A Randomized Trial to Determine if a Pre-operative Wash With a Chlorhexidine Gluconate Cloth and Chlorhexidine Gluconate Vaginal Scrub Reduces Infectious Morbidity in Patients Undergoing Cesarean Section After Labor

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PRACTICAL STUDY
Protocol from Ideate

Title
A randomized trial to determine if a pre-operative wash with a chlorhexidine cloth and chlorhexidine vaginal scrub reduces infectious morbidity in patients undergoing cesarean section after labor

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Lay Summary
Surgical site infections are the second most common cause of infections accounting for 15% of all l infections among hospitalized patients and 38% of infections in patients undergoing surgery. In obstetric patients, surgical site infections occur in 5-10% of cesarean sections, which is a higher rate than seen in vaginal deliveries. Additionally, infections are thought to be highest in those patients who have cesarean sections after undergoing labor.

Chlorhexidine is a chemical antiseptic that reduces bacteria found on the skin but it is not clear if it decreases the risk of surgical site infections.

Historically, chlorhexidine has been studied and used in orthopedic and cardiac implant surgeries. Research on the use of chlorhexidine for SSI prevention in cesarean sections is limited. This study intends to evaluate the effectiveness of use of both chlorhexidine gluconate (CHG) wipe and vaginal scrub in reducing SSI in patients undergoing cesarean section that have previously been laboring. Patients will be randomized to one of two groups: wash with both a pre-operative CHG cloth and vaginal scrub prior to surgery (in addition to standard preoperative scrub) and standard preoperative scrub.

Objective
The objective of this study is to determine if the rate of infectious morbidity is reduced with the use of chlorhexidine gluconate cloths and chlorhexidine vaginal scrub prior to cesarean section in patients previously undergoing labor.

Background
Surgical site infections (SSI) are the second most common cause of nosocomial infections accounting for 15% of all nosocomial infections among hospitalized patients and 38% of nosocomial infections in surgical patients. In obstetric patients, infectious morbidity (i.e. SSI, endometritis) occurs in 5-10% of cesarean sections, which is 5-fold higher than vaginal deliveries. Additionally, infectious morbidity is thought to be highest in those patients who have cesarean sections after undergoing labor.

Chlorhexidine, chemical antiseptic effective on gram positive and gram negative bacteria, reduces skin microflora/colonization but it is not clear if it decreases the risk of SSI.

Historically, chlorhexidine has been studied and used in orthopedic and cardiac implant surgeries. Research on the use of chlorhexidine for SSI prevention in cesarean sections is limited. This study intends to evaluate the effectiveness of use of both chlorhexidine gluconate (CHG) wipe and vaginal scrub with betadyne in reducing SSI in patients undergoing cesarean section that have previously been laboring. Patients will be randomized to one of two groups: wash with a pre-operative CHG cloth and chlorhexidine scrub prior to surgery (in addition to standard preoperative scrub) and standard preoperative scrub.

Primary and Secondary Study Endpoints

The primary outcome will be SSI and postpartum endometritis. Secondary outcomes include other maternal complications or interventions, neonatal ICU admissions, maternal length of stay or readmissions.

Subjects
800

Specify Other Setting of Human Research
Mount Sinai Hospital labor and delivery floor

Feasibility of Meeting Recruitment Goals
Researchers will have access to all patients scheduled for delivery at Mount Sinai Medical Center. About 1800 deliveries by cesarean section occur each year at Mount Sinai. Of these, approximately 800 are cesarean sections after failed labor. Assuming a primary outcome rate of 20% in the control arm, a sample size of 329 in each group would give 80% power to detect a 40% reduction in surgical site infection between the active group and control. We aim to recruit 400 patients per group (for a total of 800 patients) to account for patient drop out or non-compliance.

Due to the amount of deliveries and volume, we anticipate these recruitment goals to be feasible.

Facilities to Be Used for Conducting Research
Labor and Delivery floor at Mount Sinai Hospital

Inclusion Criteria
The study will be offered to women at > 24 weeks gestation who are admitted in labor or admitted for induction of labor at Mount Sinai Hospital.

Exclusion Criteria
Exclusion criteria include allergy to chlorhexidine, and unplanned or emergency cesarean section.

Other Aspects that Could Increase Subjects Vulnerability
The risks to subjects are inherent to the labor process itself outside of the study. The only difference in care is the use of a 2% chlorhexidine wipe and vaginal scrub in addition to standard preoperative preparation. This may potentially decrease the risk of surgical site infection in women who undergo cesarean section after labor. The only inherent risk of using the wipe and scrub is allergy to 2% chlorhexidine gluoconate and this population will be screened by the provider consenting the patient for participation and excluded accordingly.

The patients in our study are all laboring women. All women in this study will have access to labor analgesia as requested by the patient. In addition, enrollment in this study will not alter the current strategies regarding labor analgesia or labor protocols.

Safeguard to protect subjects rights and welfare
There is always the risk of loss of confidentiality; however, there are procedures in place to minimize this risk. To ensure confidentiality, the following system will be adhered to: when subjects are enrolled in this study, they will be assigned a unique identification code. Corresponding medical record numbers for each code (keycode) will be stored in a password locked document on the MFM server that can be accessed only by members of the research team. At the conclusion of the data extraction, the outcome variable will be assessed and the key codes to the medical record numbers will no longer be necessary and that information will be permanently erased from the keycode file. Electronic data with identifiers will be encrypted according to Data Security Standards.

Duration of an individual subjects participation in the study
After informed consent has been obtained, the duration of the subject participation will occur from the time they are admitted until 6 weeks post procedure.

Duration Anticipated to Enroll all study subjects
We expect to enroll patients over a two-year period. We will allow an additional 6 months to perform data analysis.

Procedures for subjects to request withdrawal
A patient may request to withdraw from the study at any time by notifying their obstetric provider.

Procedures for Investigator to Withdraw subjects
The only occasion whereby a subject may be withdrawn is when the cesarean delivery suddenly needs to be performed in an urgent manner.

How Participants will be identified
Patients presenting to labor and delivery for admission for labor will be identified.

How Research will be introduced to participants ***
The study personnel on the labor floor will present the study to the patient in addition to consenting the patient for routine admission for labor and delivery.

Women who are in early labor, in addition to being induced for labor, will be approached by study personnel. Women who are actively delivering will not be approached or included in the study.

How Participants will be screened
The participants will be screened according to the previously mentioned inclusion criteria. The participants will either be screened by obstetrical providers (residents, midwives, physician assistants) who work regularly on the labor floor at the time of admission or a research coordinator/medical student who is under the training of an obstetrical provider for consideration of participation to the study.

All research-related discussions will be held in the patient's private room. Any questions will be answered and fully discussed to maximize patient comfort. If they meet eligibility criteria and chose to participate they will be randomized and receive care within the accepted standards. The electronic medical records will be used for patient information.

Risks to Subjects
The risks to subjects are inherent to the cesarean section process itself outside of the study. The only difference in care is use of chlorhexidine gluconate in one arm of the study. This may result in a decreased rate of infectious morbidity.

If used as instructed, the only potential unforeseeable risk is an allergic reaction to the chlorhexidine gluconate. Allergic reaction could include itching or hives, swelling in the face or hands, swelling or tingling in the mouth or throat, chest tightness, and/or trouble breathing.

The patients in our study are all consented to possible cesarean section upon admission for various indications. The inherent nature of cesarean section requires an abdominal surgery. As standard of care, all women in this study will be provided with analgesia. In addition, enrollment in this study will not alter the current strategies regarding cesarean section.

Description of Procedures taken to lessen the probability of magnitude of risks
There is always the risk of loss of confidentiality; however, there are procedures in place to minimize this risk. To ensure confidentiality, the following system will be adhered to: When subjects are enrolled in this study, they will be assigned a unique identification code. Corresponding medical record numbers for each code (key code) will be stored in a password locked document on the maternal-fetal medicine (MFM) server that can be accessed only by members of the research team. At the conclusion of the data extraction, the outcome variable will be assessed and the key codes to the medical record numbers will no longer be necessary and that information will be permanently erased from the key code file. Electronic data with identifiers will be encrypted according to Data Security Standards.

Provisions for Research Related Harm / Injury
The patients will receive standard obstetric care and have access to the obstetric staff (physicians, nursing) as well as all of the resources on the labor floor including the use of the operating room, blood bank, and continuous fetal

monitoring. Any potential adverse events are inherent to the operative delivery itself and regardless of the study. Any complications that occur during cesarean section will be managed by the obstetricians and anesthesiologists. As standard of care, a physician is present during a cesarean section and is experience in managing complications. The patient is billed as per standard scheduled cesarean section regardless of complications due to the surgery.

Expected Direct Benefit to Subjects
Direct benefit to subject is unknown. However, the potential benefit is that we may find a reduction in infectious morbidity related to cesarean section.

Benefit to Society
Direct benefit to society is unknown. However, the potential benefit is that we may find a reduction in infectious morbidity related to the cesarean section surgery which may reduce subsequent healthcare costs due to decreased re-admissions for surgical site infections.

Provisions to Protect the Privacy Interests of Subjects ***
The patients will be approached upon admission to the labor and delivery floor by a physician. Their participation will not require any additional examinations. All research-related discussions will be held in a private location. Any questions will be answered and fully discussed to maximize patient comfort. If they choose to participate they will be randomized and receive care within the accepted standards. If a patient must be called to find out how the wound is healing, the research team members placing the call will not leave a message or speak to anyone except the patient herself. When called, she will be asked if she can discuss the research study at that time, ensuring patient privacy and comfort.

Economic Impact on Subjects
There are no foreseeable costs that subjects may incur through participation in the research.

Data for Assessing Potential Risks to Pregnant Women and Fetuses
The risks to pregnant women and fetuses are inherent to the cesarean section process itself outside of the study. The only difference in care is use of chlorhexidine gluconate in one arm of the study. This may result in a decreased rate of infectious morbidity.

If used as instructed, the only potential unforeseeable risk is an allergic reaction to the chlorhexidine gluconate. Allergic reaction could include itching or hives, swelling in the face or hands, swelling or tingling in the mouth or throat, chest tightness, and/or trouble breathing.

Description of the study design
This is a prospective randomized trial.

The study will be offered to women who are admitted to Mount Sinai Medical Center to undergo labor. The eligible women will be randomized to use of a 2% chlorhexidine gluconate (CHG) cloth and vaginal scrub (in addition to standard preoperative scrub) or standard preoperative scrub alone. Participants will not be blinded to the arm in which they have been assigned. This study intends to show that the use of chlorhexidine cloth and vaginal scrub prior to cesarean section will reduce the rate of SSI in women who have previously been laboring.

Researchers will have access to all patients scheduled for delivery at Mount Sinai Medical Center. About 1800 deliveries by cesarean section occur each year at Mount Sinai. Of these, approximately 800 are cesarean sections after failed labor. Assuming a primary outcome rate of 20% in the control arm, a sample size of 329 in each group would give 80% power to detect a 40% reduction in surgical site infection between the active group and control. We aim to recruit 400 patients per group (for a total of 800 patients) to account for patient drop out or non-compliance

Description of Procedures Being Performed
This study intends to evaluate the effectiveness of a chlorhexidine gluconate (CHG) cloth and vaginal scrub in reducing SSI in patients undergoing cesarean section who have previously been laboring. Patients will be randomized to one of two groups: administration of a 2% CHG cloth and vaginal scrub (in addition to standard preoperative care) prior to cesarean delivery or standard preoperative care.

Description of the Source Records that Will Be Used to Collect Data about Subjects
All data will be extracted from electronic medical records (EMR) and phone calls made to subjects if they do not present for their postpartum visit.

Description of Data that Will Be Collected Including Long-Term Follow-Up
Data that will be collected from the EMR include maternal demographics (age, race, BMI, parity) as well as outcomes including surgical site infection and postpartum endometritis. In addition data will be collected regarding other outcomes including maternal complications or interventions, neonatal ICU admissions, maternal length of stay or readmissions. This data collection will start from time of enrollment to 6 weeks postpartum.

Where and When Consent Will Be Obtained
Consent will be obtained upon admission to the labor and delivery floor at Mount Sinai Hospital.

Waiting Period for Obtaining Consent
The patient can be approached and consented starting from admission to labor and delivery and can still be consented to participate in the study at a later time in labor if not already delivered by cesarean section.

Description of Health Information That Will Be Viewed, Recorded, or Generated
Health information collected will include maternal age, parity, gestational age, medical problems, number of previous cesarean sections, indication for cesarean section, time from incision to delivery, type of anesthetic, type and use of prophylactic antibiotics and type of wound closure. Maternal outcomes including estimated blood loss (EBL) will be reviewed. Charts will be reviewed through the 6 week postpartum visit in order to determine how well the skin at the incision site is healing. If patients do not visit Mount Sinai Medical Center for their 2 week wound check, they will be called and asked the following questions: Were you treated for wound infection? Did you experience wound separation or any other wound complications?

Description of Non-Health Information That Will Be Viewed or Recorded
Data collected will include demographic variables such as age, parity, body mass index (BMI) and race.

How PHI Will Be Protected from Improper Use or Disclosure
No specimens will be sent out or received in this trial.
All data is de-identified; patients are followed by subject number. Identifiable patient information (consent forms & consent documentation) are kept separately from any data collected. All consent documentation is stored in a locked cabinet at [redacted]. Identifiable enrollment statistics are kept in a password-protected computer (Excel) spreadsheet that is only accessible by members of the research team on a departmental J Drive.

When and How PHI Will Be Destroyed
The key code and data points will be destroyed 7 years after data analysis is complete.

Description of PHI that Will Be Shared
PHI that will be shared will include maternal demographics and maternal outcomes as previously described. Maternal demographics and information collected will include age, parity, BMI, race, gestational age, and number of previous cesarean sections. Additional information will be recorded and shared including time from incision to delivery, type of anesthetic, antibiotic use, type of wound closure, and EBL. Charts will be reviewed through the 6 week postpartum visit in order to determine how well the skin at the incision site is healing.

Justification for Sharing PHI
The PHI will be shared for means of data analysis by members of the research team and statisticians.

With Whom Directly PHI Will Be Shared
The PHI will be shared with members of the research team

Location Where Data Will Be Stored
All research data will be stored in a password-protected database maintained on a secure network drive on the hospital server.

Duration Data Will Be Stored
The key code and data points will be destroyed 7 years after analysis is complete.

Steps That Will Be Taken to Secure the Data During Storage, Use, and Transmission
To minimize risk of loss of confidentiality, study subjects will be assigned a unique identification code. The unique ID code will be linked to the subject's medical record number. The linking key code will be encrypted and stored separately on a secure excel spreadsheet accessible only by the PI and research staff. All research data will be stored in a password-protected database maintained on a secure network drive on the hospital server.

Steps That Will Be Taken to Secure the Data During Storage, Use, and Transmission
To minimize risk of loss of confidentiality, study subjects will be assigned a unique identification code. The unique ID code will be linked to the subject's medical record number. The linking key code will be encrypted and stored separately on a secure excel spreadsheet accessible only by the PI and research staff. All research data will be stored in a password-protected database maintained on a secure network drive on the hospital server.

Data Analysis Plan Including Any Statistical Procedures
Data will be analyzed on an intention to treat basis. Statistical analysis will be performed by SAS using X 2 test or Fisher exact test (categorical variables) and student t test or Mann-Whitney U test (continuous variables). Statistical significance will be set at $p<0.05$.

Study Fund Account (or alternate departmental / fund account, if study is not yet established)
[redacted]

Generic Name
4% chlorhexidine gluconate

Brand Name
BD E-Z Scrub 107 Surgical Scrub Brush/Sponge 4% Chlorhexidine-Gluconate

IND Number
[redacted]

Name of IND Holder
Angela Bianco

Drug / Biologic Description (Manufacturer/Generic Name/Form/Strength)
Drug: BD E-Z Scrub 107 Surgical Scrub Brush/Sponge 4% Chlorhexidine-Gluconate

Biologic Description: Antiseptic
Manufacturer: Becton, Dickinson and Company
Generic Name: 4% chlorhexidine gluconate
Form: Scrub Brush/Sponge
Strength: 4% chlorhexidine gluconate w/v