Vaginal cleansing with chlorhexidine gluconate or povidone-iodine prior to cesarean delivery: a randomized comparator-controlled trial

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BACKGROUND: Several randomized controlled trials have demonstrated that preoperative abdominal skin preparation with chlorhexidine gluconate is superior to povidone-iodine for the prevention of surgical site infections. Despite these results, povidone-iodine is still the most commonly used agent for vaginal preparation, even though it may not be ideal.

OBJECTIVES: The objectives of the study were as follows: (1) to determine whether vaginal cleansing with a 4% chlorhexidine gluconate solution results in fewer wound infections as compared with povidone-iodine when used for vaginal antisepsis prior to cesarean delivery and (2) to compare rates of patient reported side-effects associated with vaginal application of 4% chlorhexidine gluconate solution and 10% povidone-iodine.

STUDY DESIGN: This is a block randomized, comparator-controlled, open-label trial. Women undergoing nonemergent cesarean delivery were randomized to receive vaginal cleansing with either 4% chlorhexidine solution or 10% povidone-iodine solution prior to skin incision. The primary outcome was wound site infection occurring within 14 days of cesarean delivery including superficial or deep surgical site infection. Secondary outcomes included rates of endometritis, postoperative fever, and side effects (vaginal dryness, irritation, and desquamitization) occurring within 14 days of cesarean delivery. Risks were reported as odds ratios with 95% confidence intervals, with $P < .05$ considered as significant.

RESULTS: From Dec. 1, 2016, through Feb. 28, 2018, a total of 1,114 patients met the inclusion criteria: 524 were randomized to the chlorhexidine gluconate arm and 590 to the povidone-iodine arm. Both arms were similar with regard to age, parity, body mass index, gestational age at delivery, indication for cesarean delivery, and incidence of membrane rupture. The rate of wound infection was significantly lower in the chlorhexidine arm as compared with povidone-iodine (0.6% vs 2.0%; $P = .039$, odds ratio, 0.28, 95% confidence interval, 0.08–0.98). Rates of endometritis (0.4% vs 0.5%, $P = 1.000$) and postoperative fever (2.5% and 2.7%, $P = 0.892$) were similar for the chlorhexidine and povidone-iodine groups, respectively. No adverse effects on the vaginal mucosa were noted for either solution.

CONCLUSION: Vaginal cleansing with a 4% chlorhexidine solution prior to cesarean delivery resulted in fewer overall wound infections when compared with povidone-iodine solution with no patient-reported adverse reactions.

Key words: cesarean delivery, chlorhexidine gluconate, povidone-iodine, preoperative abdominal skin preparation, surgical site infections, vaginal cleansing

EDITOR'S NOTE

This practice-changing RCT shows that vaginal cleansing with 4% chlorhexidine, as compared as with 10% povidone-iodine, before a non-scheduled (for arrest disorders, maternal request while laboring, Category II fetal heart tracings, or failed inductions with a trial of labor) cesarean, is associated with significantly lower rates of wound infection, even in women who get pre-op antibiotics and chlorhexidine skin cleansing. While there are several RCTs comparing povidone-iodine to placebo/no treatment, and some comparing chlorhexidine to placebo/no treatment, this is the first published RCT comparing the two interventions.

EDITOR'S CHOICE

In a 2018 Cochrane systematic review, 10 randomized controlled trials (RCTs) evaluated the effect of vaginal cleansing on postcesarean infectious morbidity.[1] Vaginal preparation immediately before a cesarean delivery was shown to significantly reduce the incidence of postcesarean endometritis from 8.7% in the control groups to 3.8% in the vaginal cleansing groups (risk ratio [RR], 0.36, 95% confidence interval [CI], 0.20–0.63, 10 trials, 3283 women).[1]

Two trials reported a lower risk of a composite outcome of wound complication or endometritis in women receiving preoperative vaginal preparation.[1] Of the 10 RCTs, 8 studies evaluated povidone-iodine and 2 evaluated chlorhexidine gluconate against placebo or no treatment.[1] In contrast to the results of the Cochrane review, one 2018 study found that vaginal preparation before a cesarean delivery was not significantly associated with lower surgical site infection rates in women who underwent cesarean delivery during labor.[2]

For abdominal preoperative skin preparation, prior RCTs have demonstrated superiority of chlorhexidine gluconate compared with povidone-iodine for the prevention of surgical site infections.[3,4] However, more recently, the Chlorhexidine-Alcohol versus Povidone-Iodine for Cesarean Antisepsis trial did not show any benefit of preoperative skin preparation with chlorhexidine.[5]

2589-9333/free

https://doi.org/10.1016/j.ajogmf.2019.03.004

AJOG at a Glance

Why was this study conducted?

In contrast to povidone-iodine, chlorhexidine is bactericidal, is not inactivated in the presence of blood, and has extended residual activity from 24 to 72 hours after application. This study was conducted to determine whether vaginal cleansing with a 4% chlorhexidine gluconate solution results in fewer surgical site infections compared with povidone-iodine when used for vaginal antisepsis before cesarean delivery.

Key findings

The rate of wound infection was significantly lower in the chlorhexidine arm as compared with the povidone-iodine arm.

What does this add to what is known?

Previous studies have demonstrated superiority of chlorhexidine for abdominal preparation in reducing surgical site infection. This is the first randomized trial to compare the efficacy of vaginal preparation with 4% chlorhexidine gluconate as compared with povidone-iodine prior to cesarean delivery for the prevention of surgical site infection.

Although povidone-iodine is the most commonly used antiseptic for surgical preparation of the vagina, it is not an ideal agent for several reasons. First, in the acidic milieu of the normal vagina (pH 3.8−4.5), the efficacy of iodine's disinfecting properties is diminished.[6] Second, iodophores are inactivated in the presence of blood, which can be ubiquitous in the vagina at the time of a delivery.[7] Inactivation of the iodophores completely discontinues the antimicrobial effect of povidone-iodine.

Additionally, systemic absorption of iodine from the vagina is a safety concern because the vagina lacks protective keratinized epithelium. In contrast to povidone-iodine, which is bacteriostatic, chlorhexidine gluconate is bactericidal. It acts by causing destruction of bacterial cell membranes, leading to a decrease in bacterial colony counts.[8] In addition, chlorhexidine gluconate has been shown to possess extended residual activity that can persist from 24 hours up to 3 days after application.[9]

This study is the first randomized trial to compare the efficacy of vaginal preparation with 4% chlorhexidine gluconate as compared with 10% povidone-iodine prior to cesarean delivery for the prevention of surgical site infections.

Materials and Methods

This randomized, comparator-controlled, open-label institutional review board−approved study (ClinicalTrials.gov identifier, NCT02915289) was conducted at Richmond University Medical Center (Staten Island, NY), a high-risk tertiary care center for obstetrics and neonatology.

From Dec. 1, 2016 through Feb. 28, 2018, all women undergoing nonemergent cesarean delivery were included in the study. This population included patients who underwent a cesarean delivery for arrest disorders, maternal request while laboring, category II fetal heart tracings, or failed inductions with a trial of labor. Exclusion criteria were emergent cesarean deliveries, face presentation, or known or suspected allergy to chlorhexidine or iodine.

A computer-generated calendar block randomization method was utilized. Blocks ranging from 5 to 14 days were randomly assigned to either the povidone iodine solution or the chlorhexidine gluconate solution throughout the study duration. Any patient who consented to the study during a particular block was cleansed with the solution assigned to that block. Attending surgeons and operating room staff were made aware of the computer-generated solution assigned for the given day via a sign posted in the operating room. The resident physicians were trained in the proper prepping technique and were responsible for preoperative preparation.

Patients received prophylactic antibiotics at least 30 minutes prior to skin incision.[10] After placement of the Foley catheter, the assigned solution was used to prepare the surgical field from the vaginal apex to the introitus with attention to the anterior, posterior, and lateral aspects of the vaginal walls. Three passes were required.

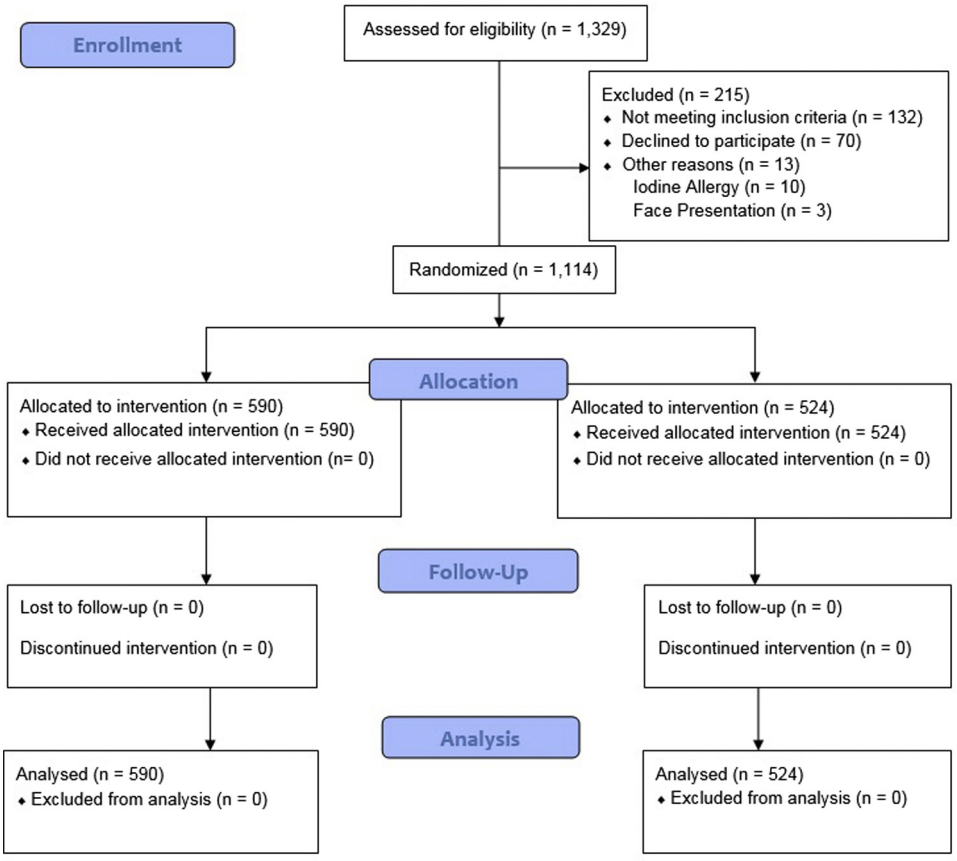
Women in the povidone iodine arm of the study received preparation with the povidone iodine preparation kit (Aplicare Povidine iodine paint sponge sticks, 10%; Aplicare Inc, Meriden, CT) that was consistent with those used for vaginal preparation in other settings. Women in the chlorhexidine gluconate arm of the study received vaginal preparation with a 4% chlorhexidine gluconate solution (BD E-Z Scrub 107 surgical scrub brush/sponge 4% CHG; (Becton, Dickinson and Company, Franklin Lakes, NJ).

The BD E-Z Scrub 107 surgical scrub brush/sponge was readily available in our operating room because it is routinely used for preoperative hand scrubbing. The sponge was detached from the plastic brush, and the plastic brush was disposed of. The sponge, which was presaturated with the 4% chlorhexidine solution, was attached to a sterile sponge stick and used to clean the vagina.

To control for variations, subjects also received periurethral preparation with either povidone iodine or chlorhexidine gluconate, depending on the arm of the study to which they were randomized, prior to placement of the Foley catheter. Abdominal application with a 70% chlorhexidine gluconate isopropyl alcohol solution prior to skin incision was standardized for all patients.

Operational definitions for outcomes were established prior to the start of the study. The primary outcome was wound site infection occurring within 14 days of cesarean delivery including superficial or deep surgical site infection. Wound infection was defined as erythema

FIGURE
Flow diagram for study selection



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surrounding the incision site characterized by cellulitis or pus-like incisional drainage in the presence or absence of fever requiring antibiotic treatment or wound care.

Patients were followed up for the occurrence of wound infection after hospital discharge via a standardized telephone interview. Phone calls were made 14–20 days after discharge, depending on when the patient answered the phone. The telephone interview followed a standardized questionnaire that asked the following: (1) were you diagnosed with a wound infection within 14 days of your surgery? and (2) were you readmitted to the hospital? If so, what was the reason for readmission?

Both the telephone questionnaire and data collection were conducted by the same research assistant who was blinded to randomization. Hospital records were obtained and reviewed if the subject reported that they were evaluated at an outside institution.

As a secondary follow-up, the operating attending physician was contacted by blinded study personnel and asked whether the patient was diagnosed or treated for a wound infection. If we were unable to contact the patient, she was considered lost to follow-up but was still included in the intent-to-treat analysis.

Secondary outcomes included rates of endometritis, in-hospital postoperative fever, and side effects (vaginal dryness, irritation, and desquamatization) occurring within 14 days of cesarean delivery. Endometritis was defined as temperature of 100.4°F or higher occurring 24 hours after surgery with uterine fundal tenderness or foul-smelling vaginal discharge. Vaginal side effects were assessed by direct questioning during daily postpartum rounds and during the telephone interview.

An a priori power analysis for a χ^2 test was conducted in G-POWER 3.1 (Faul and Erdfelder) to determine a sufficient sample size using an alpha of 0.05 and 1 degree of freedom. A small-medium effect size ($w = 0.23$) was determined based on data by Amer-Alshiek et al[11] that noted a 7.36% decrease in abdominal infection with chlorhexidine preparation compared with an iodine-containing preparation.

Given that the incidence of post-cesarean wound infection is approximately 7% on our labor and delivery unit, we estimated needing to enroll a total of 1050 patients for 80% power. Statistical analysis was carried out using IBM SPSS 22.0 (IBM Corp., Armonk, NY).

Univariate analysis for continuous variables was compared using the Student t test or Mann-Whitney U test. Categorical data was compared using χ^2 or Fisher exact tests. Risks were reported

TABLE 1
Maternal, clinical, and delivery characteristics

Characteristics	Povidone-iodine (n = 590)	4% Chlorhexidine gluconate (n = 524)	*P* value
Age, y	32.61 ± 5.22	32.49 ± 5.56	.705
BMI, kg/m^2	32.99 ± 6.63	32.48 ± 6.42	.195
Gestational age, wks	39 (24.2–41.5)	39 (25.1–42.0)	.596
Race			
White	424 (71.9)	395 (75.4)	.084
Black	68 (11.5)	53 (10.1)	
Hispanic	76 (12.9)	53 (10.1)	
Asian/Pacific Islander	22 (3.7)	23 (4.3)	
Insurance status			
Uninsured/government assistance	147 (25.2)	126 (24.4)	.747
Privately insured	436 (74.8)	391 (75.6)	
Gravidity	2 (1–15)	2 (1–9)	.308
Parity	1 (1–8)	1 (0–6)	.773
Pregestational diabetes	6 (1)	5 (1)	.999[a]
Gestational diabetes	42 (7.2)	23 (4.4)	.050
Preeclampsia	22 (3.8)	14 (2.7)	.315
Gestational hypertension	36 (6.1)	20 (3.8)	.080
Rupture of membranes before cesarean delivery	186 (31.5)	169 (32.3)	.810
Duration of rupture, min	521 (34–26,317)	618 (22–15,346)	.890
Trial of labor before cesarean delivery	316 (53.6)	261 (49.8)	.200
Type of cesarean delivery			
Primary	317 (53.9)	287 (54.8)	.774
Repeat	271 (46.1)	237 (45.2)	
Type of wound closure			
Suture	112 (19.3)	94 (18.3)	.677
Staples	468 (80.7)	419 (81.7)	
Subcutaneous layer reapproximated with 2-0 plain gut suture	416 (71.6)	332 (64.6)	.013
Estimated blood loss, mL	800 (300–2500)	800 (500–3000)	.815

BMI, body mass index.

[a] Fisher exact test.

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as odd ratios with 95% confidence intervals, with a value of $P < .05$ considered as significant.

Results

From Dec. 1, 2016, through Feb. 28, 2018, 1329 women were assessed for eligibility, 215 of which were excluded for the following reasons: 132 women did not meet inclusion criteria, 70 declined to participate, 10 had an iodine allergy, and 3 had face presentation. A total of 1114 patients were randomly assigned to be in 1 of 2 study groups: a povidone-iodine arm (n = 590) or a 4% chlorhexidine gluconate arm (n = 524) (Figure).

Both arms were comparable with regard to age, gravidity, parity, body mass index, gestational age at delivery, race, insurance status, and type of cesarean delivery performed (Table 1). Similarly, there were no differences found among comorbidities including pregestational diabetes, gestational diabetes, preeclampsia, and gestational hypertension among randomization groups (Table 2).

The predetermined primary outcome, occurrence of wound infection, was significantly higher in the

TABLE 2
Outcomes by study group

Outcomes	Povidone-iodine (n = 590)	4% Chlorhexidine gluconate (n = 524)	*P* value
Wound infection	12 (2.0)	3 (0.6)	.039
Endometritis	3 (0.5)	2 (0.4)	.999
Postoperative fever	15 (2.7)	14 (2.5)	.892[a]
Readmission	3 (0.5)	3 (0.6)	.999

All values are presented as n (percentage). All *P* values use a 2-sided Fisher's exact test except those marked with a superscript letter. which use Chi-square.

[a] *P* values use a χ^2 test.

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povidone-iodine arm as compared with the chlorhexidine arm (2% vs 0.6%, $P = .039$, odds ratio [OR], 0.28, 95% CI, 0.08−0.98) (Table 2). Rates of postcesarean endometritis (0.5% vs 0.4%; $P = .999$), postoperative fever >100.4°F (2.7% vs 2.5%; $P = .892$), and hospital readmission (0.5% vs 0.6%, $P = .999$) were similar in the povidone-iodine and chlorhexidine arms, respectively.

All 5 patients who were diagnosed with endometritis were laboring before cesarean delivery (3 from the povidone-iodine arm and 2 from the chlorhexidine arm). Three patients from the povidone-iodine group were readmitted to the hospital: one for wound cellulitis with a 4 cm separation, one for a wound infection with discharge, and one for acute blood loss with retained blood clots requiring blood transfusion. The patients with the wound cellulitis and wound infection both required antibiotic treatment. Three patients from the chlorhexidine group were readmitted: one for a superficial wound infection, one for pyelonephritis, and one for endometritis. The patient with the wound infection and the patient with endometritis received antibiotic treatment. There were no side effects related to the vaginal cleansing solutions used in either arm.

More patients in the povidone-iodine group (71.6% vs 64.6%, $P = .013$, OR, 0.72, 95% CI, 0.56−0.93) had reapproximation of the subcutaneous tissue with plain gut suture. However, there were no differences in wound infection rates between those who had reapproximation and those who did not (1.2% vs 1.7%, respectively, $P = .577$) (Table 3). The occurrence of wound infection was similar between those who had skin closure with staples compared with skin closure with suture (1.7% vs 0%, $P = .089$) (Table 3). Wound infections developed more frequently in patients with pregestational diabetes than in patients without the condition (9.1% vs 1.3%, $P = .140$); however, it did not reach statistical significance.

Incidence of membrane rupture prior to cesarean delivery was similar between the povidone-iodine and chlorhexidine arms (31.5% vs 32.3%, $P = .810$, respectively). Subanalysis of patients with ruptured membranes prior to cesarean delivery showed no differences with respect to primary or secondary outcomes.

Comment

We found that the risk of wound infection after cesarean delivery was significantly lower when a 4% chlorhexidine gluconate solution was used for preoperative vaginal preparation as compared with a 10% povidone-iodine solution. Prior to conducting this study, we found that the incidence of postcesarean wound infection was approximately 7% on our labor and delivery unit.

We realize that the outcomes of our study reflect a much lower percentage of wound infections, and we propose several explanations as to why this may be true. Before this study began, there was no strict policy regarding vaginal preparation before cesarean delivery; some surgeons used a vaginal preparation, while others did not. The fact that vaginal preparation was used consistently with either povidone-iodine or chlorhexidine during the study period may have contributed to the lower rate of infection. The lower wound infection rate in our study may also be attributed to our department's active use of protocol to reflect best practice techniques and improve patient outcomes (Table 4). Additionally, the 7% wound infection rate was derived from a nonstringent coded database. For the purposes of this study, strict criteria were used to define the primary and secondary outcomes prospectively. The less specific criteria that was used for coding may have included some cases that would not meet the criteria for wound infections in our study.

Secondary outcomes, including rates of postcesarean endometritis and postoperative fever were similar, regardless of which type of vaginal preparation was used. This finding may be because the overall incidence of endometritis in our patient population was surprisingly low, at 0.4%, given that the national rate is approximately 11% for cesarean deliveries performed after the onset of labor and 1.7% for those performed electively.[18] The same factors that may have affected our rate of wound infection could have also accounted for our low incidence of endometritis.

After conducting a subanalysis, our results showed that women in either the povidone-iodine or chlorohexidine arm with ruptured membranes had similar rates of primary and secondary outcomes. This is consistent with a 2018 Cochrane review that showed that there was insufficient evidence to suggest that women with ruptured membranes prior to cesarean delivery benefit more from vaginal cleansing compared with those without ruptured membranes.[1,19-21] However, a recent meta-analysis by Berghella and colleagues[22] found that vaginal cleansing prior to cesarean delivery reduced the incidence of endometritis. Subgroup analysis demonstrated that the reduction in the incidence of endometritis was limited to

TABLE 3
Wound infection rates

Characteristics	Wound infection	*P* value
Insurance		
Uninsured	2/273 (0.7)	.382
Privately insured	13/827 (1.6)	
Pregestational diabetes		
Yes	1/11 (9.1)	.140
No	14/1096 (1.3)	
Gestational diabetes		
Yes	1/65 (1.5)	.599
No	14/1042 (1.3)	
Preeclampsia		
Yes	2/36 (5.6)	.083
No	13/1072 (1.2)	
Gestational hypertension		
Yes	1/56 (1.8)	.543
No	14/1052 (1.3)	
Rupture of membranes before cesarean delivery		
Yes	3/344 (0.9)	.574
No	12/769 (1.6)	
Scheduled cesarean delivery vs trial of labor		
Scheduled	8/536 (1.5)	.797
Trial of labor	7/577 (1.2)	
Subcutaneous layer reapproximated with 2-0 plain gut suture		
Yes	9/748 (1.2)	.577
No	6/347 (1.7)	
Skin closure		
Suture	0/206 (0)	.089
Staples	15/887 (1.7)	

All values are presented as the number of patients within a group who were diagnosed with a wound infection/number of women in the group (percentage). All *P* values use a Fisher exact test.

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women in labor before cesarean delivery (8.1% compared with 13.8%; RR, 0.52, 95% CI, 0.28−0.97) or those with ruptured membranes (4.3% compared with 20.1%; RR, 0.23, 95% CI, 0.10−0.52).[22] The lack of a difference in rates of endometritis in our study between women with ruptured membranes and those without may be due to the fact that endometritis is an ascending infection. For women with ruptured membranes, bacteria from the vagina may have already ascended and colonized in the uterus prior to vaginal cleansing, which may have negated any beneficial effect. Additionally, women with preterm premature rupture of membranes and those diagnosed with clinical chorioamnionitis were not excluded from the study. These patients received antibiotics in labor, which may have minimized the incidence of endometritis.

The safety and efficacy of vaginal application of chlorhexidine gluconate in low concentrations has been well established in the literature, with several studies that include more than 4500 women.[6,23,24] One small randomized trial of 50 patients compared the efficacy of 4% chlorhexidine gluconate and 10% povidone-iodine for preparation of the vagina prior to vaginal hysterectomy.[6] The primary endpoint was the number of bacterial colonies noted on serial cultures obtained throughout the surgery. Thirty minutes after application, those in the iodine group were 6 times more likely to have contaminated cultures compared with those in the chlorhexidine group.

Two other randomized trials have investigated the use of chlorhexidine prior to cesarean delivery; however, none used povidone iodine as a comparator.[25,26] Evidence from the 2 studies is conflicting. Rouse et al[25] studied 1024 patients randomized to chlorhexidine or placebo and found no differences among rates of endometritis. A smaller study of 218 women by Ahmed et al[26] found a significant reduction in overall postcesarean delivery infectious morbidity with use of chlorhexidine compared with no vaginal cleansing (8.8% vs 24.4%, respectively, $P = .003$, RR, 0.3 [95% CI, 0.2−0.7]).

The US product labeling of chlorhexidine gluconate specifies to avoid genital use; however, solutions with low concentrations of alcohol may be used off label in the vagina as an antiseptic for both obstetric and gynecological procedures.[27] In the United States, 4% chlorhexidine gluconate (containing 4% isopropyl alcohol) is often used off label to prepare the vagina in cases of iodine allergy. To avoid irritation, chlorhexidine gluconate with high concentrations of alcohol, such as those commonly used for skin preparation (containing 70% isopropyl alcohol) should not be used in the vagina.

Based on the results of our study, the use of 4% chlorhexidine gluconate vaginal preparation is effective in lowering the incidence of surgical site wound infections and resulted in no adverse reactions. Given that the incidence of endometritis was lower than anticipated, a larger sample size would be necessary to evaluate this outcome.

TABLE 4
Strategies in place to decrease surgical site infections after cesarean delivery at Richmond University Medical Center, Staten Island

Antepartum	
Prophylactic antibiotics[a]	Patients receive prophylactic antibiotics consisting of a single dose of IV cefazolin (3 g for women ≥120 kg and 2 g for women <120 kg) at least 30 minutes prior to skin incision.[10] Alternative prophylactic antibiotics include 600 mg IV clindamycin or 500 mg IV erythromycin for patients with a penicillin allergy.
Antibiotics for nonscheduled CD[a]	Patients undergoing cesarean delivery during labor or after membrane rupture receive 500 mg of IV azithromycin in addition to the standard prophylactic antibiotics.[12]
Abdominal skin preparation[a]	Abdominal application with a 70% chlorhexidine gluconate isopropyl alcohol solution prior to skin incision as per the manufacturer's instructions.
Vaginal cleansing[a]	Vaginal cleansing as per study protocol with either a 4% chlorhexidine or 10% povidone-iodine solution.
Intraoperative	
Prevention of maternal hypothermia[a]	Forced-air warming blankets are routinely used to prevent intraoperative hypothermia as well as maintaining an ambient temperature at 73ºF in the obstetrical operating rooms.[13,14]
Incision for obese patients	A modified Joel-Cohen incision technique for obese patients is strongly encouraged to avoid making the incision under the panniculus.[15]
Placenta extraction	Placental removal by umbilical cord traction is strongly recommend at our institution; however, choice is ultimately left to provider discretion.[16]
Instrument/glove change[a]	Prior to closure of the fascia, all scrubbed personnel change gloves. A separate sterile instrument pack (scissors, needle holder, tissue forceps) is used to close the fascia, subcutaneous tissue, and skin.
Subcutaneous closure[a]	Subcutaneous approximation with a 2-0 plain suture for all women with >2 cm of subcutaneous tissue
Skin closure	Skin is closed with staples or subcuticular suture. This is left to provider choice. If staples are used, we encourage removal by postoperative day 7.
Postpartum	
Dressing removal[a]	Dressings are left in place for 24 hours postoperatively.
Additional antibiotics for obese patients[b]	Patients with a BMI >35 kg/m^2 are given oral cephalexin (500 mg) and metronidazole (500 mg) every 8 hours for a total of 48 hours postoperatively.[17]
Negative-pressure wound therapy[b]	A negative-pressure wound therapy system PICO 7 (Smith and Nephew Medical Ltd, London, UK) is offered to patients with a BMI >35 kg/m^2. This PICO dressing is kept in place until postoperative day 7.

BMI, body mass index; *CD*, cesarean delivery; *IV*, intravenous.

[a] Departmental policy was in effect during study period; [b] New departmental policy was put into effect after study closure.

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Strengths of this study included a large number of patients to evaluate the primary outcome and randomization to eliminate the effects of variation in care. Use of skin-preparation procedures and antibiotic prophylaxis was standardized between both groups. Certain aspects of the cesarean procedure including the reapproximation of subcutaneous tissue with suture, or skin closure with either suture or staples, were left to the discretion of the surgeon. This allows our data to be generalizable for various surgical techniques.

We used active surveillance, including telephone calls to patients and providers, to minimize loss to follow-up and to track the incidence of primary and secondary outcomes. This is important because most postcesarean delivery infections occur after discharge from the hospital. Both data analysis and the telephone surveys were conducted by researchers who were blinded to the randomization of patients, thereby limiting bias.

Our study also has some limitations. First, we conducted the trial at a single site, which raises a question about the potential generalizability of our findings to other hospital settings. Second, the study was not randomized by patient but rather by calendar-generated time blocks. However, this method of randomization still allowed our schedule to be unpredictable to providers and study staff while ensuring that the study could continue during the hours that study personnel were unavailable.

Patients were equally likely to be assigned to a particular cleansing solution based on the day of their cesarean delivery. Random variation in the number of cesarean deliveries that occurred on each assigned day accounted for the discrepancy in numbers between participants in each group.

Finally, blinding was not possible for this study because the povidone-iodine solution and chlorhexidine solution were different colors. Using a dummy solution was considered. It was ultimately decided against because it may have confounded the results as the participants would have needed to have their vaginas cleaned twice.

Vaginal cleansing with a 4% chlorhexidine solution prior to cesarean delivery resulted in a significant reduction of overall surgical site wound infection up to 14 days after cesarean delivery when compared with the povidone-iodine solution. A 4% solution of chlorhexidine gluconate solution did not have any patient-reported adverse effects on the vaginal mucosa. Given that the overall rate of postcesarean endometritis

was lower than anticipated, a larger sample size would be required to assess for this outcome. ■

Acknowledgment

This study had a Clinical Trial registration number of NCT02915289 (https://clinicaltrials.gov/ct2/show/NCT02915289?term=vaginal+cleansing&rank=6).

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Received Feb. 15, 2019; revised March 12, 2019; accepted March 12, 2019.

The authors report no conflicts of interest.

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