| Total | 2/121 (1.7) | 7/121 (5.8) | 9/242 (3.7) | 0.17 |

¹Fisher's exact test (prophylactic antibiotics versus no prophylactic antibiotics).

risk-associated variables that we did examine (prolonged rupture of membranes, intrapartum maternal fever, and postpartum instrumentation) were not associated with increased incidence of postpartum endometritis in this cohort and thus not a source of confounding.

In summary, we report a relatively high incidence of postpartum endometritis following manual exploration of the uterus at delivery that often resulted in hospitalization. Prophylactic antibiotic use among women who were not receiving intrapartum antibiotics for other indications was associated with significantly lower incidence of endometritis. Further larger studies are needed to confirm these findings and provide additional information regarding selection or timing of antibiotics. Until that information is available, we recommend the consideration of a single prophylactic dose of broad-spectrum antibiotics in patients undergoing manual uterine exploration who have not previously received antibiotics during their labor.

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