Stepwise implementation of vaginal cleansing and azithromycin at cesarean: a quality improvement study

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ABSTRACT

Objective: We aimed to decrease our surgical site infection (SSI) rate by 30% by sequential implementation of vaginal cleansing and azithromycin for women who underwent a cesarean delivery (CD) after having labored or experienced rupture of membranes.

Methods: This is a quality improvement project that assessed the stepwise implementation of two interventions within three time periods: (1) 12 months prior to implementation of either intervention; (2) 14 months of vaginal cleansing as infection prophylaxis; (3) 16 months of vaginal cleansing and azithromycin as infection prophylaxis. The primary outcome measure was the SSI as defined by the Center for Disease Control and Prevention and analyzed by control charts. The process measures were compliance rates of vaginal cleansing and azithromycin. Significance was detected by rules for determining a special cause variation. This study followed the SQUIRE 2.0 guidelines for reporting on quality improvement.

Results: There were 1033 patients included from the three study periods. The total rate of SSI decreased from 22.8% to 15.2% after implementing vaginal cleansing. Special cause variation was detected with an 8-point shift starting 4 months after implementation of vaginal cleansing. This decrease was sustained during the following 26 months. Adding azithromycin did not significantly lower the SSI rate further. When examined separately, deep SSI (p = .009) and endometritis (p = .001) significantly decreased in the post-intervention periods. Pre-operative vaginal cleansing compliance rose to 74%, and then further increased to 85% 1 year after implementation. Azithromycin compliance rose to 75%. Total length of postpartum stay decreased over the study periods from 3.5 ± 1.4 days to 3.2 ± 0.8 days (p = .001).

Conclusion: In this quality improvement study, implementation of vaginal cleansing decreased the SSI rate by 33%, from 22.8% to 15.2%. The addition of azithromycin did not result in any additional change in SSI rate.
CD. Such risk-based interventions are particularly important, as the risk for SSI has been reported to be two to three times higher in this population [4].

Vaginal cleansing with povidone iodine has been shown to decrease post cesarean endometritis [10,11], which is classified as a deep organ space surgical site infection by the CDC. A Cochrane review and a recent meta-analysis established that the subgroup of women who benefit from vaginal cleansing are those who have labored or experienced a rupture of membranes prior to cesarean delivery, with a decrease in the rate of endometritis from 8.8% to 4.5% [11]. As additional prophylaxis against SSI, a large randomized controlled trial (RCT) [12] recently randomized >2000 women undergoing CD to azithromycin or placebo if the women had experienced labor and found a similar significant decrease in the rate of surgical site infections. The primary outcome, which was a composite of endometritis, wound infection and other infections occurring within 6 weeks of cesarean, decreased from 12.0% to 6.1%. Despite the fact that vaginal cleansing and azithromycin are interventions that have been shown to benefit a similar population of women undergoing cesarean once in labor or after membrane rupture, throughout the United States there has not been universal uptake of these interventions [13]. For example, within the trials on vaginal cleansing included in the meta-analysis, azithromycin was not reported as utilized in any included trial [10–11]. Similarly within the sole RCT of azithromycin administration, only 26% of women received vaginal cleansing [12].

At our institution there was a perception that we had an increased rate of SSI for patients undergoing CD. We aimed to decrease our SSI rate by 30% in a high-risk population by sequential implementation of vaginal cleansing and azithromycin for women who underwent a CD after having labored or experienced a rupture of membranes.

Methods

Context

This was a stepwise quality improvement project with the goal of decreasing post-cesarean infection rates at a tertiary care facility. This study followed the SQUIRE 2.0 guidelines for reporting on quality improvement [14]. At our institution during the entire timeframe of the study, we routinely used pre-operative weight-based antibiotic dosing, skin cleansing with alcohol-based products, sterile technique, subcutaneous closure of tissue >2 cm and suture to close the incision. Our institution performed approximately 2000 deliveries a year during this timeframe. We serve an urban population and the majority of patients at our institution are African American. The average body mass index (BMI) at the delivery of our patient population is 33 kg/m².

Interventions

Part I. Vaginal cleansing

We planned to implement vaginal cleansing and azithromycin administration to women undergoing cesarean delivery in labor or after rupture of membranes (ROM). The initial intervention enacted was routine vaginal cleansing which was implemented on 1 January 2017 (see Supplement 3 for vaginal cleansing guideline). Although the evidence for azithromycin and vaginal cleansing was published within the same year, vaginal cleansing was selected as the first intervention as our group published a meta-analysis on the topic [10]. Vaginal cleansing was performed with 10% povidone iodine prior to performing the abdominal preparation and at the time of urinary catheter placement. For women with iodine or shellfish allergy, 4% chlorhexidine sponge solution was used instead of povidone iodine [15]. All providers were trained on vaginal cleansing technique, which included 30 s of cleansing the perineum from the anterior to posterior direction using a sponge stick with 10% povidone iodine or the sponge portion of a 4% chlorhexidine scrub brush. Povidone iodine supplies that were routinely used prior to vaginal delivery were used and thus no new supplies were necessary for the implementation of this protocol. In the case of urgent or emergent CD, no vaginal cleansing was performed secondary to time constraints related to delivery.

Part II. Azithromycin

The initial institutional antibiotic guideline at the time of cesarean was expanded on 10 March 2018 to include the addition of azithromycin as a second antibiotic for women in labor or those with ROM for more than four hours prior to CD (see Supplement 4 for antibiotic guideline). Azithromycin was chosen based off the external validity of the RCT evidence by Tita et al. [12] as study population generally reflected the population of our own institution. Azithromycin was not administered in the case of diagnosis of intrapartum chorioamnionitis (i.e. triple I) as these patient’s generally received ampicillin, gentamycin and clindamycin. Azithromycin was ordered if CD was planned within 1 h. Routine preoperative antibiotics (generally
weight-based dosing of cefazolin) were given preferentially prior to administration of azithromycin. The ideal timing of administration was prior to incision, although depending on the urgency of the CD, routine preoperative antibiotics and azithromycin were sometimes given after skin incision.

A multidisciplinary approach included members from the following teams: anesthesiologists, labor and delivery nursing and nursing leadership, operating room technologists, resident and attending obstetricians, and maternal-fetal medicine fellows and attendings. This team met in the planning process, reviewed the available evidence, and agreed on the implementation. Specifics for the guideline, including supplies needed for vaginal cleansing and number of intravenous lines for azithromycin were clarified with appropriate teams and specified in the guidelines.

Over the course of our implementation we underwent a series of plan, do, study, act (PDSA) cycles as outlined in Supplement 1. For vaginal cleansing, a guideline was developed and feasibility meetings with labor and delivery nursing leadership helped determine that povidone iodine from vaginal delivery kits could be used. Implementation occurred on labor and delivery and was announced at daily sign outs. As resident teams were the ones to perform vaginal cleansing, a resident teaching session occurred to demonstrate the method of vaginal cleansing and allow providers to practice. Reminder emails were sent out when the compliance rate was found to be at approximately 50% in the first two months of implementation of vaginal cleansing. The results of compliance statistics, as well as infectious outcomes, were reviewed as a department at departmental research conferences. A new electronic medical record was implemented during the study period and prepopulated operative notes included reinforcement for performing vaginal cleansing. Operating room staff also reminded providers when inclusion criteria were met and often provided supplies for providers to perform vaginal cleansing at the time of cesarean delivery.

For azithromycin, a similar guideline was developed and implemented by the same guidelines committee and research team. The guideline team worked with the electronic medical record (EMR) to generate a best practice advisory alert that came into the EMR screen for the ordering physician whenever a case request for cesarean was processed for a patient already registered as being in labor or having ruptured membranes.

**Measures**

Women were included for analysis if they had a singleton pregnancy and underwent cesarean delivery during labor or rupture of membranes prior to CD between 1 January 2016 and 30 June 2019. Exclusion criteria were multiple pregnancies, pregnancies less than 24 weeks gestation, and intrauterine fetal demise. Patient demographics and intrapartum characteristics were collected for women during the study time period including Group B Streptococcus (GBS) status, diagnosis of chorioamnionitis (Triple I), indication for CD and postpartum hemorrhage (defined as greater than 1-liter (L) blood loss).

The primary outcome measure of this study was the rate of any SSI as defined by the Center for Disease Control and Prevention (CDC) and analyzed by control charts [16]. In evaluating the impact of our primary intervention, we also analyzed the SSI data by the three separate time periods in order to separate out types of infections. The process measures were implementation of both interventions. The adherence rate was defined as the percentage of eligible patients meeting inclusion criteria that received vaginal cleansing and/or azithromycin in the appropriate timeframe. Secondary outcome measures included rates of infections stratified by subtype (superficial, deep, organ space). Other maternal postoperative outcomes included length of stay, post-discharge office visits and emergency department visits for concern for infection, and readmission rates during the six-week postpartum period. Postoperative fever was defined as any fever \( \geq 100.4 \) degrees Fahrenheit following CD during the hospitalization. Postpartum endometritis (defined as an organ space infection [16]) was defined as diagnosis by the treating provider within 6 weeks after delivery. The general diagnostic criteria for endometritis used at our institution included postoperative fever \( \geq 100.4 \) degrees Fahrenheit without another obvious infectious source plus one or more of the following: fundal tenderness, maternal tachycardia, foul smelling lochia, or leukocytosis.

**Analysis**

The primary outcome measure and process measures were analyzed by control charts and significance was determined by rules for determining special cause variation, according to Provost and Murray in the Healthcare Data Guide, and was selected *a priori* [17]. Special cause variation are rules that identify unexpected variations in quality improvement data that result from unusual occurrences. These rules are as
follows: (1) A single point outside the control limits (either above the upper control limit or below the lower control limit); (2) At least 6 consecutive points all increasing or all decreasing; (3) Eight or more consecutive points all on the same side of the center line (all above the line or all below the line); (4) Two out of three points in the outer third of the chart; (5) At least 15 consecutive points in the inner third of the chart [17]. Control charts were generated using the QI Charts macro within Microsoft Excel. The demographics and secondary outcomes were evaluated by grouping as three separate timeframes of interventions for traditional statistical analysis. The first timeframe was pre-intervention (12 months: 1 January 2016–31 December 2016). The second timeframe was after the implementation of vaginal cleansing (14 months: 1 January 2017–9 March 2018). The third timeframe included both azithromycin administration and vaginal cleansing (16 months: 10 March 2018–30 June 2019). Statistical analyses comparing groups were performed in SPSS version 24. Independent T-test was used to evaluate continuous data, while Pearson Chi-square test was used to evaluate categorical data. Logistical regression was used to evaluate secondary outcomes and was controlled for baseline characteristics with \( p \leq 0.05 \). This project was approved by the local Institutional Board Review.

**Ethical considerations**

No ethical concerns arose during implementation or studying either intervention.

**Results**

Within the timeframe of the study, there were 1992 cesarean deliveries, 1003 of which were performed on women who were in labor or had ROM and thus qualified for inclusion (Figure 1). Demographics between the three study timeframes showed no significant differences between groups (Supplement 2). Body mass index (BMI) at the time of delivery could not be reliably obtained from the older EMR in the pre-intervention group and thus is not reported, but the mean BMI was 33 in the vaginal cleansing only group as well as the vaginal cleansing and azithromycin group. Preoperative characteristics (Table 1) were significant for a decrease in number of patients who were GBS positive from 34% to 25% within the study period. The proportion of CD performed for the arrest of labor decreased in the study period from 40% to 36% (Table 1).

For the primary outcome, we analyzed the data using a P-chart, showing a center line shift from 22.8% to 15.2% with the special cause variation signal of 8-points shift below the center line starting 4 months after implementation of vaginal cleansing. This decrease was sustained during the following 26 months. Adding azithromycin did not significantly further lower the rate of SSI (Figure 2(A)). When examined types of SSI separately; deep SSI decreased from 2% to 0% (\( p = .009 \)) (Table 2). Similarly, endometritis, which is considered an organ space SSI per CDC criteria, significantly decreased from 16% to 10% and 11% (\( p = .03 \)) in the post-intervention periods. The total length of postpartum stay decreased over the study period.
periods within this population from 3.5 ± 1.4 days to 3.2 ± 0.8 days ($p = .001$) (Table 2).

Our process measures demonstrated that pre-operative vaginal cleansing compliance rose to 74%, and then further increased to 85% 1 year after implementation (Figure 2(B)). Azithromycin IV compliance rose to 75% and remained sustained (Figure 2(C)).

**Discussion**

**Summary**

In this quality improvement study, we evaluated women at high risk for developing SSI and found a 33% decrease. This decrease occurred after the initiation of vaginal cleansing and did not appear to be further impacted by azithromycin. The process measures were both successfully implemented with compliance rates >75%.

**Interpretation**

After successful implementation of vaginal cleansing and subsequent decrease in SSI we had hoped to see a further decrease in the rate of SSI by the stepwise addition of azithromycin. It was surprising that the addition of azithromycin did not further decrease the rate of post-cesarean SSI. Given the nature of the quality improvement study, we are unable to report a direct reason for the lack of further decrease in SSI. Our population is >40% African American and the majority had membrane rupture >6 h, both factors that increase the risk of infection [18]. We also anecdotally note that when azithromycin is ordered from pharmacy there was, at times, a delay and it often was not started until after skin incision. While the timing of administration was not recorded in our study, this delay could have contributed as well.

Throughout the world, there has not been universal uptake of these two implemented interventions. Indeed, other papers have questioned if using both azithromycin and vaginal cleansing are necessary to prevent post-cesarean infection [13] La Rosa et al. performed a secondary analysis of the RCT of azithromycin administration wherein the post-operative infectious outcomes were compared by their institutional policy of administering vaginal cleansing. Of the 2013 patients included in analysis, 523 were delivered at an institution with a policy regarding vaginal cleansing. They found no difference in SSI if there was an institutional policy regarding the use of vaginal cleansing. As mentioned within their paper, these data were limited as they were unable to report if the patients actually received vaginal cleansing.

Other groups have previously shown benefits to utilizing bundles to decrease SSI in post-cesarean delivery. Kawakita et al. implemented a bundle of interventions that included both vaginal cleansing and azithromycin to all cesarean deliveries regardless of if labor occurred or not and demonstrated a decrease in surgical site infections from 4.5% to 2.2% [19]. They report a significantly lower SSI rate than our rate as they included scheduled cesarean deliveries which have a lower risk post-operative wound infection. The same data was investigated to see if the bundle of care decreased racial disparities seen in the rate of SSI, and they found that the bundle decreased infections in black women but did not eliminate racial disparities [20]. These data demonstrate the benefits of implementing a bundle to decrease SSI.

Strengths of our study include that it is focused on a group of women at highest risk of SSI. We demonstrate successful uptake of our process measures and we detail these interventions in our PDSA cycles. We provided analysis by both control charts and standard research methods, using control charts to demonstrate, with more precision, the timing of the improvement of our main outcome measure to our interventions. Women who are in labor or have ruptured membranes generally qualify for both vaginal

| Table 1. Preoperative and intraoperative characteristics. |
|----------------------------------------------------------|
| **Standard care** | **Vaginal cleansing only** | **Vaginal cleansing and azithromycin** | **p-Value** |
| Standard care (n = 291) | Vaginal cleansing only (n = 335) | Vaginal cleansing and azithromycin (n = 407) | |
| Chorioamnionitis 62 (21%) | 74 (23%) | 68 (17%) | .1 |
| Indication for cesarean: | | | |
| Arrest of labor 115 (40%) | 114 (34%) | 145 (36%) | .03 |
| Fetal indications 110 (38%) | 117 (35%) | 145 (36%) | |
| Repeat/Elective 21 (7%) | 26 (8%) | 33 (8%) | |
| Other 19 (7%) | 31 (9%) | 12 (3%) | |
| Failed induction 16 (5%) | 19 (6%) | 35 (9%) | |
| Malpresentation 10 (3%) | 22 (7%) | 26 (6%) | |
| Emergent cesarean 27 (9%) | 33 (10%) | 31 (8%) | .1 |
| Postpartum hemorrhage > 1000 cc 31 (11%) | 91 (27%) | 63 (15%) | .1 |

Numbers expressed in n (%). Bold values indicate statistical significance. GBS: Group B Streptococcus; Ave: average; hr: hour; NA: not applicable.
Figure 2. Control charts A. Primary outcome, any surgical site infections (SSI) as defined by CDC. (A) Percentage of patients with SSI by month, red circle indicates special cause variation was seen with an 8-point shift below the mean. (B) Percentage of patients receiving vaginal cleansing. (C) Percentage of patients receiving azithromycin.
cleansing and azithromycin by our institutional guidelines. Thus, it has been observed that providers couple these interventions together. This is reflected as the compliance with vaginal cleansing increased further with the institution of azithromycin.

**Limitations**

As with any quality-improvement project, there are limitations to generalizability in other patient populations. Given the design of the study, we are unable to account for all other contributors that may have impacted our results. For example, the postoperative length of stay demonstrated a significant decrease only during the time frame of vaginal cleansing and azithromycin but may not be directly attributed to the interventions. Additionally, other quality improvement initiative occurred during this time frame that could have also affected the length of stay. There is also a possibility of a type I error given the decreasing rates of GBS and cesarean performed for arrest of labor in our population. Additionally, the rate of infection seen in our cohort was higher than that seen in the RCT and meta-analysis from which we based our processes for implementation. We attribute this to three possible causes: (1) demographic differences, with the majority of patients having ruptured membranes >6 h and a large proportion of patients being African American. (2) The fact that we are studying only women in labor or with ruptured membranes who are at high risk of developing infection. (3) The rates of outcomes within intervention and the placebo groups of a randomized controlled trial may not always be equivalent to the rates in a population [21].

**Conclusions**

In this quality improvement study, implementation of vaginal cleansing decreased the SSI rate by 33%, from 22.8% to 15.2%. The addition of azithromycin IV did not result in any additional change in SSI rate. Future directions may include implementing postoperative oral antibiotic regimens in patients at high risk of developing an SSI, as such has been shown to be beneficial in obese patients [22].

**Disclosure statement**

No potential conflict of interest was reported by the author(s).

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**Data availability statement**
De-identified data set available upon reasonable request.

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**Table 2. Primary and secondary outcomes.**

|                                     | Standard care (n = 291) | Vaginal cleansing only (n = 335) | Vaginal cleansing and azithromycin (n = 407) | p-Value  |
|-------------------------------------|-------------------------|----------------------------------|---------------------------------------------|----------|
| All surgical site infections        | 64 (22%)                | 57 (17%)                         | 62 (15%)                                    | a        |
| Superficial                         | 18 (6%)                 | 27 (8%)                          | 17 (4%)                                     | .9       |
| Deep                                | 5 (2%)                  | 1 (0%)                           | 0 (0%)                                      | .009     |
| Organ spaceb                         | 48 (16%)                | 33 (10%)                         | 46 (11%)                                    | .03      |
| Secondary outcomes                  |                         |                                  |                                             |          |
| Length of postpartum stay           | 3.5 ± 1.4               | 3.5 ± 1.5                        | 3.2 ± 0.8                                   | .001     |
| Postoperative emergency department visit | 12 (4%)            | 19 (6%)                          | 26 (6%)                                     | .4       |
| Office evaluation for infection     | 27 (9%)                 | 24 (7%)                          | 33 (8%)                                     | .6       |
| Readmissions for infection          | 10 (3%)                 | 13 (4%)                          | 9 (2%)                                      | .4       |
| Treated as outpatients              | 18 (6%)                 | 18 (5%)                          | 15 (4%)                                     | .2       |
| Treated as inpatients               | 10 (3%)                 | 10 (3%)                          | 8 (2%)                                      | .4       |

Data are presented as: n complication/total cesarean delivery, (percentage) and p value. Bold values indicate statistical significance.

a The p-value for all surgical site infections is not included as the primary outcome was analyzed by control charts and the rules of special cause variation.

b All organ space infections were diagnosed cases of postpartum endometritis.
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