

UNIVERSITY *of* WASHINGTON

# Vaginal Preparation Prior to Cesarean Delivery

Obstetric Consensus Conference

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## INTRODUCTION

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Post-operative infections are the most common cause of postpartum morbidity and significantly affect maternal well-being as well as hospital readmissions.<sup>1</sup> The greatest risk factor for postpartum infection is cesarean section, which is associated with a 5-20 fold increased risk of infection compared to vaginal delivery.<sup>2</sup> Approximately 30% of deliveries nationwide and 40% of deliveries at the University of Washington occur by cesarean section. The most frequent postpartum infectious complications are endometritis (6-27%), fever (5-24%), and wound infection (2-9%).<sup>3</sup>

Despite the use of pre-operative antibiotics, which have reduced infection rates by 60-70%, infection continues to be an important preventable cause of post-cesarean morbidity.<sup>4,5</sup> Endometritis is thought to occur primarily through ascending infection of anaerobic vaginal bacteria, which are typically not covered by pre-operative antibiotics. In gynecologic surgery, vaginal preparation prior to surgery has been demonstrated to significantly reduce the risk of post-operative infections by reducing the burden of vaginal bacteria.<sup>6</sup> Recently, several randomized controlled trials have been performed to investigate whether vaginal preparation at the time of cesarean section can further reduce the risk of post-operative infections. Additionally, the American College of Obstetricians and Gynecologists (ACOG) recently updated practice recommendations in September 2018 for infection prophylaxis on labor and delivery.<sup>7</sup> The purpose of this consensus conference is to review the literature on vaginal preparation prior to cesarean delivery to determine whether we should institute this practice at the University of Washington.

## BACKGROUND

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ACOG published an updated practice bulletin on “Use of Prophylactic Antibiotics in Labor and Delivery”.<sup>7</sup> In this Practice Bulletin No. 199, ACOG presents vaginal cleansing literature prior to cesarean delivery, categorizing available data as Level A evidence: based on good and consistent scientific evidence. In their recommendations and conclusions, ACOG states that “vaginal cleansing before cesarean delivery in laboring patients and those with ruptured membranes using either povidone-iodine or chlorhexidine gluconate may be considered.”

A number of small randomized controlled trials at primarily single institutions have been performed evaluating the effectiveness of vaginal preparation prior to cesarean delivery in reducing post-operative infection. These trials are of varying size, quality, and design, however, two recent meta-analyses have been performed evaluating the majority of available literature on the topic. This consensus conference primarily focuses on the Haas Cochrane review published in 2018 and Caissutti a meta-analysis published in *Obstetrics and Gynecology* in 2017.<sup>8,9</sup> The Caissutti publication is the bulk contributor to the September 2018 ACOG Practice Bulletin recommendations.

Haas reviewed eleven randomized control trials (RCT) involving a total of 3403 women.<sup>8</sup> The inclusion criteria were an RCT with vaginal preparation prior to cesarean delivery with any type of antiseptic solution less than one hour prior to delivery. Both unlabored and laboring cesarean deliveries were included in the 7 trials. Exclusion criteria included vaginal preparation performed during labor prior to the decision to perform a cesarean had been made, or studies without pre-operative antibiotics as that is the standard of care in current practice. Ten of eleven studies in this meta-analysis used betadine vaginal preparation (povidone iodine 10% solution) or chlorhexidine vaginal preparation versus either saline or no preparation in the control group. The primary outcome was the rate of postpartum

endometritis and secondary outcomes were postpartum fever, wound infection, wound complications and side effects of vaginal preparation. Sub-analysis examined these same outcomes between patients with cesarean delivery after labor versus unlabored delivery, as well as patients with rupture of membranes compared to intact membranes. The quality of the evidence using GRADE was rated as moderate.

The primary finding of the Haas analysis was a significant 64% reduction in post-cesarean endometritis from 8.7% in the control patients compared to 3.8% in the patients receiving pre-cesarean vaginal preparation, with a relative risk of 0.36 (95% CI 0.20 - 0.63). A composite outcome of wound complication or endometritis also showed a significant 54% reduction in the vaginal preparation group (RR 0.46, 95% CI 0.26-0.82). Stratifying by labor versus unlabored, subgroup analysis revealed a significant reduction in the rate of postoperative endometritis in patients in labor who received vaginal preparation (4.7% versus 11.1%; RR 0.41, 95% CI 0.19 - 0.89), however the unlabored group did not reach statistical significance (RR 1.00, 85% CI 0.35 – 2.84). Stratification by membrane status showed that vaginal preparation resulted in a significant reduction in postoperative endometritis in patients both with and without ruptured membranes. In women with ruptured membranes, post-cesarean endometritis was reduced from 17.9% to 4.3% in the vaginal preparation group (RR 0.24, 95% CI 0.10 - 0.55). For women with intact membranes who received vaginal preparation, post-cesarean endometritis was reduced by 50% (RR 0.50, 95%CI 0.31-0.82). There were trends towards slight reductions in postoperative fever and wound infection, which did not reach statistical significance (RR 0.87, 95% CI 0.72-1.05 and RR 0.74, 95%CI 0.49-1.11, respectively). There were no adverse events noted in any of the trials from the betadine or chlorhexidine vaginal preparation. Based on these results, the authors recommended that “vaginal preparation with povidone-iodine or chlorhexidine solution compared to saline or not cleansing immediately before cesarean delivery probably reduces the risk of post-cesarean endometritis.” (Haas DM, 2018)

The Caissutti meta-analysis reviewed fifteen RCTs involving a total of 4744 women.<sup>9</sup> RCTs comparing vaginal preparation within one hour of delivery versus a control group were included. Prophylactic surgical antibiotics were used on all included trials. Eleven studies used betadine (range 1-10% solution), three studies used chlorhexidine (0.2-0.4% solution), one study used dilute cetramide (an antiseptic solution similar to chlorhexidine, specific concentration not available), and one study used metronidazole 0.5% vaginal gel for vaginal preparation in the intervention groups. The most common preparation technique was a sponge stick in the vagina for 30 seconds. Similar to the Haas study, the primary outcome was postpartum endometritis and secondary outcomes were postoperative fever, wound infection, and wound complications. Subgroup analysis included patients in labor versus unlabored, rupture of membranes versus intact membranes, type of antiseptic solution for vaginal preparation, and timing of prophylactic antibiotics. 13 trials had no treatment or saline placebo in the control group. One trial directly compared betadine to chlorhexidine. The overall risk of bias was considered low

For the primary outcome of the Caissutti study, there was a significant 48% reduction in post-cesarean endometritis among patients who received vaginal preparation prior to cesarean section (8.8% in control patients versus 4.5% in patients with vaginal preparation RR 0.52, 95% CI 0.37 to 0.72). Similar to Haas, the greatest benefit was seen in patients in labor and with ruptured membranes. Vaginal preparation resulted in a significant reduction in endometritis for women in labor (8.1% versus 13.8%, RR 0.52, 95%CI 0.28-0.97), however the subgroup of unlabored women showed only a trend in the primary outcome (3.5% versus 6.6%, RR 0.62, 95%CI 0.34-1.15). There was a statistically significant reduction in the rate of endometritis for women receiving vaginal cleansing with ruptured membranes (4.3% versus 20.1%, RR 0.23, 95% CI 0.10-0.52). However, for women with intact membranes, there was a non-significant trend in postoperative endometritis (4.4% versus 6.8%, RR 0.71, 95% CI 0.40-1.24). Among the secondary outcomes, there was an overall significant risk reduction in postoperative

fever (9.4% versus 14.9%, RR 0.65, CI 0.50 to 0.86) and non-significant trends towards reductions in wound infection (2.9% versus 3.8%, RR 0.74, CI 0.53 to 1.05) and wound complications (5.1% versus 7.1%, RR 0.71, CI 0.43 to 1.17) in patients with vaginal preparation compared to controls. Based on these results the authors recommended vaginal preparation in patients undergoing cesarean delivery who are in labor or have rupture of membranes.

In subgroup analysis of antiseptic type, Caissutti et al also compared rates of postpartum endometritis between patients receiving vaginal preparation with betadine versus dilute chlorhexidine. The 10 trials that used betadine vaginal preparation concurred with the overall analysis, finding a decreased rate of postoperative endometritis with betadine vaginal preparation (2.8 % versus 6.3%, RR 0.42, CI 0.25 to 0.71). The 3 trials that used dilute chlorhexidine vaginal preparation did not reach statistical significance for the primary outcome of postoperative endometritis (8.5% versus 17.5%, RR 0.45, CI 0.14 to 1.52), however there were significantly fewer patients in the analysis who received chlorhexidine (330), compared to betadine (1959). The only head-to-head RCT comparing betadine preparation to chlorhexidine demonstrated potential slight improvement in reduction in postpartum endometritis in patients receiving chlorhexidine preparation compared to betadine (4.3% compared to 8.6%, respectively) although this was a small study with less than fifty patients per group and a non-significant RR of 2.04 (95% CI 0.39 to 10.62).<sup>10</sup>

Although all studies in these analyses included prophylactic surgical antibiotics as is the current standard of care, there was variation in the timing of antibiotic administration (some studies were administered prior to skin incision and in others administered after cord clamping). Only 6 of the RCTs included in the Caissutti publication specifically stated timing of antibiotic administration prior to skin incision, which is now standard practice. In subgroup analysis, these 6 studies similarly demonstrated a significant risk reduction in postpartum endometritis (2.0% in vaginal preparation compared to 6.1% in control patients; RR 0.33, CI 0.17 to 0.63) indicating benefit for vaginal preparation in patients most similar to our practice. The preoperative antibiotics in these studies were typically cephalosporins. These analyses did not include preoperative azithromycin, which has been demonstrated to have additional benefit in reducing postoperative infections in patients with obesity and rupture of membranes who are at the highest risk for postpartum infection at time of cesarean delivery.<sup>11</sup> A recent secondary analysis of patients receiving vaginal preparation with betadine compared to no preparation in patients who received adjuvant treatment with preoperative azithromycin in addition to cephalosporin was published by La Rosa et al in August 2018.<sup>12</sup> This analysis failed to demonstrate significant reduction in superficial or deep surgical site infection (5.5% versus 4.1%, OR 1.38, CI 0.87-2.17) in patients receiving vaginal preparation compared to no preparation. A composite secondary outcome of endometritis, wound infection or other infections was also non-significant. The La Rosa study suggests there may be less benefit for vaginal preparation among patients receiving adjuvant azithromycin.

There is one additional trial published by Ahmed et al in 2017, evaluating chlorhexidine vaginal wipes as a method of pre-cesarean vaginal preparation.<sup>13</sup> In this study, the authors performed a trial among 218 women randomized to 1-minute vaginal preparation with a 0.25% chlorhexidine wipe compared to controls with no prep immediately prior to cesarean delivery. They demonstrated a significant reduction in the rate of endometritis in the intervention group compared to the control group (2.9% versus 13.2%,  $p < 0.05$ ). ACOG Practice Bulletin 199 cites the Ahmed study as support for the use of vaginal preparation prior to cesarean delivery.

## DISCUSSION

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Overall these findings indicate a statistically significant benefit to the addition of vaginal preparation at the time of cesarean delivery towards reducing rates of postpartum endometritis. The benefit was most pronounced in patients undergoing cesarean section in the setting of labor or rupture of membranes. This is consistent with the current theory of endometritis etiology due to ascending infection of vaginal flora, which would be expected to be reduced by vaginal preparation. The reduction of postpartum endometritis was still seen in patients who received surgical antibiotic prophylaxis prior to skin incision, which is standard of care at the University of Washington. There may be reduced efficacy of vaginal preparation in patients who receive adjuvant azithromycin prior to cesarean delivery, however, there is limited literature on this subset of patients undergoing cesarean delivery.

After evaluation of the above evidence, the American College of Obstetricians and Gynecologists supports consideration of vaginal cleansing before cesarean delivery in laboring patients and those with ruptured membranes using either betadine (povidone-iodine) or chlorhexidine gluconate.<sup>7</sup>

In terms of potential adverse effects, there were no maternal or fetal complications associated with vaginal preparation with either betadine or chlorhexidine in any of the studies in these analyses. There have been case reports of allergic reactions to vaginal preparation with either betadine or chlorhexidine leading to desquamation, however, these are very rare. Although chlorhexidine solutions with high concentrations of alcohol are contraindicated for surgical preparation in the vagina, the safety of vaginal preparation with dilute chlorhexidine solutions less than 4% concentration has been demonstrated in multiple studies and is endorsed by ACOG.<sup>7</sup>

Prior pediatric literature has suggested potential neonatal risks of depressed thyroid function due to repeated betadine exposure, typically in the setting of direct skin preparation on the infant prior to a pediatric surgical procedure.<sup>14-17</sup> This older literature was reviewed by the neonatology faculty at UWMC. It was concluded by neonatology that vaginal preparation with betadine 10% solution would result in minimal potential fetal exposure due to short interval between vaginal cleansing and delivery, as well as our current practice of cleaning and drying the infant immediately after delivery. Concern for neonatal thyroid suppression was low.

The cost of vaginal preparation is low: approximately \$1.70 for one 113g bottle of chlorhexidine and \$1.40 for one 118mL bottle of betadine.<sup>9</sup> In the above meta-analyses, there does not appear to be a clear superiority of vaginal preparation with chlorhexidine versus betadine. Due to the majority of data and lower cost with betadine preparation, we recommend betadine preparation as first choice with the option of dilute 4% chlorhexidine for patients with betadine allergy. Additional nursing time will be needed to perform vaginal preparation prior to cesarean delivery. Most studies used 30 seconds of vaginal preparation, which could be added to the current practice of urethral preparation prior to Foley catheter placement with minimal additional time.

The reduction in postoperative endometritis with vaginal preparation was most robust in the subgroups of laboring patients and those patients with ruptured membranes. However, the Haas Cochrane review also demonstrated significant reductions in post-cesarean endometritis for women with intact membranes, while the Caissutti meta-analyses demonstrated a trend in the reduction of postoperative infectious morbidity for non-laboring patients. No increase in adverse outcomes was seen in any meta-analyses subgroup who received vaginal preparation. Due to the difficulty of initiating selective clinical practices on a busy Labor and Delivery unit, and the overall benefit for all patients of a low cost and low

risk intervention, universal application of vaginal preparation at the time of cesarean section will prevent missed opportunities for patients eligible for this intervention.

Based on the above available literature, we recommend universal vaginal preparation prior to cesarean delivery at the University of Washington.

## SUMMARY RECOMMENDATIONS

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All patients should receive a 30 second vaginal preparation prior to cesarean delivery. Vaginal preparation will be performed with 10% betadine by nursing at the time of Foley placement in the operating room. For patients with a Foley in place prior to entry into the operative room, vaginal preparation can be performed immediately prior to the sterile abdominal preparation. A single sterile 4 x 8 sponge can be moistened with betadine and held with a ring forcep for application of the vaginal preparation, gently covering all surfaces within the vagina during the 30 seconds.

### Exceptions:

- Patients with betadine allergy should receive alternative vaginal preparation with 4% chlorhexidine, applied in an identical manner with a 4 x 8 sponge and ring forcep for 30 seconds
- Patients with need for emergent cesarean delivery should not receive vaginal preparation prior to delivery, in order to expedite delivery and maternal/fetal safety

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