Review

Vaginal Cleansing Before Cesarean Delivery

A Systematic Review and Meta-analysis

Claudia Caissutti, MD, Gabriele Saccone, MD, Fabrizio Zullo, MD, Johanna Quist-Nelson, MD, Laura Felder, MD, Andrea Ciardulli, MD, and Vincenzo Berghella, MD

OBJECTIVE: To assess the efficacy of vaginal cleansing before cesarean delivery in reducing postoperative endometritis.

DATA SOURCES: MEDLINE, Ovid, EMBASE, Scopus, Clinicaltrials.gov, and Cochrane Library were searched from their inception to January 2017.

METHODS OF STUDY SELECTION: Selection criteria included all randomized controlled trials comparing vaginal cleansing (ie, intervention group) with a control group (ie, either placebo or no intervention) in women undergoing cesarean delivery. Any method of vaginal cleansing with any type of antiseptic solution was included. The primary outcome was the incidence of endometritis. Meta-analysis was performed using the random-effects model of DerSimonian and Laird to produce summary treatment effects in terms of relative risk (RR) with 95% CI.

TABULATION, INTEGRATION, AND RESULTS: Sixteen trials (4,837 women) on vaginal cleansing immediately before cesarean delivery were identified as relevant and included in the review. In most of the included studies, 10% povidone–iodine was used as an intervention. The most common way to perform the vaginal cleansing was the use of a sponge stick for approximately 30 seconds. Women who received vaginal cleansing before cesarean delivery had a significantly lower incidence of endometritis (4.5% compared with 8.8%; RR 0.52, 95% CI 0.37–0.72; 15 studies, 4,726 participants) and of postoperative fever (9.4% compared with 14.9%; RR 0.65, 95% CI 0.50–0.86; 11 studies, 4,098 participants) compared with the control group. In the planned subgroup analyses, the reduction in the incidence of endometritis with vaginal cleansing was limited to women in labor before cesarean delivery (8.1% compared with 13.8%; RR 0.52, 95% CI 0.28–0.97; four studies, 440 participants) or those with ruptured membranes (4.3% compared with 20.1%; RR 0.23, 95% CI 0.10–0.52; three studies, 272 participants).

CONCLUSION: Vaginal cleansing immediately before cesarean delivery in women in labor and in women with ruptured membranes reduces the risk of postoperative endometritis. Because it is generally inexpensive and a simple intervention, we recommend preoperative vaginal preparation before cesarean delivery in these women with sponge stick preparation of povidone–iodine 10% for at least 30 seconds. More data are needed to assess whether this intervention may be also useful for cesarean deliveries performed in women not in labor and for those without ruptured membranes.

SYSTEMATIC REVIEW REGISTRATION: PROSPERO International prospective register of systematic reviews, https://www.crd.york.ac.uk/PROSPERO/, CRD42017054843.

(Obstet Gynecol 2017;130:527–38)
DOI: 10.1097/AOG.0000000000002167

The most important risk factor for postpartum maternal infection is cesarean delivery.[1] Women undergoing cesarean delivery have a 5- to 20-fold greater risk for infection and infectious morbidity compared with those undergoing a vaginal birth.[1]

Postcesarean delivery infection is a major health problem, which can cause maternal morbidity and mortality. The most frequent postcesarean infective complications are endometritis (6–27%), clinically significant fever (5–24%), and wound infection (2–9%).[2]

From the Department of Experimental Clinical and Medical Science, DISM, Clinic of Obstetrics and Gynecology, University of Udine, Udine, and the Department of Neuroscience, Reproductive Sciences and Dentistry, School of Medicine, University of Naples Federico II, Naples, Italy; the Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, Pennsylvania; and the Department of Obstetrics and Gynecology, Catholic University of Sacred Heart, Rome, Italy.

Each author has indicated that he or she has met the journal's requirements for authorship.

Corresponding author: Vincenzo Berghella, MD, Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Thomas Jefferson University, 833 Chestnut Street, Philadelphia, PA 19107; email: vincenzo.berghella@jefferson.edu.

Financial Disclosure
The authors did not report any potential conflicts of interest.

ISSN: 0029-7844/17

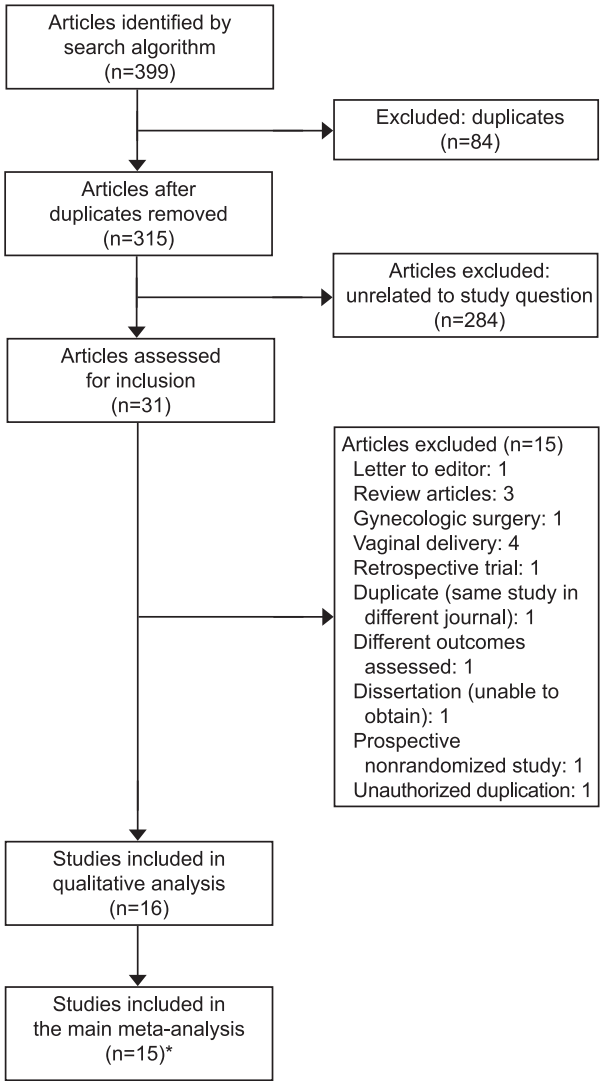

Fig. 1. Flow diagram of studies identified in the systematic review. *One study was analyzed separately.

Caissutti. Vaginal Preparation Before Cesarean Delivery. Obstet Gynecol 2017.

Postpartum endometritis occurs after 1–3% of all deliveries and it is up to 10 times more common after cesarean delivery.[1,2]

The main cause of endometritis is ascending infection by mostly anaerobic bacteria from the vagina.[3] Compared with placebo or no treatment, presurgical broad-spectrum antibiotic prophylaxis administration in women undergoing cesarean delivery reduced the incidence of infectious complications by 60–70%.[4,5] It is unclear whether additional benefit could be obtained by cleansing the vagina with antibacterial agents. In the last few years several randomized controlled trials (RCTs) have investigated the efficacy of vaginal cleansing with antiseptic solutions before cesarean delivery.[6] In a Cochrane review, Haas et al[6] pooled data from five RCTs evaluating the effects of vaginal cleansing with povidone–iodine on postcesarean infectious morbidity. They showed with a low quality of evidence that vaginal preparation with povidone–iodine immediately before cesarean delivery may reduce the risk of postoperative endometritis.

The aim of this review was to assess the efficacy of vaginal cleansing before cesarean delivery in reducing postoperative endometritis through a systematic review of RCTs and a meta-analysis.

SOURCES

This review was performed according to a protocol recommended for systematic review.[7] The review protocol was designed a priori to define methods for collecting, extracting, and analyzing data. The research was conducted with the use of MEDLINE, Ovid, EMBASE, Scopus, Clinicaltrials.gov, and Cochrane Library as electronic databases by two independent reviewers (C.C., L.F.). The trials were identified with the use of a combination of the following text words: "vaginal irrigation," "cesarean," "pregnancy," "infection," "caesarean," "endometritis," "povidone-iodine," "chlorhexidine," "trial," and "randomized" from the inception of each database to January 2017. Review of articles also included the abstracts of all references that were retrieved from the search. No restrictions for language or geographic location were applied.

STUDY SELECTION

Selection criteria included all RCTs comparing vaginal cleansing (ie, intervention group) with a control group (ie, either placebo or no intervention) in women undergoing cesarean delivery. Trials in women undergoing vaginal delivery were excluded as were trials not reporting any of our outcomes of interest.[8] Any method of vaginal cleansing (eg, douches, wipes, sponges) with any type of antiseptic solution (eg, povidone–iodine, chlorhexidine) was included. Trials comparing different solutions were also included but analyzed separately.

Only trials in which vaginal preparation was performed no more than 1 hour before surgery were included. This review addressed the use of preoperative vaginal cleansing after the decision to perform cesarean delivery had been made and did not address the use of vaginal preparation during labor.

The risk of bias in each included study was assessed by using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions.* Seven domains related to risk of bias were assessed in each

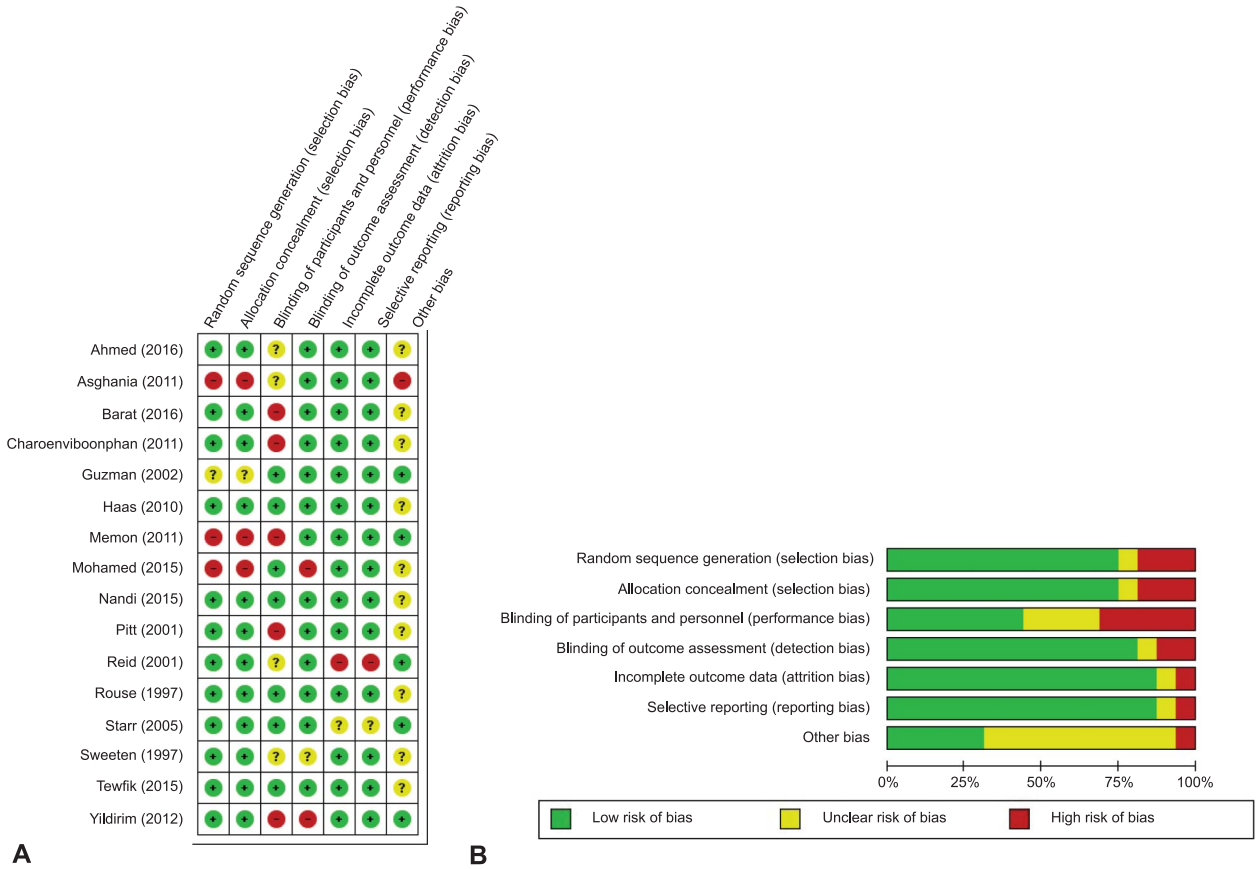

Fig. 2. Assessment of risk of bias. **A.** Summary of risk of bias for each trial. *Plus sign* indicates low risk of bias, *minus sign* indicates high risk of bias, and *question mark* indicates unclear risk of bias. **B.** Risk of bias items presented as percentages across all included studies.

Caissutti. Vaginal Preparation Before Cesarean Delivery. Obstet Gynecol 2017.

included trial because there is evidence that these issues are associated with biased estimates of treatment effect: 1) random sequence generation, 2) allocation concealment, 3) blinding of participants and personnel, 4) blinding of outcome assessment, 5) incomplete outcome data, 6) selective reporting, and 7) other bias. Review authors' judgments were categorized as "low risk," "high risk," or "unclear risk" of bias.[7]

For each trial, data regarding vaginal cleansing procedure and incidence of infective complications were extracted and carefully reviewed. We planned to review the type of solution used and duration of the procedure.

The primary outcome was the incidence of endometritis as defined by the original trials. Secondary outcomes were postoperative wound infection; postoperative fever greater than 38°C or 100.4°F; and other wound complications including postoperative wound seroma or hematoma.

For the primary outcome, the following subgroup analyses were planned:

1. Women in labor compared with those not in labor;
2. Women with ruptured membranes compared with those with intact membranes;
3. Type of antiseptic solution; and
4. Time of use of prophylactic antibiotics.

We also excluded studies in which prophylactic surgical antibiotics were explicitly not used. Surgical prophylaxis with intravenous antibiotics before or during cesarean deliveries has been clearly demonstrated as beneficial in reducing postoperative infectious morbidities. Thus, it is the standard of care. Inclusion of trials not using general surgical antibiotic prophylaxis would not represent the current standard of care and the results would not be translatable into current practice.

The data analysis was completed independently by two authors (A.C., G.S.) using Review Manager

Table 1. Characteristics of the Included Trials

Author, Year	Country	Sample Size (Intervention vs control)	Inclusion Criteria
Rouse, 1997[10]	United States	130 (62 vs 68)*	Patients admitted for delivery at 24 wk of gestation or greater
Sweeten, 1997[2]	United States	64 (32 vs 32)*	Patient in labor with intact membranes at 36 wk of gestation or greater
Pitt, 2001[11]	United States	224 (112 vs 112)	Patients 24 wk of gestation or greater undergoing cesarean delivery, no intrapartum infections
Reid, 2001[12]	United States	430 (217 vs 213)	Patients undergoing cesarean delivery
Guzman, 2002[13]	United States	160 (80 vs 80)	Patients undergoing planned cesarean delivery
Starr, 2005[14]	United States	308 (142 vs 166)	Patients undergoing nonemergent planned cesarean delivery
Haas, 2010[15]	United States	300 (155 vs 145)	Patients undergoing cesarean delivery
Asghani, 2011[16]	Iran	568 (284 vs 284)	Patients undergoing cesarean delivery
Memon, 2011[17]	Pakistan	200 (100 vs 100)	Patients undergoing cesarean delivery
Charoenviboonphan, 2011[18]	Thailand	599 (299 vs 300)	Patients undergoing cesarean delivery
Yildirim, 2012[19]	Turkey	669 (334 vs 335)	Patients undergoing cesarean delivery at 39 wk of gestation or greater
Mohamed, 2015[21]	Egypt	200 (100 vs 100)	Patient undergoing nonemergent planned cesarean delivery at 39 wk of gestation or greater
Nandi, 2015[22]	Bangladesh	274 (136 vs 138)	Patients undergoing cesarean delivery
Tewfik, 2015[23]	Egypt	93 (46 vs 47)	Patient undergoing nonemergent planned cesarean delivery at 39 wk of gestation or greater
Ahmed, 2016[24]	Egypt	218 (109 vs 109)	Singletons undergoing nonemergent planned cesarean delivery at 39 wk of gestation or greater
Barat, 2016[25]	Iran	400 (200 vs 200)	Singletons undergoing nonemergent planned cesarean delivery at 39 wk of gestation or greater

DM, diabetes mellitus; BMI, body mass index; ROM, rupture of membranes at the time of randomization; PROM, prelabor rupture of membranes.
Data are total number (number in the intervention group vs number in the control group).
* We considered only women who underwent cesarean delivery.

Exclusion Criteria	Intervention Group (Vaginal Cleansing)	Control Group	Primary Outcome(s)
Contraindication to digital cervical examination, active genital herpes, chorioamnionitis before randomization, or known or suspected allergy to chlorhexidine	225 mL chlorhexidine diacetate 0.2%	Placebo (sterile water)	Intrapartum chorioamnionitis, postpartum endometritis
Contraindication to digital cervical examination, active genital herpes, chorioamnionitis before randomization, malpresentation, or known or suspected allergy to chlorhexidine	20 mL chlorhexidine diacetate 0.4%	Placebo (sterile water)	Intraamniotic infection
Patients with chorioamnionitis or suspected allergy to metronidazole	Metronidazole 0.5% 5 g vaginal gel (37.5 mg)	Placebo (5 g vaginal gel)	Postcesarean endometritis
Highly emergent cesarean delivery, allergy to povidone–iodine, iodine, or shellfish; bleeding placenta previa; and active genital herpes	Sponge stick preparation of povidone–iodine 10%	No treatment	Fever, endometritis
Emergent need for delivery, allergy, or placenta previa	Sponge stick preparation of povidone–iodine in vagina for 3 min	Placebo (sponge stick preparation of saline in vagina for 3 min)	Postcesarean endometritis
Placenta previa, diagnosis of chorioamnionitis	Sponge stick preparation of povidone–iodine in vagina for 30 s	No treatment	Postoperative febrile morbidity, endometritis, wound infection
Allergy to iodine-containing solutions or planned cesarean hysterectomy	Sponge stick preparation of povidone–iodine 1% in vagina	No treatment	Postoperative fever, endometritis, early wound complications
Povidone–iodine hypersensitivity; active chorioamnionitis; gestational herpes; abnormal vaginal discharge during pregnancy (foul-smelling discharge with pruritus, which could stain underwear); emergency cesarean delivery	Sponge stick preparation of povidone–iodine 10% in vagina for 30 s	No treatment	Febrile morbidity, endometritis, wound infection
Allergy to iodine-containing solutions and bleeding placenta previa	Sponge stick preparation of povidone–iodine 10% in vagina	No treatment	Febrile morbidity, endometritis, wound infection
Allergy to iodine-containing solutions and bleeding placenta previa	Sponge stick preparation of povidone–iodine 1% in vagina	No treatment	Postoperative fever, endometritis, wound infection, length of hospital stay
Umbilical cord prolapse, placenta previa, allergy to povidone–iodine	Sponge stick preparation of povidone–iodine in vagina for 30 s	No treatment	Postoperative fever, endometritis, wound infection
DM, anemia, history of postcesarean delivery infection, obstructed labor, preeclampsia, allergy to Cetrimide	Vaginal preparation with diluted Cetrimide 50 cc	No treatment	Postpartum morbidity
Cesarean delivery with deeply engaged head, bleeding placenta previa, active genital herpes, and allergy to iodine	Vaginal scrub with povidone–iodine 5%	No treatment	Endometritis, abdominal wound infection
BMI greater than 30 kg/m^2, ROM, antepartum hemorrhage, chronic steroid or immunosuppressive treatment	Vaginal preparation with povidone–iodine	Vaginal preparation with chlorhexidine	Postoperative fever and endometritis
PROM, placenta previa, immunocompromised status	Vaginal cleansing with sterile gauze pieces 225 mL chlorhexidine diacetate 0.2% for approximately 1 min	Placebo (sterile water)	Adverse postcesarean infectious morbidities
Allergy to povidone–iodine, antepartum hemorrhage, ROM diabetes	Sponge stick preparation of povidone–iodine 10% in vagina for 30 s	No treatment	Postoperative fever, postpartum endometritis, early wound complications

Table 2. Technical Characteristics of Cesarean Delivery

Author, Year	Time of Cesarean Delivery	Patients in Labor (n)	Patients With ROM at Randomization (n)
Rouse, 1997[10]	Planned, after labor or emergent	56/62 vs 60/68	Not stated
Sweeten, 1997[2]	After labor or emergent	32/32 vs 32/32	0/32 vs 0/32
Pitt, 2001[11]	Planned, after labor or emergent	64/112 vs 67/112	10/112 vs 16/112
Reid, 2001[12]	Planned, or after labor	107/217 vs 104/213	Not stated
Guzman, 2002[13]	Planned	None	36/80 vs 36/80
Starr, 2005[14]	Planned	None	86/142 vs 113/166
Haas, 2010[15]	Planned, after labor or emergent	45/155 vs 50/145	34/155 vs 42/145
Asghania, 2011[16]	Planned, after labor or emergent	Not stated	Not stated
Memon, 2011[17]	Planned, after labor or emergent	31/100 vs 38/100	25/100 vs 33/100
Charoenviboonphan, 2011[18]	Planned, after labor or emergent	Not stated	Not stated
Yildirim, 2012[19]	Planned, after labor or emergent	115/334 vs 97/335	68/334 vs 56/335
Mohamed, 2015[21]	Planned	None	5/100 vs 4/100
Nandi, 2015[22]	Planned, after labor or emergent	92/136 vs 94/138	16/136 and 18/138
Tewfik, 2015[23]	Planned	None	None
Ahmed, 2016[24]	Planned	None	None
Barat, 2016[25]	Planned	None	None

ROM, rupture of membranes; bpm, beats per minute.
Data are number in the intervention group vs number in the control group.

5.3. The completed analyses were then compared, and any difference was resolved by discussion with a third reviewer (V.B.). Data from each eligible study were extracted without modification of original data onto custom-made data collection forms. For continuous outcomes, means±SDs were extracted and imported into Review Manager 5.3. Meta-analysis was performed using the random-effects model of DerSimonian and Laird to produce summary treatment effects in terms of mean difference or relative risk (RR) with

Chorioamnionitis (n)	Timing of Antibiotics	Definition of Endometritis
Not stated	All patients after cord clamping	Temperature greater than 100.4˚F, a diagnosis of endometritis by the managing physicians, one or more symptoms or signs: uterine tenderness, maternal tachycardia (greater than 100 bpm), purulent or foul-smelling cervical discharge, or maternal leukocytosis (greater than 12,000 cells/mL^3)
Not stated	All patients after cord clamping	Temperature greater than 100˚F with two of the following criteria: maternal tachycardia, uterine tenderness, foul-smelling amniotic fluid, maternal leukocytosis, or fetal tachycardia.
Not stated	89/112 vs 95/112 (after cord clamping) and 23/112 vs 17/112 (before incision)	Oral temperature 38˚C or greater on any 2 postoperative d (excluding the first 24 h) and one or more sign: uterine tenderness to palpation, maternal tachycardia (at least 100 bpm), foul-smelling vaginal discharge, or maternal leukocytosis (greater than 12,000/mm^3)
68/500	322/430 (after cord clamping) and 172/430 (antepartum)	Postoperative fever with a physician's note indicating uterine or abdominal pain or tenderness, preceding an order for broad-spectrum, intravenous antibiotics, without other apparent source of serious infection
Not stated	Not stated	Temperature greater than 100.4˚F at least twice, 24 h after surgery, or of greater than 101˚F at any time after surgery, with abdominal or uterine tenderness
Not stated	All patients after cord clamping	Temperature greater than 38.4˚C persisting beyond the first postoperative d, with uterine tenderness and foul lochia, in the absence of physical or laboratory evidence of other infection
5/155 vs 9/145	All patients after cord clamping	Uterine tenderness plus postoperative fever requiring antibiotic administration
Not stated	All patients before incision	Temperature greater than 38.4˚C persisting beyond the first postoperative d, in association with uterine tenderness and foul lochia, in the absence of physical or laboratory evidence of other infection
4/100 vs 6/100	All patients before incision	Postoperative fever greater than 38.4˚C with uterine tenderness and foul-smelling lochia requiring broad-spectrum intravenous antibiotic administration
Not stated	Not stated	Postoperative fever greater than 38.4˚C with uterine tenderness and foul-smelling lochia requiring broad-spectrum intravenous antibiotic administration
Not stated	All patients before incision	Body temperature greater than 38.5˚C with concomitant foul-smelling discharge or abnormally tender uterus on bimanual examination
Not stated	All patients before incision and postoperatively	Presence of fever, purulent lochia and fundal tenderness, needed antibiotic therapy
Not stated	All patients after cord clamping	Uterine tenderness plus postoperative fever with leucocytosis
Not stated	All patients before incision and postoperatively	Fever 38˚C, uterine tenderness, and offensive vaginal discharge that necessitate antibiotic treatment
Not stated	All patients before incision	Postoperative fever greater than 38.4˚C at least twice 24 h after delivery associated with uterine tenderness and persistent offensive lochia
Not stated	All patients after cord clamping and postoperatively	Fever greater than 38˚C with uterine tenderness and foul-smelling lochia, which require a wide variety of intravenous antibiotics

95% CI. Heterogeneity was measured using Higgins I^2. Potential publication biases were assessed statistically by using Begg's and Egger's tests. The meta-analysis was reported following the Preferred Reporting Item for Systematic Reviews and Meta-analyses statement.[9] Before data extraction, the review was registered with the PROSPERO International Prospective Register of Systematic Reviews (Registration Number: CRD42017054843).

RESULTS

Seventeen RCTs[2,10–25] were identified as relevant and met the inclusion criteria (Fig. 1). However, Ameer et al[20] was excluded because it was an unauthorized

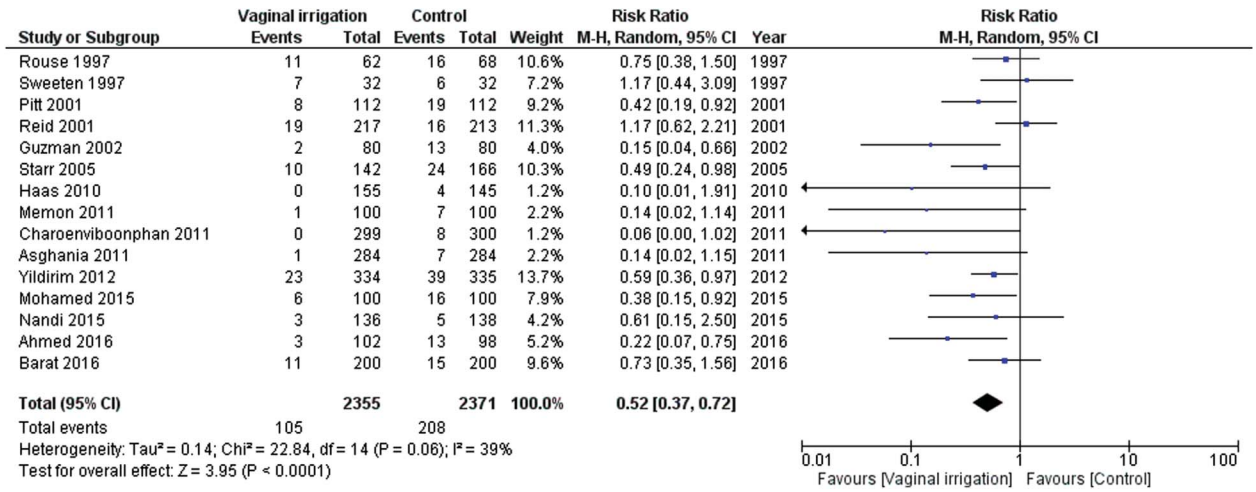

Fig. 3. Forest plot for the risk of endometritis. M-H, Mantel-Haenszel; df, degrees of freedom.
Caissutti. Vaginal Preparation Before Cesarean Delivery. Obstet Gynecol 2017.

duplication of Starr et al.[14] Therefore, 16 RCTs (n=4,837 women)[10–19,21–25] were included in the systematic review, of which 15 RCTs,[10–22,24,25] involving 4,744 women randomized to either vaginal cleansing before cesarean delivery or control (ie, either placebo or no treatment), contributed data to the quantitative meta-analysis. One trial[23] compared vaginal preparation with povidone–iodine with vaginal preparation with chlorhexidine and therefore was analyzed separately. Publication bias, assessed statistically by using Begg's and Egger's tests, showed no significant bias (*P*=.33 and *P*=.27, respectively).

The overall risk of bias was low. Most of the included studies had a low risk of bias in "random sequence generation." In three trials, the method of random sequence generation was judged as inadequate. Adequate methods for allocation of women were used in all the included trials, but one in which details on methods used to conceal allocation were not reported and in three that were judged as inadequate. Regarding "incomplete outcome data," 14 RCTs were judged as "low risk" of bias, one as "unclear," and one as "high risk" of bias (Fig. 2). The studies came from different countries, including both high-income and low- and middle-income countries. Seven trials originated from the United States. The year of the trials' publication ranged from 1997 to 2016, and most of them were published after 2010. Six trials included only women undergoing planned, scheduled, nonemergent cesarean delivery, and nine included also laboring women or emergent cesarean delivery, whereas Sweeten et al[2] included only laboring women (Table 1). Of the nine studies that included also laboring women, two RCTs did not state the number of included laboring women, whereas seven RCTs included overall 1,020 of 2,227 laboring women (510/1,116 and 510/1,111 in the intervention and the control groups, respectively) (Table 2). Four trials explicitly included only women at 39 weeks of gestation or greater (Table 1).

In most of the included studies (11 RCTs), povidone–iodine was used as an intervention. Of them, four did not report the percentage of the solution, four used 10% povidone–iodine, two used 1%, and one used 5%. Two trials used 225 mL chlorhexidine diacetate 0.2%, one used 20 mL chlorhexidine diacetate 0.4%, and one trial used metronidazole 0.5% 5 g vaginal gel; the other trial used Cetrimide 50 cc. In five double-blind RCTs,[2,10,11,13,24] which used placebo as a control, neither the participants nor the investigators were aware of the treatment assignment. Ten trials used no treatment as control. Tewfik et al[23] compared povidone–iodine (intervention group) with chlorhexidine (control group) (Table 1). The most common way to perform the vaginal cleansing was the use of a sponge stick (nine RCTs) for approximately 30 seconds (four RCTs). In one trial, the sponge stick was used for 3 minutes and in one for 60 seconds. One study used vaginal gel, one used vaginal scrubs, one used sterile gauze, and three did not specify these details. Sweeten et al[2] used a syringe to perform vaginal cleansing.

All trials used prophylactic or intraoperative surgical antibiotics. Six studies used antibiotics before incision, six after cord clamping, two trials either before incision or after cord clamping, and the other two did not report timing of antibiotics. In three studies, antibiotics were administrated also

Table 3. Primary and Secondary Outcomes Comparing Vaginal Cleansing With No Vaginal Cleansing

Author, Year	Endometritis	Postoperative Fever	Wound Infection	Others Wound Complications*
Rouse, 1997[10]	11/62 (17.7) vs 16/68 (23.5)	Not reported	Not reported	1/62 (1.6) vs 2/68 (2.9)
Sweeten, 1997[2]	7/32 (21.9) vs 6/32 (18.8)	Not reported	Not reported	Not reported
Pitt, 2001[11]	8/112 (7.1) vs 19/112 (17.0)	15/112 (13.4) vs 21/112 (18.8)	5/112 (4.5) vs 3/112 (2.7)	Not reported
Reid, 2001[12]	19/217 (8.8) vs 16/213 (7.5)	12/217 (5.5) vs 13/213 (6.1)	Not reported	12/217 (5.5) vs 18/213 (8.5)
Guzman, 2002[13]	2/80 (2.5) vs 13/80 (16.3)	Not reported	Not reported	7/80 (8.8) vs 4/80 (5.0)
Starr, 2005[14]	10/142 (7.0) vs 24/166 (14.5)	34/142 (23.9) vs 47/166 (28.3)	1/142 (0.7) vs 2/166 (1.2)	Not reported
Haas, 2010[15]	0/155 (0.0) vs 4/145 (2.8)	2/155 (1.3) vs 7/145 (4.8)	7/155 (4.5) vs 10/145 (6.9)	6/155 (3.9) vs 12/145 (8.3)
Asghania, 2011[16]	1/284 (0.3) vs 7/284 (2.5)	14/284 (4.9) vs 17/284 (6.0)	10/284 (3.5) vs 9/284 (3.2)	Not reported
Memon, 2011[17]	1/100 (1.0) vs 7/100 (7.0)	4/100 (4.0) vs 6/100 (6.0)	1/100 (1.0) vs 3/100 (3.0)	Not reported
Charoenviboonphan, 2011[18]	0/299 (0.0) vs 8/300 (2.7)	34/299 (11.4) vs 93/300 (31.0)	1/299 (0.3) vs 4/300 (1.3)	Not reported
Yildirim, 2012[19]	23/334 (6.9) vs 39/335 (11.6)	55/334 (16.5) vs 61/335 (18.2)	6/334 (1.8) vs 9/335 (2.7)	Not reported
Mohamed, 2015[21]	6/100 (6.0) vs 16/100 (16.0)	10/100 (10.0) vs 23/100 (23.0)	5/100 (5.0) vs 9/100 (9.0)	Not reported
Nandi, 2015[22]	3/136 (2.2) vs 5/138 (3.6)	Not reported	4/136 (2.9) vs 7/138 (5.1)	Not reported
Tewfik, 2015[23],†	Not reported	Not reported	Not reported	Not reported
Ahmed, 2016[24]	3/102 (2.9) vs 13/98 (13.3)	2/102 (2.0) vs 4/98 (4.1)	4/102 (3.9) vs 7/98 (7.1)	Not reported
Barat, 2016[25]	11/200 (5.5) vs 15/200 (7.5)	10/200 (5.0) vs 14/200 (7.0)	12/200 (6.0) vs 13/200 (6.5)	Not reported
Total	105/2,355 (4.5) vs 208/2,371 (8.8)	192/2,041 (9.4) vs 306/2,057 (14.9)	56/1,964 (2.9) vs 76/1,978 (3.8)	26/514 (5.1) vs 36/506 (7.1)
RR (95% CI)	**0.52 (0.37–0.72)**	**0.65 (0.50–0.86)**	0.74 (0.53–1.05)	0.71 (0.43–1.17)
I^2 (%)	39	49	0	1

RR, relative risk.
Data are as number in the intervention group (%) vs number in the control group (%) unless otherwise specified.
Bold indicates statistically significant data.
* Other wound complications: seroma, hematoma, wound separation, cellulitis.
† Excluded from the main analysis.

postoperatively (Table 2). Data on placental removal and on peritoneal closure were not available in any of the trials.

Fifteen RCTs, involving 4,744 women and comparing vaginal cleansing with either placebo or no treatment, were included in the quantitative meta-analysis. Women who received vaginal cleansing before cesarean delivery had a significantly lower incidence of endometritis (4.5% compared with 8.8%; RR 0.52, 95% CI 0.37–0.72; Fig. 3) and postoperative fever (9.4% compared with 14.9%; RR 0.65, 95% CI 0.50–0.86) compared with the control group. No statistically significant differences were found in the incidence of postoperative wound infection or other wound complications (Table 3). Side effects such as allergy were not recorded in the included trials.

Three trials stratified data for women in labor compared with not in labor,[15,17,19] and one included only laboring women.[2] There was a statistically significant reduction in the incidence of endometritis for women in labor before cesarean delivery who received vaginal cleansing (8.1% compared with 13.8%; RR 0.52, 95% CI 0.28–0.97; four studies, 440 participants). The subgroup analysis for women who were not in labor before the operation did not show a statistically significant benefit in the primary outcome (3.5% compared with 6.6%; RR 0.62, 95% CI 0.34–1.15; three studies, 793 participants).

Three trials stratified data for women with ruptured membranes compared with women without ruptured membranes.[13,15,19] One trial explicitly included only women with intact membranes at the time of randomization.[2] There was a statistically significant reduction in the rate of endometritis for women receiving vaginal cleansing with ruptured membranes (4.3% compared with 20.1%; RR 0.23, 95% CI 0.10–0.52; three studies, 272 participants). For women with intact membranes at the time of

cesarean delivery, the rate of postoperative endometritis was not significantly reduced in the vaginal preparation group (4.4% compared with 6.8%; RR 0.71, 95% CI 0.40–1.24; three studies, 857 participants).

The subgroup analysis of the 10 trials that used povidone–iodine as the intervention compared with placebo or no treatment concurred with the overall analysis in the significant decrease of endometritis (2.8% compared with 6.3%; RR 0.42, 95% CI 0.25–0.71); no differences were found in the subgroup analysis of the three trials that used chlorhexidine as the intervention compared with placebo or no treatment (8.5% compared with 17.5%; RR 0.45, 95% CI 0.14–1.52; 330 participants).

The subgroup analysis of the six RCTs in which all women received antibiotics before incision also concurred with the overall analysis in the significant decrease of endometritis (2.0% compared with 6.1%; RR 0.33, 95% CI 0.17–0.63; six studies, 2,167 participants).

Only one study directly compared povidone–iodine with chlorhexidine and therefore meta-analyses for these data were not available.[23] However, they found no statistically significant difference in the incidence of endometritis comparing vaginal cleansing with povidone–iodine with vaginal cleansing with chlorhexidine (8.6% compared with 4.3%; RR 2.04, 95% CI 0.39–10.62; 93 participants).

DISCUSSION

This meta-analysis showed that vaginal cleansing before cesarean delivery reduces the incidence of postpartum endometritis compared with no such cleansing. Subgroup analyses demonstrated that the reduction in postoperative endometritis is significant only for women in labor and for those with ruptured membranes. Ruptured membranes are a known risk factor for postcesarean infectious morbidity and therefore the use of vaginal preparation in this subset of women makes particular sense. The risk of bias of the included trials is reasonably moderate with few areas being identified as potential sources of bias. In most of the included studies, 10% povidone–iodine was used as the intervention. The most common way to perform the vaginal cleansing was the use of a sponge stick for approximately 30 seconds. No side effects such as allergy were reported in any of the trials.

We also found a 67% decrease in the rate of endometritis from vaginal cleansing in the subgroup of women who received prophylactic antibiotics before skin incision. Surgical prophylaxis with intravenous antibiotics before cesarean delivery has been clearly demonstrated as beneficial in reducing postoperative infection morbidity.[5] Thus, it is the standard of care and these findings could translate to current practice.

Limitations of our study are mostly inherent to the limitations of the included studies. Only four trials used placebo as a control and were double-blind. Data regarding optimal dose and optimal type of antiseptic to use were limited. Although povidone–iodine was the most commonly used antiseptic, the efficacy of chlorhexidine, although nonsignificant, was similar (RR 0.42 for povidone–iodine compared with 0.45 for chlorhexidine). Moreover, the one RCT comparing povidone–iodine and chlorhexidine vaginal cleansing failed to find any statistically significant difference.[23] Many of the subset analyses, including comparison of povidone–iodine and chlorhexidine, had small sample sizes and may be underpowered to detect statistically significant differences. Alcohol-containing preparations have not been studied and should probably be avoided.

Some published trials comparing vaginal cleansing with either placebo or no treatment were excluded because they included both vaginal and cesarean delivery without stratifying data for mode of delivery. Inclusion of data of cesarean delivery only from these RCTs could modify our findings. Finally, there was high variability of study implementation such as timing of antibiotics, placental removal technique, diagnosis of endometritis, and socioeconomic status of enrolled women. These variables could have affected our findings. The inclusion of a study with metronidazole may be a confounder, because metronidazole is an antibiotic instead of an antiseptic preparation.

Our data concur with a prior Cochrane review.[6] Haas et al pooled data from only five RCTs (1,766 women) evaluating the effects of vaginal cleansing with povidone–iodine on postcesarean infectious morbidity. They showed with a low quality of evidence that vaginal preparation with povidone–iodine immediately before cesarean delivery may reduce the risk of postoperative endometritis. However, there remains a lack of widespread uptake and previously published guidelines on vaginal preparation have not been modified to include cesarean delivery. Moreover, several more trials have been published after the Cochrane review was completed.[20–26]

The concept of vaginal cleansing is not new to the field of obstetrics and gynecology. Since the 1970s it has been demonstrated that a povidone–iodine vaginal scrub before vaginal surgery or abdominal hysterectomy is associated with lower postoperative infectious morbidity.[26] Prior studies showed that

vaginal cleansing decreased the number of vaginal bacterial species by 98%,[27] especially Enterococcus species.[28] By cleansing the vagina before cesarean delivery, there may be less bacterial load in the vagina that might cause postoperative endometritis. In terms of costs, vaginal cleansing with either povidone–iodine or chlorhexidine is a low-cost intervention, approximately $1.7 per 113-g bottle of chlorhexidine and $1.4 per 118-mL surgical scrub with povidone–iodine.[29]

In summary, vaginal cleansing immediately before cesarean delivery in women in labor and in women with ruptured membranes reduces the risk of postoperative endometritis. Because it is generally an inexpensive and simple intervention, we recommend preoperative vaginal preparation in these women before cesarean delivery with a sponge stick preparation of povidone–iodine 10% for at least 30 seconds. More data are needed to assess whether this intervention may be also useful before cesarean delivery in women not in labor and for those without ruptured membranes.

REFERENCES

1. Declercq E, Barger M, Cabral HJ, Evans SR, Kotelchuck M, Simon C, et al. Maternal outcomes associated with planned primary cesarean births compared with planned vaginal births. Obstet Gynecol 2007;109:669–77.
2. Sweeten KM, Eriksen NL, Bianco JD. Chlorhexidine versus sterile water vaginal wash during labor to prevent peripartum infection. Am J Obstet Gynecol 1997;176:426–30.
3. Larsen B, Galask RP. Vaginal microbial flora: practical and theoretic relevance. Obstet Gynecol 1980;55(suppl):100S–13.
4. French LM, Smaill FM. Antibiotic regimens for endometritis after delivery. The Cochrane Database of Systematic Reviews 2004, Issue 2. Art. No.: CD001067. DOI: 10.1002/14651858.CD001067.
5. Smaill FM, Grivell RM. Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section. The Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD007482. DOI: 10.1002/14651858.CD007482.pub3.
6. Haas DM, Morgan S, Contreras K. Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections. The Cochrane Database of Systematic Reviews 2014, Issue 9. Art. No.: CD007892. DOI: 10.1002/14651858.CD007892.pub4.
7. Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions, version 5.1.0 (update March 2011). Available at: training.cochrane.org/handbook. Retrieved July 19, 2017.
8. Göymen A, Şimşek Y, Özdurak Hİ, Özkaplan ŞE, Akpak YK, Özdamar Ö, et al. Effect of vaginal cleansing on postoperative factors in elective caesarean sections: a prospective, randomized controlled trial. J Matern Fetal Neonatal Med 2017;30:442–445.
9. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62:1006–12.
10. Rouse DJ, Hauth JC, Andrews WW, Mills BB, Maher JE. Chlorhexidine vaginal irrigation for the prevention of peripartal infection: a placebo-controlled randomized clinical trial. Am J Obstet Gynecol 1997;176:617–22.
11. Pitt C, Sanchez-Ramos L, Kaunitz AM. Adjunctive intravaginal metronidazole for the prevention of postcesarean endometritis: a randomized controlled trial. Obstet Gynecol 2001;98:745–50.
12. Reid VC, Hartmann KE, McMahon M, Fry EP. Vaginal preparation with povidone iodine and postcesarean infectious morbidity: a randomized controlled trial. Obstet Gynecol 2001;97:147–52.
13. Guzman MA, Prien SD, Blann DW. Post-cesarean related infection and vaginal preparation with povidone-iodine revisited. Prim Care Update Ob Gyns 2002;9:206–9.
14. Starr RV, Zurawski J, Ismail M. Preoperative vaginal preparation with povidone-iodine and the risk of postcesarean endometritis. Obstet Gynecol 2005;105:1024–9.
15. Haas DM, Pazouki F, Smith RR, Fry AM, Podzielinski I, Al-Darei SM, et al. Vaginal cleansing before cesarean delivery to reduce postoperative infectious morbidity: a randomized, controlled trial. Am J Obstet Gynecol 2010;202:310.e1–6.
16. Asghania M, Mirblouk F, Shakiba M, Faraji R. Preoperative vaginal preparation with povidone-iodine on post-caesarean infectious morbidity. J Obstet Gynaecol 2011;31:400–3.
17. Memon S, Qazi RA, Bibi S, Parveen N. Effect of preoperative vaginal cleansing with an antiseptic solution to reduce post caesarean infectious morbidity. J Pak Med Assoc 2011;61:1179–83.
18. Charoenviboonphan P. Preoperative vaginal painting with 1% povidone-iodine before cesarean delivery to reduce postoperative febrile morbidity: a randomized control trial. Region 4-5 Med J 2011;30:118–24.
19. Yildirim G, Güngördük K, Asicioğlu O, Basaran T, Temizkan O, Davas I, et al. Does vaginal preparation with povidone-iodine prior to caesarean delivery reduce the risk of endometritis? A randomized controlled trial. J Matern Fetal Neonatal Med 2012;25:2316–21.
20. Ameer AA. Evaluation of the risk of postcesarean endometritis with preoperative vaginal preparation with povidone–iodine: a randomized controlled study. Middle East Fertil Soc J 2015;20:246–50.
21. Mohamed H, Hassan S, Hemida R. Vaginal preparation with antiseptic solution before cesarean section for reducing post partum morbidity. OSR-JNHS 2015;4:75–80.
22. Nandi JK, Saha DP, Pal S, Barman S, Mitra A. Antiseptic vaginal preparation before cesarean delivery to reduce post operative infection: a randomised controlled trial. JMSCR 2015;3:4310–5.
23. Tewfik H, Ibrahim A, Hanafi S, Fahmy A, Abdelrazak KM, Abdelazim IA. Preoperative vaginal preparation using povidone iodine versus chlorhexidine solutions in prevention of endometritis in elective cesarean section. Int J Curr Microbiol App Sci 2015;4:486–92.
24. Ahmed MR, Aref NK, Sayed Ahmed WA, Arain FR. Chlorhexidine vaginal wipes prior to elective cesarean section: does it reduce infectious morbidity? A randomized trial. J Matern Fetal Neonatal Med 2017;30:1484–7.
25. Barat S, Bouzari Z, Ghanbarpour A, Zabihi Z. Impact of preoperative vaginal preparation with povidone iodine on post cesarean infection. Caspian J Reprod Med 2016;2:2–8.

26. Haeri AD, Klopper LL, Forder AA, Baillie P. Effect of different pre-operative vaginal preparations on morbidity of patients undergoing abdominal hysterectomy. S Afr Med J 1976;50: 1984–6.

27. Osborne NG, Wright RC. Effect of preoperative scrub on the bacterial flora of the endocervix and vagina. Obstet Gynecol 1977;50:148–51.

28. Amstey MS, Jones AP. Preparation of the vagina for surgery. A comparison of povidone-iodine and saline solution. JAMA 1981;245:836–41.

29. Lee I, Agarwal RK, Lee BY, Fishman NO, Umsheid CA. Systematic review and cost analysis comparing use of chlorhexidine with use of iodine for preoperative skin antisepsis to prevent surgical site infection. Infect Control Hosp Epidemiol 2010;31:1219–29.