

# 207526  
Date 6/3/2019

## **The Role of Adherent Occlusive Antimicrobial Absorbent Foam Dressing in Prevention of Cesarean Section Wound Complications**

### **Background and Significance:**

Cesarean delivery rates continue to increase in the United States, accounting for 33% of all births in 2011 (1). Patients undergoing cesarean delivery are at a greater risk of postpartum infection when compared to vaginal delivery. Additionally, the most prominent risk factor for postpartum infection is cesarean delivery. The spectrum of puerperal infections ranges from surgical site infections (SSI), endometritis, and abscess to pelvic thrombophlebitis, bacteremia, and sepsis (2). 2.5-16% wound complication post csection which includes seroma, hematoma, infection, separation and dehiscence. Risk factors for wound complication include medical disorders such as diabetes, tobacco use, preeclampsia, obesity, frequent vaginal exams, internal monitoring and emergent cesarean. (3) Reported rates of post-cesarean wound infection range from 2.71-11.4% (4-8). Risk factors for post-cesarean SSIs include prolonged operating time, body mass index (BMI) greater than 30, and increased thickness of subcutaneous tissue (5,6). Furthermore, patients undergoing cesarean delivery experience increased risk of rehospitalization within 30 days postpartum, as the majority of SSIs become apparent following discharge (9, 10). SSI is the principal reason for readmission following cesarean delivery (9).

Wound infection is an economic and social burden to the health care system. Of the major health care-associated infections—central line-associated bloodstream infection, ventilator-associated pneumonia, SSI, Clostridium difficile infection, and catheter-associated urinary tract infection—SSI contributes the most to the total annual cost of health care-associated infections (11,12).

The increased risk of postpartum infection following cesarean delivery has motivated research to establish practices now accepted as standards of care. The routine use of prophylactic antibiotics in women undergoing cesarean delivery reduces the risk of fever, wound infection, endometritis, serious infectious morbidity, maternal urinary tract infections, and decreased maternal length of stay in the hospital (13). Vaginal cleansing with an antiseptic solution immediately prior to cesarean delivery reduces the risk of endometritis but has not been found to reduce the number of fevers or wound complications (14). However, despite these measures, post-cesarean wound complications, with disruption and/or infection still occurs.

Of the heavy metals, silver possesses antibacterial activity and thus, has been used in medicine for centuries. Well-known uses of silver include silver nitrate drops to

prevent gonococcal ophthalmia neonatorum and silver sulfadiazine to prevent burn wound infections (15). While the antimicrobial mechanism of silver is not completely understood, proposed pathways include oxidative destruction catalyzed by silver, targeting of membrane proteins, affinity for sulfhydryl groups, and blocking or destroying host-cell receptors (16).

Silver-containing wound dressings and topical agents are widely used for burn injuries and chronic wounds, such as ulcers. Wound dressings and creams containing silver may help promote wound healing as well as prevent local infections. The use of silver for wound management is limited and, as a result, the literature investigating its use and recommendations for its use in wound management remain inconclusive. In a recent prospective, randomized controlled trial involving SSI following colorectal surgery, the total incidence of SSI was significantly lower in the silver nylon dressing group versus the control group (17). However, other studies have failed to show a statistically significant reduction in SSIs with the use of silver-impregnated dressings (18-20).

Evidence to support the use of silver-containing dressings to limit and treat post-cesarean SSIs is particularly limited. Connery et al. (2012) conducted a retrospective review to evaluate the effectiveness of silver-containing dressings versus traditional wound dressings in reducing additional postoperative visits associated with SSIs in patients undergoing cesarean delivery. Although they did not find a significant difference between the experimental and control groups, the study was limited due to small number of study subjects and a higher number of medical comorbidities in the study group (21).

Despite measures to decrease the risk of postpartum infection following cesarean delivery, the rate of SSI remains prominent. Wound infections are responsible for longer hospital stays, readmissions, and ultimately, increased costs to the healthcare system. Silver-containing dressings may prevent wound infection. The purpose of the current study is to determine if the use of a silver-impregnated dressing decreases the incidence of SSI following cesarean delivery.

**Purpose:** To investigate the role of an adherent soft silicone anti-microbial occlusive foam silver-impregnated dressing for primary cesarean delivery.

**Primary Aims:**

1. To determine the primary cesarean wound complication rate using the adherent soft silicone silver impregnated anti-microbial occlusive foam dressing silver-impregnated dressing

**Secondary Aims:**

1. To assess pain scores by VAS in primary C-section patients using the adherent soft silicone silver impregnated anti-microbial occlusive foam dressing silver-impregnated dressing

2. To assess cosmetic appearance of the incision based on Stony Brook scar evaluation scale scores for those patients using the adherent soft silicone silver impregnated anti-microbial occlusive foam dressing silver-impregnated dressing.

## **Methods and Materials**

### *Study Population and Recruitment*

This single-center, prospective, observational trial will include women between 18 and 45 years of age with viable pregnancies (24 weeks or greater) undergoing primary cesarean delivery at Loyola University Medical Center, Maywood, Illinois.

### ***Inclusion criteria:***

Participants must meet all of the following criteria:

- Consent to undergo cesarean delivery
- Between the ages of 18 and 45
- Primary C-section
- Subcuticular skin closure
- Able to consent, fill out study documents, and complete all study procedures and follow-up visits

### ***Exclusion criteria:***

- Patients with an allergy to silver
- Inability to obtain informed consent
- Staples
- Repeat C-section
- Vertical skin incision
- Intrapartum fever of 100F or >

## **Enrollment**

Women will be approached for voluntary study participation upon admission to labor and delivery or the antepartum unit. A member of the research team will explain the purpose and procedures of the study. Potential participants who meet the inclusion criteria and sign the research consent document will be enrolled. A signed copy of the research consent document will be given to the subject. The investigator will keep the original research consent document, in keeping with prevailing research regulations.

## **Protection of Human Subjects**

### *Recruitment and Informed Consent*

Participants will be counseled by the study personnel (investigator or study coordinator) prior to signing informed consent for study participation. All study procedures will be approved by the LUMC Institutional Review Board.

### Protection and Informed Consent

This protocol will comply with all prevailing regulations that govern human subject research. Our research team is directly responsible for monitoring the safety of study participants. All adverse events will be documented and reported to our IRB in a timely manner. Finally, the research team and our IRB will report serious adverse events that affect study conduct to the appropriate NIH program officers.

In addition, strict research procedures will be followed to minimize risks to the privacy of participants. Patient identifiers will not be included on any study documents, and identifying information will not appear in any electronic database. Once a patient consents to join the study, they will be assigned a study ID number, which will then be used to refer to that patient for the duration of the study. Documents linking patient identifiers and study ID will be kept in a locked cabinet, separate from other study documents.

### **Study Flow and Measurements**

As part of clinical care, all patients who are admitted to Loyola's labor and delivery or antepartum unit undergo a standardized history and physical examination. At the time of recruitment for the study, all study participants will undergo a standardized baseline obstetric evaluation, which includes:

- Demographics: age, self-reported race and ethnicity, medications, allergies, prior medical and surgical history, obstetric and gynecologic history
- Examination: gestational age, maternal BMI, rupture of membranes, labor, temperature, blood pressure

### **Methodology of Measurements:**

Women who are admitted to labor and delivery or the antepartum unit will be invited to participate. Those who require a cesarean delivery will undergo standard perioperative management: surgical skin preparation with Chloroprep solution, vaginal betadine prep, and prophylactic antibiotics. Women, who consented to participate, have a Pfannensteil incision and subcuticular skin closure will have the study dressing, *Mepilex Border AG*, placed.

*Mepilex Border Ag* is produced by Molynycke Health Care, and is a commercially available adherent soft silicone anti-microbial occlusive foam silver-impregnated dressing. This dressing was designed to aid in healing of wounds at high risk for infection, such as postoperative wounds, with provision of localized antimicrobial

activity. The high risk for wound infection and complications in our population led to selection of this dressing. No contraindications have been identified.

The cesarean delivery technique may differ among health care providers at our institution but generally follows usual practice, including perioperative prophylactic antibiotics and surgical skin preparation with Chloroprep solution, vaginal betadine prep, saline irrigation of the subcutaneous layer, and the use of cautery to obtain hemostasis. In addition, the subcutaneous layer is reapproximated with 3-0 Vicryl for all women with a subcutaneous layer greater than 2.0 cm. The skin will be closed with continuous absorbable suture, e.g. 3-0 Vicryl or Monocryl. Women with subcuticular suture will have adhesive strips applied with benzoin prior to the placement of the dressing.

If not participating, the wound will be dressed with a standard dressing. The standard dressing will be removed by 24 hours postoperatively. The study dressing will be removed during the first 7 days post-op only to allow/require dressing changes due to clinical signs of infection, leakage, or if the dressing falls off. Otherwise the study dressing will be removed on postoperative day 7 by a physician.

Obstetric physicians will perform a standardized physical examination of the wound dressing on each postoperative day, at 7 days post-operatively on dressing removal, and the wound will be examined also at the standard 6 weeks postpartum examination for patients in both groups. For patients who do not return for their postpartum visit at 7 days and 6 weeks, a standardized phone evaluation will be conducted by trained study personnel; any report of wound complication will be documented in the medical record.

The **primary outcome variable** will be a composite of wound disruption and/or infection occurring within 4 weeks postoperative (**wound complication rate: SSI**). Wound disruption will be defined as any separation of the wound (ranging from small skin defects to entire separation of the wound) and subcutaneous skin dehiscence, i.e. from seroma or hematoma. Wound infection will be classified by the Centers for Disease Control and Prevention (CDC) guidelines (22). **Secondary outcomes will include:** pain measured at 24h, 48 h, 7 days at dressing removal, and 6 weeks after cesarean delivery using a ten-point visual analog scale (VAS) from 0 to 10 (with 0 indicating no pain and 10 indicating worst conceivable pain), cosmesis score (as defined by the Stony Brook Scar Evaluation Scale (23)) 7 days and 6 weeks postoperatively, mobility assessment, readmission to the hospital, post discharge fever or antibiotic therapy, and additional clinic visits (both routine and unscheduled). Please see Figures 1 and 2. Additionally, all patients will be queried on degree of satisfaction on a scale of 1-10 as will clinicians queried on ease of use.

In addition, deidentified demographic and outcome data on those who had a primary csection with transverse incision closed in a subcuticular fashion who did not participate in the silver dressing during the same time period were collected.

## Analysis Plan

### Statistical Considerations:

*Data Management:* Data forms collected will be converted to equivalent electronic data entry forms with use of REDCap. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. REDCap is hosted on secure servers located in the Loyola Medical School Campus and supported by the IT department. Project staff will be trained in the use of REDCap for entry of study data. Appropriate logic and limits checking (including cross-form validity checks) will be implemented in REDCap to facilitate accurate and consistent data entry. Study information within the virtual environment will be available for participant tracking activities such as production of result and reminder letters, scheduling of interim telephone contacts, and scheduling and tracking of follow-up visits.

*Statistical Analysis:* It has been argued that the current rate of wound complication is about 10%. We postulate that patients following this treatment will experience a lower rate of wound complication. The incidence of infection will be estimated as the proportion of patients who developed infection by the end of the study period. Confounded-adjusted rates will be estimated using generalized linear models (identity link, binomial family). We will apply a one-sample, two-sided, 5% significance Z-test to compare the rate of infection with the new treatment to the historical 10%.

In addition, comparisons between the silver dressing group and the contemporary comparison group will be made by T-test, Chi-square, Fishers exact test, logistic regression modeling.

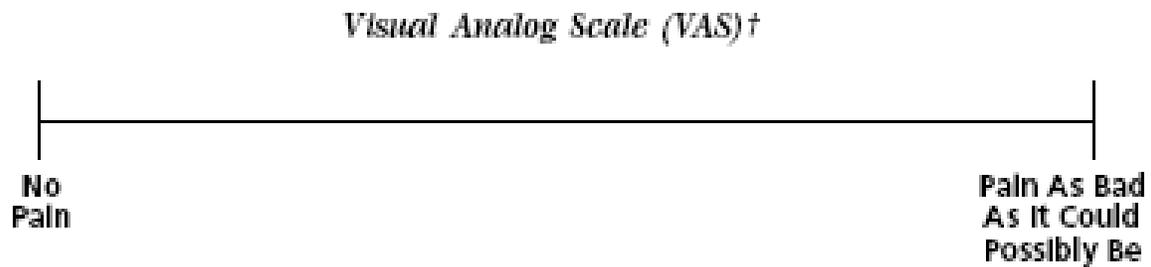
*Sample Size/Power Justification:* As stated above, we are interested in demonstrating that the rate of wound complication is lower than the historical 10% value found in the literature. We will accrue **185 patients** to detect a 5% difference (10% vs 5%) using the one-sample Z-test with 80% statistical power. Testing via the generalized linear model to adjust for confounders will increase the statistical power to detect differences.

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**Figure 1. Visual Analog Scale (VAS)**

| Category | Response           | Score |
|----------|--------------------|-------|
| Width    | >2mm               | 0     |
|          | </=2mm             | 1     |
| Height   | Elevated/Depressed | 0     |

|                                      |   |          |
|--------------------------------------|---|----------|
|                                      | <b>Flat</b>                               | <b>1</b> |
| Color (compared to surrounding skin) | <b>Darker (red, purple, brown, black)</b> | <b>0</b> |
|                                      | <b>Same or lighter</b>                    | <b>1</b> |
| Hatch/Suture Marks                   | <b>Present</b>                            | <b>0</b> |
|                                      | <b>Absent</b>                             | <b>1</b> |
| Overall Appearance                   | <b>Poor</b>                               | <b>0</b> |
|                                      | <b>Good</b>                               | <b>1</b> |
| Total Score                          | -----                                     |          |

**Figure 2. Stony Brook Scar Evaluation Scale**