STUDY PROTOCOL 4/1/2024

TITLE: Glue versus subcuticular suture for cesarean closure: a randomized controlled trial

Short Title: GLUE Study

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Study Background and Rationale

The incidence of cesarean delivery in the United States has increased significantly over the past few decades, with an incidence of 33% in New York State alone per the CDC's National Center for Health Statistics in 2019 [1]. Despite the abundance of existing literature on the benefits of subcuticular skin closure over staples, there is limited data on other methods of cesarean skin closure, such as tissue adhesives and skin glue. This method has recently been examined in the non-obstetric literature due to possible advantages of decreased operative time, the ability to provide a waterproof barrier, and antimicrobial properties of tissue adhesives [2-3].

Dermabond Prineo is a tissue adhesive that has been used for skin closure in the gynecologic, plastics, and cardiothoracic surgery literature, but has not yet been utilized for obstetric surgery. Known advantages of Dermabond Prineo in comparison to subcuticular suture include greater skin holding strength, which has been shown in non-obstetric studies to be 40% stronger compared to 4-0 sutures and 33% stronger than staples. Dermabond Prineo has been shown to have better cosmetic results according to patient and observer scar assessment scales, and shorter closure time by up to 84% as it dries in 60 seconds. This method eliminates the need for postsurgical dressings, and has a waterproof antimicrobial barrier that has been shown in invitro studies to be 99% effective for 72 hours against SSI organisms. In comparison, traditional dissolvable suture can be a site of bacterial colonization for infection, and can create inconsistent suture tension distribution across the incision which can compromise both the integrity and cosmesis of the closure. Cesarean section incisions closed with suture are typically covered with a sterile dressing; however, these dressings do not have antimicrobial properties, and may increase the risk for infection if removed too early or too late as patients are unable to shower with the bandage on. In comparison, patients with Dermabond Prineo can shower immediately after surgery, as the mesh layer falls off on its own or can be removed in 7-14 days [4-6].

We propose a quality assessment initiative, through a randomized controlled trial designed to investigate the role of tissue adhesives such as Dermabond Prineo on outcomes such as cesarean wound cosmesis, operative times, and SSI.

Objective

The primary outcome of the current study is to assess patient satisfaction with cesarean scar cosmesis when comparing standard subcuticular suture closure to the Dermabond Prineo tissue adhesive system. This outcome will be assessed with the validated Patient Scar Assessment Scale

(PSAS) [7]. This questionnaire has previously been used in the skin staples versus suture obstetric literature [8].

Primary Research Question / Hypothesis

Does Dermabond Prineo provide improved patient scar satisfaction when compared to standard subcuticular suture?

Secondary Research Questions

1. Does Dermabond Prineo decrease the rate of wound complications after cesarean section when compared to standard subcuticular suture?

2. Does Dermabond Prineo decrease overall skin closure time and operative time at the time of cesarean section when compared to standard subcuticular suture?

3. Is Dermabond Prineo associated with decreased postoperative pain scores after cesarean section when compared to standard subcuticular suture?

Exposure

Dermabond Prineo
Standard subcuticular suture

Arms

Group 1: Dermabond Prineo for skin closure at time of cesarean section
Group 2: Standard subcuticular suture for skin closure at time of cesarean section

Study Design

This will be a prospective randomized, open label trial as both surgeons and patients will know what type of closure technique is utilized. Two study groups will be defined as described above. In group 1, Dermabond Prineo will be utilized in place of standard subcuticular closure at the time of cesarean skin closure. In group 2, standard subcuticular closure will be utilized at the time of cesarean skin closure. All patients will be randomized immediately preoperatively as part of the multidisciplinary preoperative briefing process. See procedure below for further details.

Inclusion Criteria

· Women age 18 years or older

· Admitted to CHONY Labor and Delivery unit

· All women scheduled for primary or repeat cesarean deliveries

· All women undergoing intrapartum or antepartum cesarean delivery

· Pfannenstiel skin incision

· Birth of a live infant at time of cesarean delivery

Exclusion Criteria

· Vertical skin incision

· Cesarean hysterectomy

· Emergency or stat cesarean delivery excluding standard preoperative preparation measures (i.e. use of Chlorhexidine skin prep, vaginal prep, etc)

· Intrapartum stillbirth

· Planned postpartum follow up at another facility

· Contraindications to routine postpartum pain medications

· Allergy to skin glue/adhesive

Sample Size Calculation

The primary outcome of our study will be the Patient Scar Assessment Scale (PSAS), which has a range of potential scores from 6-60). The following assumptions were used for the parameters in our sample size calculation:

Power: 80%
Alpha level: 0.05 (two-sided)
Mean ± SD for suture group: 20 ± 6
Effect size: 20% reduction (relative to the control group)
Loss to follow up: 20%
Allocation Ratio: 1:1
The distributions of both groups are assumed to be normal.
The standard deviation for both groups is assumed to be the same.
The results were calculated in Stata/BE 17.0

With these assumptions, our total sample size is calculated to be 188 total patients, with 94 patients in each arm.

Procedures

Permission from primary teams will be sought on Columbia University Medical Center: New York Presbyterian – Children's Hospital of New York (CHONY) labor and delivery and informed consent obtained from women willing to participate in the study. Women scheduled for cesarean delivery will be contacted by the research team via 1 of 3 options: 1) via telephone to obtain telephone consent in the week prior to their scheduled procedure; 2) in person at the last outpatient visit prior to their scheduled c-section; 3) in person at the time of admission to labor and delivery for their scheduled procedure if they cannot be contacted beforehand. Women admitted to the antepartum service or labor and delivery for induction of labor or spontaneous labor who then undergo intrapartum cesarean delivery will be consented at the time the decision is made to proceed with cesarean.

Once consent is obtained, randomization will be performed using a computer-generated algorithm. Consenting women will be randomly assigned in a 1:1 ratio to each group by trained research personnel. Women meeting inclusion criteria will be randomized to two groups: 1) experimental arm: Dermabond Prineo skin closure at the time of cesarean section; or 2) control arm: standard subcuticular skin closure at the time of cesarean section. Following randomization, the assigned intervention will be announced to the surgical team at the time of the surgical time-out in the operating room, dictating either standard subcuticular skin closure or closure with Dermabond Prineo, both of which will be available in the Labor and Delivery operating rooms. Those who receive standard subcuticular skin closure will have their incision covered by a standard pressure dressing, as per routine protocol. Those who receive Dermabond Prineo will forego the application of an additional pressure dressing, as one of the benefits of the Dermabond Prineo closure is that an overlying dressing is no longer necessary. Thus, this is an open label trial as both the surgical team and the patient will be able to visualize what type of closure technique was utilized.

In addition to the overall operative time, the total skin closure time will be documented by the surgical staff for all women enrolled in the study. For the standard subcuticular skin closure group, the total skin closure time will include the time the first subcuticular skin suture is placed, to the completion of the pressure dressing application. For the Dermabond Prineo closure group, the total skin closure time will include the time the Dermabond mesh is first applied, to the completion of the removal of the outer adhesive edge once the Dermabond glue dries.

Regardless of group assignment, standard perioperative interventions as part of the perioperative bundle to prevent and decrease the incidence of cesarean section SSIs will be utilized, including the use of chlorhexidine skin prep, hair removal around the surgical site, preoperative antibiotic administration for surgical prophylaxis, vaginal prep for laboring patients, and subcutaneous skin closure with suture for subcutaneous depth of more than 2cm. Labor and delivery management, as well as intraoperative surgical technique, will otherwise be at the discretion of the obstetric care providers. Patients who require stat cesarean delivery with the use of Betadine skin prep, intraoperative cesarean hysterectomy, or vertical skin incision will be excluded from the study.

All patients will receive routine postoperative care. However, postpartum nursing and clinical staff will be educated via in-services on additional postoperative considerations for patients who receive Dermabond Prineo skin closure; namely, that they are able to shower immediately postoperatively as they will not have a postoperative surgical dressing, and that the adhesive should not be removed during their postoperative stay. Otherwise, routine postoperative considerations will apply to both groups, including keeping the incision clean and dry.

Postoperative wound assessment for both groups will occur at 2 separate time intervals: 1) immediate postoperative wound assessment on postoperative day 3 by the surgical team of both the composite primary outcome, as well as postoperative pain scores; 2) postoperative follow up at 4-6 weeks via a telehealth research visit to assess the primary outcome via the Patient Scar Assessment Scale (PSAS) questionnaire.

In terms of immediate postoperative wound assessment on postoperative day 3, a member of the surgical team will perform a standard postoperative wound assessment prior to hospital discharge to assess for evidence of the wound complications, including the presence or absence of superficial SSI, deep SSI, endometritis, and/or wound disruption. Postoperative pain scores are also documented for all patients by postpartum nursing staff as part of routine postoperative care, and will be assessed for patients in both groups.

Long term postoperative follow up will then be assessed by the research team at 4-6 week postoperative follow up visits. Patients will be consented, at the time of initial consent to the study, to a short telehealth video or telephone visit at 4-6 weeks postoperative. This research visit will administer the Patient Scar Assessment Scale (PSAS) questionnaire to assess for our primary outcome of patient scar satisfaction. Additionally, chart review will be performed at this time to assess for the presence of other secondary outcomes, such as wound complication.

The research team will perform chart review to abstract maternal demographics, delivery information, and maternal and neonatal outcomes from maternal and neonatal medical records. This information will be entered into REDCap, a web-based data collection system. Once the study is underway, an interim analysis using the previously described statistical methodology may be appropriate to ensure that there is not a disproportionate incidence of the primary composite outcome or other adverse outcome in the experimental group.

Study Drugs or Devices

Dermabond Prineo is a product that is already available at New York Presbyterian Hospital, and has been used regularly by our gynecologic oncology colleagues for skin closure after cesarean hysterectomy. In services will be performed by the Dermabond Ethicon team via in- person or video training on Labor and Delivery for the surgical team and nursing staff, followed by distribution of the product in the L&D operating rooms. The in-services will serve to familiarize the surgical teams and clinical staff on the appropriate use and application of Dermabond Prineo at time of cesarean skin closure, as well as postpartum aftercare as described above for the postpartum clinical staff. Postoperative patient education will be individualized according to the type of skin closure patients receive; postoperative surgical dressings will be removed on POD2-3 for standard subcuticular skin closure, versus at 7-14 days for the Dermabond Prineo group.

Study Questionnaires

The Patient Scar Assessment Scale (POSAS) is a patient questionnaire that has been validated in prior studies, including in the dermatologic and plastics literature [11, 15-18]. PSAS includes assessment of scar related pain, itchiness, color, stiffness, thickness, and irregularity (ranked 1-10 w/ 1 representing normal skin). This survey will be administered via telehealth video visits at a 4-6 week postoperative research visit, as previously described in "Procedures". A copy of these questionnaires can be found at the end of this protocol.

Potential Risks

Given that the study is not introducing new medications or treatments, there are no additional significant risks anticipated to patients enrolled in the study except for the presumed baseline risk to all patients during cesarean delivery, which includes but is not limited to risk of bleeding, infection, injury to surrounding organs, and wound complications, such as wound infection, separation, hematoma, or fascial dehiscence.. In all cases, obstetric providers will take standard precautions to minimize surgical site infection (SSI). As part of routine post-delivery care, all patients will have vital signs, urine output, blood count, and symptoms monitored closely after delivery to quickly identify and treat patients with SSI or wound infection.

As discussed previously, standard perioperative interventions as part of the perioperative bundle to prevent and decrease the incidence of cesarean section SSIs will be utilized for all patients in the study, including the use of chlorhexidine skin prep, hair removal around the surgical site, preoperative antibiotic administration for surgical prophylaxis, strict glycemic control, vaginal prep for laboring patients, and subcutaneous skin closure with suture for subcutaneous depth of more than 2cm. These interventions have been demonstrated in prior studies to effectively decrease the incidence of cesarean section SSI [3], and remain the standard of care at our institution. These precautions will continue to be applied during our study.

For both randomization groups, routine postoperative care to decrease cesarean section SSI will also continue to be utilized, including patient and postpartum nursing education on appropriate wound care. Patients who receive standard subcuticular skin closure will have their surgical dressings removed on POD2-3 and will be encouraged to shower following dressing removal, as is the current standard of care at our institution. Patients who receive Dermabond Prineo skin closure will keep the Dermabond mesh in place until day 7-14, or until the mesh falls off on its own. Every attempt will be made to keep the incision clean and dry for both study groups, and any postoperative SSI or wound infection will be treated with wound exploration and/or antibiotics, as deemed clinically appropriate.

As previously described, an interim analysis may be conducted once the study is underway to ensure that there is not a disproportionate incidence of the primary composite outcome or other adverse outcome in the Dermabond Prineo group, although this has not been shown in any prior studies involving this skin closure method. Although unlikely, it is possible that participating in this study may involve risks to the patient that are not expected. No neonatal risks are anticipated as part of this study, as the intervention will occur following delivery.

Potential Benefits

If patients decide to participate in this research study, they may or may not directly benefit from their participation. However, if the patient is randomized to Dermabond Prineo closure, they may potentially benefit from increased satisfaction with their cesarean incision. Patients randomized to the Dermabond Prineo group may also potentially benefit from secondary outcomes, such as decreased incidence of SSI, skin closure and overall operative time, lower postoperative pain scores, and higher observer and patient satisfaction scores.

In addition, the data gathered on the above primary and secondary outcomes will serve to increase the general knowledge base regarding the use of tissue adhesives at time of cesarean section skin closure, and subsequently benefit patients and clinicians in the future.

Alternatives

The alternative to this study is to not participate in the study, and to continue receiving standard intraoperative and postoperative care.

Data and Safety Monitoring

Data will be stored in a secured REDCAP database and only accessed on a password protected computer. We will abide by the OBGYN departmental data safety and monitoring policy. The data will be used only by those investigators involved in the study. The data will not be shared with other researchers. The data will not become a part of the subjects' permanent record. Once all of the data abstraction is complete and before data is ready for analysis, the REDCAP Manager will remove all identifiers from the file and send the coded file to the data analysts. This study will be monitored in accordance with the Department of OBGYN Quality Assurance Monitoring standard operating procedure.

Detailed information concerning adverse events (AEs) will be collected by research personnel and evaluated throughout the trial (including enrollment through the 6 week follow up period). All adverse events will be causally assessed by the Principal Investigator and reported per the CUMC HRPO policy of reporting Adverse events.
https://research.columbia.edu/sites/default/files/content/HRPO/Unanticipated%20Problems%20Pol icy.FINAL%20VERSION.012408.pdf

Feasibility/Timeline

There are approximately 30 cesarean deliveries per week at our institution. Assuming that 90% meet eligibility criteria, and assuming that 50% of patients agree to participate in the study, we will be able to recruit 1-2 patients per day. Thus, recruitment and enrollment will take approximately 4-6 months to reach the expected sample size of 188 patients.

Anticipated Budget

This goal of this proposal is to secure a charitable donation from Ethicon for 94 Dermabond Prineo units for use in this study as the experimental arm. The results of this study will aim to promote this product as an alternative to cesarean skin closure, and to increase its routine use at Columbia University Medical Center for our high volume obstetric practice. We cannot promote or endorse the use of this product until it has been shown to be a safe and non-inferior alternative to our current standard of skin closure with skin sutures at the time of cesarean delivery. Thus, we will need a donation of the Dermabond Prineo product in order to meet this goal.

References

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