



Original Research Article

Preoperative Vaginal Preparation using Povidone Iodine versus Chlorhexidine Solutions in Prevention of Endometritis in Elective Cesarean Section

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ABSTRACT

Keywords

Povidone iodine,
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Objective of the study is to compare the efficacy of povidone iodine versus chlorhexidine in prevention of postpartum endometritis and related febrile morbidity in women undergoing elective cesarean section. Term pregnant women who were admitted for planned elective cesarean delivery were studied. Recruited eligible women were randomized into one of two groups: group A, including women who were subjected to pre-operative vaginal preparation with povidone iodine; and group B, including women who were subjected to pre-operative vaginal preparation with chlorhexidine. The study outcome measures development of postpartum endometritis. Use of chlorhexidine rather than povidone iodine was significantly associated with 3-fold reduction in the risk of post-operative fever (relative risk was 3.07, 95% CI; 1.07 - 8.81); absolute risk reduction (ARR) was 17.6%. Use of chlorhexidine rather than povidone iodine was associated with 2-fold reduction in the risks of endometritis and wound infection (relative risk was 2.04, 95% CI; 0.3-10.62 and 2.04, 95% CI; 0.19-21.7; respectively), ARR was 4.4% and 2.2%; respectively. Chlorhexidine seems to be more effective than povidone iodine as a vaginal antiseptic preparation applied immediately prior to elective CS in reduction of postpartum fever. Generally, providers should implement the simple pre-operative vaginal preparation with antiseptics before cesarean deliveries.

Introduction

Cesarean section (CS) is currently one of the most common surgical procedures performed in concurrent obstetrics. Post-operative infectious morbidity is one of the main adverse sequelae in cesarean deliveries (Haas *et al.*, 2014). Endometritis can complicate cesarean delivery at a rate ranging between 6 and 27% (Smaill and Hofmeyr, 2002).

In addition; cesarean deliveries frequently complicated by maternal fever and wound complications including seroma, hematoma, infection and separation (Chongsuvivatwong *et al.*, 2010).

It has found that most of the pathogenic organisms that are responsible for such post-

operative infectious complications in cesarean section colonize from the vagina (Watts et al, 1991). Prophylactic antibiotic has been a standard practice in cesarean section and shown to be effective in prevention of postoperative endometritis and surgical site sepsis (Starr *et al.*, 2005).

Nevertheless, despite the wide use of prophylactic antibiotics, post-operative sepsis remains a serious complication (Haas *et al.*, 2014). Vaginal antiseptic preparation using povidone iodine has been a common practice prior to abdominal and vaginal hysterectomies and shown to reduce the risk of postoperative sepsis (Culligan *et al.*, 2005).

Likewise, vaginal antiseptic preparation using povidone iodine was used prior to cesarean section procedures and was found to reduce the risk of postpartum endometritis (Haas *et al.*, 2014).

There are no published data that compare different antiseptic preparations prior to cesarean section. Chlorhexidine is a broad-spectrum antiseptic that has used extensively for many decades in hospital and other clinical settings.

It has given as maternal vaginal lavage, full-body newborn skin cleansing, and/or umbilical cord cleansing to prevent infection in neonates (Lumbiganon *et al.*, 2004). Chlorhexidine gluconate shown to be more effective than povidone iodine in decreasing the bacterial colony counts that found in the operative field for vaginal hysterectomy (Culligan *et al.*, 2005).

The study designed to compare the efficacy of povidone iodine versus chlorhexidine in prevention of postpartum endometritis and related febrile morbidity in women undergoing elective cesarean section.

Patients and Methods

This randomized controlled trial conducted at the labor/delivery ward at Ain Shams University Maternity Hospital during the period between September 2014 and February 2015. The study protocol was in agreement with the Helsinki Declaration for Ethical Medical Research, last updated in Brazil 2013 and approved by the Ethical Research Committee at Obstetrics and Gynecology Department, Ain Shams University, Cairo, Egypt. Term pregnant women who admitted from causality for planned elective cesarean delivery were studied. Obese women who had a Pre-pregnancy body mass index (BMI) > 30 kg/m², those who were in labor, those who had ruptured fetal membranes, antepartum hemorrhage or those who maintained on chronic steroid or immunosuppressive treatment excluded from this trial. Women who had intra-operative or post-operative events that independently may raise the risk of endometritis excluded from the analysis. All participating women signed informed written consent after thorough explanation of the purpose and procedure of the study. Recruited eligible women randomized into one of two groups: group A, including women who subjected to pre-operative vaginal preparation with povidone iodine (Betadine[®] vaginal antiseptic solution, SEDICO, Egypt); and group B, including women who subjected to pre-operative vaginal preparation with chlorhexidine (Chlorhexidine[®] antiseptic solution, SEDICO, Egypt). Randomization performed using Computer-generated randomization system. Concealed random allocation applied. Random allocation numbers enclosed in opaque serially numbered envelopes, only opened after recruitment. All included women received pre-operative prophylactic antibiotic (1 gm cephradine Intravenous) at the time of induction of

anesthesia. After induction of anesthesia, indwelling Foley's urinary catheter inserted under complete aseptic conditions. Vaginal preparation using the allocated antiseptic solution performed. Skin was prepared using povidone iodine. Low transverse (modified Pfannenstiel) incision performed. C-shaped incision of the lower uterine segment performed. After delivery of the fetus, the placenta and membranes delivered using controlled cord traction. The uterus closed in two layers. The fascia is closed using delayed absorbable number 1 polyglactin (Vicryl[®], Ethicon, United States) continuous sutures. The skin closed using non-absorbable number 3/0 polypropylene (Prolene[®], Ethicon, United States) subcuticular sutures. CS procedures performed by by lecturer of the causality (lecturer of the causality; who had passed the residency program for 3 years and having an experience for 3 years as assistant lecturer, with MD degree), assisted by a registrar of the causality (Amr *et al.*, 2014). Postoperatively, the included women received two doses of the same antibiotic 8 hours apart.

The study outcome measures were development of postoperative fever, defined as any temperature $\geq 38^{\circ}\text{C}$ after 24 hours postoperatively and postpartum endometritis (defined as fever $\geq 38^{\circ}\text{C}$, uterine tenderness and offensive vaginal discharge that necessitate antibiotic treatment).

Sample size and statistical analysis

The required sample size was calculated using G* Power software, version 3.17 for sample size calculation [*Heinrich Heine Universität; Düsseldorf; Germany], setting the α -error probability at 0.05, power [1- β error probability] at 0.95%, and effective sample size [w] at 0.3. The effective size [w] was calculated as follows: $w = \sqrt{\chi^2/N}$,

where X^2 is the chi-square test and N is the total sample size.

Data were collected and statistically analyzed using SPSS (Statistical Package for Social Sciences); computer software version 18 (Chicago, IL, USA). Mean and SD (standard deviation) were used to represent numerical variables, while, number and percentage were used to represent categorical variables. Independent student's t-test, used for numeric parametric variables, and Chi-square (χ^2) test for categorical variables analysis. The risk association presented in terms of risk ratios (RRs) and their 95% confidence intervals, as well as the absolute risk reduction (ARR) calculated. P value <0.05 was considered significant.

Results and Discussion

Three hundred and eleven women admitted to undergo elective CS were approached; 106 of them were recruited in the current trial. Figure 1 shows details of approach and recruitment as well as the excluded cases in both groups.

There was no significant difference between group A (Povidone Iodine) and group B (Chlorhexidine group) regarding; mean age (27.12 ± 5.2 versus 28.88 ± 5.9 years; respectively), mean BMI (21.81 ± 4.2 versus 22.1 ± 5.1 ; respectively) and median parity (1 (Range; 0-4) versus 1 (Range; 0-3); respectively) (Table 1).

There was a significantly higher rate of post-operative fever in group A (Povidone Iodine) compared to group B (Chlorhexidine group) (13 (28.3%) versus 4 (8.5%); respectively). The rates of endometritis and wound infection were higher in group A (Povidone Iodine) compared to group B (Chlorhexidine group), but this difference was statistically insignificant (Table 2).

Use of chlorhexidine rather than povidone iodine was significantly associated with 3-fold reduction in the risk of post-operative fever (relative risk was 3.07, 95% CI; 1.07 - 8.81); absolute risk reduction (ARR) was 17.6%. Use of chlorhexidine rather than povidone iodine was also associated with 2-fold reduction in the risks of endometritis and wound infection (relative risk was 2.04, 95% CI; 0.3-10.62 and 2.04, 95% CI; 0.19-21.7; respectively), ARR was 4.4% and 2.2%; respectively (Table 2).

The use of vaginal antiseptic preparation prior to CS has previously been shown to reduce the risk of post-operative febrile morbidity and endometritis.

In this study; There was a significantly higher rate of post-operative fever in povidone Iodine compared to chlorhexidine group (13 (28.3%) versus 4 (8.5%); respectively). The rates of endometritis and wound infection were higher in povidone Iodine compared to chlorhexidine group, but this difference was statistically insignificant. Use of chlorhexidine rather than povidone iodine was significantly associated with 3-fold reduction in the risk of post-operative fever (RR was 3.07, 95% CI; 1.07 - 8.81) and 2-fold reduction in the risks of endometritis and wound infection (relative risk was 2.04, 95% CI; 0.3-10.62 and 2.04, 95% CI; 0.19-21.7; respectively).

A randomized controlled study which performed in 308 women undergoing non-emergent CS by Starr and colleagues to detect the effect of pre-operative vaginal preparation with povidone-iodine as a preventive intervention against post-cesarean endometritis and wound infection (Starr *et al.*, 2005). Subjects received either standard abdominal scrub alone or abdominal scrub with an additional vaginal preparation with povidone-iodine solution. Starr and colleagues, found that post-

cesarean endometritis occurred in 7% of subjects who received a pre-operative vaginal preparation and 14.5% of controls ($p<0.05$). Also, they found no measurable effect of a vaginal scrub on the development of post-operative fever or wound infection.

Starr and colleagues concluded that pre-operative vaginal scrub with povidone-iodine decreases the incidence of post-cesarean endometritis. This intervention does not seem to decrease the overall risk of post-operative fever or wound infection (Starr *et al.*, 2005).

Cochrane systematic review published in December 2014 (Seven trials randomizing 2816 women) evaluated by Hass and Co-workers to evaluate the effect of vaginal cleansing (all with povidone-iodine) on post-cesarean infectious morbidity (Haas *et al.*, 2014). They found that vaginal preparation immediately before cesarean delivery significantly reduced the incidence of post-cesarean endometritis from 8.3% in control groups to 4.3% in vaginal cleansing groups (RR 0.45, 95% CI 0.25 - 0.81). Also, they found the risk reduction was particularly strong for women who were already in labor at the time of the cesarean delivery (7.4% in the vaginal cleansing group versus 13.0% in the control group; RR 0.56, 95% CI 0.34 - 0.95) and for women with ruptured membranes (4.3% in the vaginal cleansing group versus 17.9% in the control group; RR 0.24, 95% CI 0.10 to 0.55, three trials, 272 women). Hass and Co-workers concluded that vaginal preparation with povidone-iodine solution immediately before cesarean delivery reduces the risk of post-operative endometritis (Haas *et al.*, 2014).

This benefit is particularly realized for women undergoing cesarean delivery, who are already in labor or who have ruptured membranes. Hass and co-workers also

concluded that as a simple, generally inexpensive intervention, providers should consider implementing pre-operative vaginal cleansing with povidone-iodine before performing cesarean deliveries (Haas *et al.*, 2014). To the best of our knowledge, the current study was the first randomized controlled trial that compare chlorhexidine to povidone iodine as vaginal antiseptic preparation prior to elective CS. The study has shown that chlorhexidine was significantly associated with reduced risk of post-operative fever. The rates of endometritis and wound sepsis was also reduced but not to a statistically significant level.

The only limitation in this study is recruitment of women planned for elective CS, which considered as low risk

population, further studies are needed to compare chlorhexidine to povidone iodine in high risk population specially women in labor or women with rupture of fetal membranes and delivered by cesarean section.

In conclusion, chlorhexidine seems to be more effective than povidone iodine as a vaginal antiseptic preparation applied immediately prior to elective CS in reduction of postpartum fever. Generally, providers should implement the simple and inexpensive pre-operative vaginal preparation with antiseptics before performing cesarean deliveries to reduce risk of post-operative endometritis and febrile morbidities.

Table.1 Demographic Data of two studied groups

Variable	Group A (Povidone Iodine group) (Number 46)	Group B (Chlorhexidine group) (Number 47)	P value (95% CI), Significance
Age (years) Mean ± SD (Range)	27.12 ± 5.2 (22 – 37)	28.88 ± 5.9 (24 – 38)	1 (-7.3, -1.7, 3.7), Non-Significant *
BMI (kg/m ²) Mean ± SD (Range)	21.81 ± 4.2 (19.1 – 28.9)	22.1 ± 5.1 (18.2-27.2)	0.89 (-6.1319 <-0.3< 5.5319), Non-Significant*
Parity Range Median (IQR)	0-4 1 (1 – 2)	0-3 1 (1 – 2)	P = 1 (-6.1, -0.3, 5.5), Non-Significant**

**Analysis using Chi-square (x2) test

*Analysis done using independent student’s t-test

BMI: Body mass index (calculated as weight (kg) divided by squared height (m2))

IQR: Interquartile range; SD: Standard deviation

Table.2 Postoperative fever, endometritis and wound infection in two studied groups

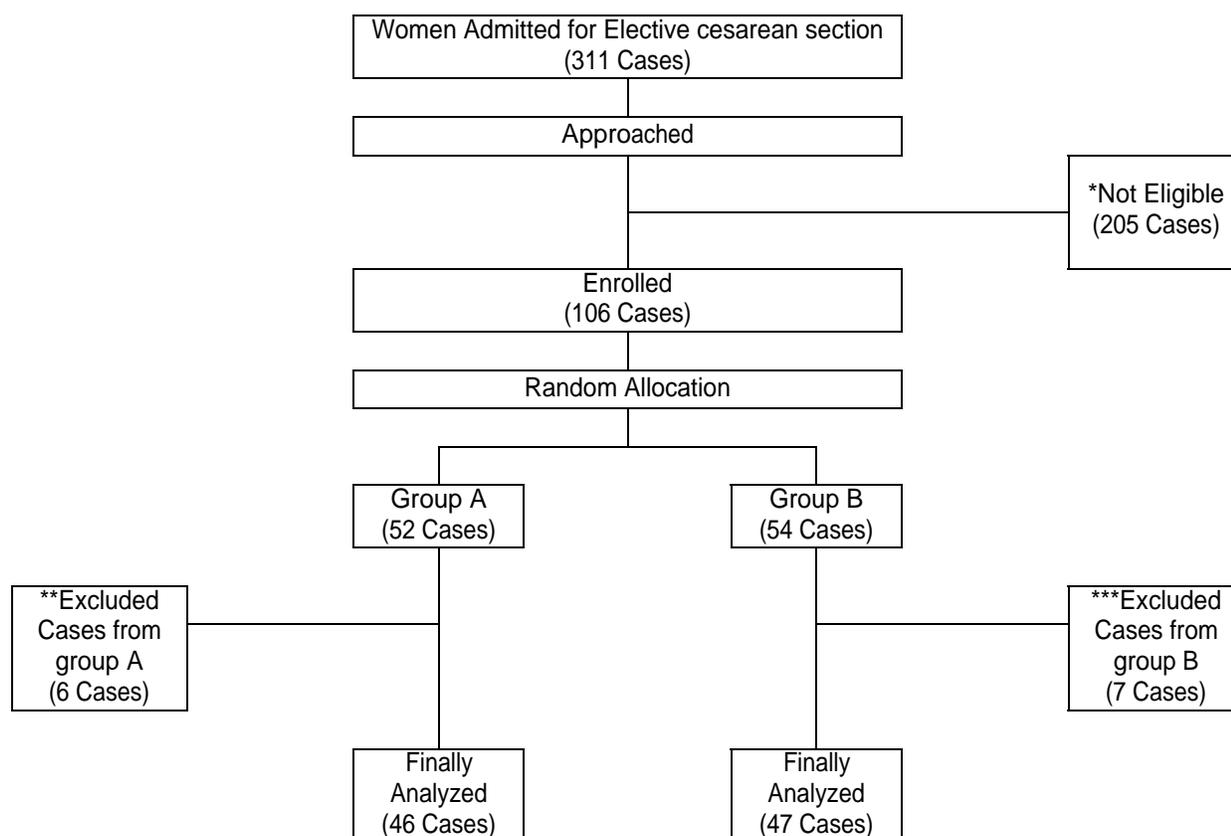
Variable	Group A (Povidone Iodine group) (Number 46)	Group B (Chlorhexidine group) (Number 47)	P Value; RR (95% CI)	ARR
Postoperative Fever	13 (28.3%)	4 (8.5%)	0.03; 3.3 (1.17 - 9.4)	17.6%
Endometritis	4 (8.7%)	2 (4.3%)	0.6; 2.04 (0.39 -10.62)	4.4%
Wound Infection	2 (4.3%)	1 (2.1%)	0.5; 2.04 (0.19 - 21.7)	2.2%

Analysis done using Chi-square test (X²) test

ARR: Absolute Risk Reduction; RR: (95% CI) relative risk and its 95% confidence interval

SD: presented as number and percentage

Figure.1 Flow diagram of the study course, excluded cases and reasons for exclusion



*Women not eligible and excluded; women in labor, with ruptured membranes, antepartum hemorrhage and women under chronic steroid therapy.

**Excluded women in group A (6 Cases); 1 case of bladder injury, 2 cases of severe intraoperative blood loss that necessitated blood transfusion, 1 case that needed manual separation of the placenta and 2 cases who did not attend for follow-up postoperatively.

***Excluded women in group B (7 Cases); 3 cases of severe intraoperative blood loss that necessitated blood transfusion, 1 case of small bowel injury, 1 case that needed manual separation of the placenta and 2 cases who did not attend for follow-up postoperatively.

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Conflict of interest: Authors declare that they have no conflict of interest in relation to this study.

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