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STUDY PROTOCOL

Study Title: The PICS Project (Prevention of Infection after Caesarean Section): Implementation of a peri-operative bundle at National Women’s, Auckland City Hospital, New Zealand.

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Study Method: Prospective cohort study/Quality improvement project

Aim

To determine whether the introduction of a peri-operative bundle of care could reduce the rate of post-caesarean section surgical site infection and complications. This includes genital-tract sepsis, endometritis, wound infection, haematoma and seroma.

Hypothesis

Implementation of an evidence-based peri-operative bundle will reduce the absolute rate of post-caesarean surgical site infection and wound complications.

We hypothesise that the peri-operative care bundle will be acceptable to all women undergoing caesarean delivery.

Background and literature review

Post-operative infection is a major cause of maternal morbidity and mortality in women undergoing caesarean section; indeed, caesarean section is considered the single-most important risk factor for post-partum infection. When compared to vaginal delivery, caesarean delivery presents a 5-to-20-fold increased risk of infection.1

The most recent report from the UK and Ireland confidential enquiry into maternal deaths and morbidity reported 24 maternal deaths from sepsis between 2013 and 2015 (MMR 0.56/100,000 maternities). There were three deaths from genital-tract sepsis after caesarean section, and two deaths from post-operative caesarean wound sepsis. Urinary tract sepsis was the cause of death in three women.2 In the last 10 years, 5.6% of the maternal mortalities in New Zealand have been due to pregnancy-related infection.

In 2014, a review of 70,000 caesarean deliveries in the USA reported endometritis rates of 6% in primary, not-in-labour caesarean section and wound infection in 1-2%.3 A study from the UK published in 2010 reported on outcomes for over 4000 women undergoing both elective and emergency caesarean section, with a surgical site infection complicating 9.6% (394 women). Whilst 88% of these were superficial wound infections, over half of these patients needed to be readmitted to hospital, contributing significantly to increased healthcare costs.4

Rates of caesarean delivery have increased significantly over the last three decades, with 32% of live births in Australia now delivered by caesarean section.In 2015, 25.5% of all deliveries were by caesarean section.5 As rates of caesarean delivery continue to rise, the incidence of complications will inevitably rise with it.

Surgical site infection, as defined by the Centers for Disease Control, is infection of the incision, organ or space that occurs after surgery.6 Risk factors for surgical site infection have been explored, and obesity and chorioamnionitis are known to increase the risk significantly. Additionally, variations in the use of pre-operative antibiotic prophylaxis outside of best practice, diagnosis of active labour, diabetes, ruptured membranes, emergency caesarean delivery, anaemia and prolonged surgical time are contributors.4

Recent evidence supports the use of pre- and intraoperative, evidence-based bundles to reduce the incidence of surgical site infection (Baseline rate 6% vs 2% post-intervention).7,8 Both deep and superficial wound infections were reduced, however it is noted that the rates of endometritis were low in the pre-intervention study period. It is not clear from the data as to whether pre-operative vaginal preparation with chlorhexidine is routine at the centres included in the systematic review. This intervention has been previously noted to reduce rates of post-operative infection significantly, particularly in the presence of ruptured membranes.9 In 2017, updated recommendations for the prevention of all surgical site infections were published by the CDC, based on a systematic review of 170 studies. Their updated recommendations include bathing with soap or antiseptic the night before surgery, antibiotic administration prior to skin incision, alcohol-based skin preparation and maintenance of normo-glycaemia and normo-thermia post-operatively. It was recommended that these interventions be incorporated into surgical quality improvement programs to improve patient outcomes.10

A recent retrospective study published in May 2020 demonstrated a significant reduction in surgical site infection rates after caesarean section following implementation of in infection prevention bundle (Mean rate 2.4 pre vs 1.1 post).11 A peri-operative surgical bundle has therefore been designed to be implemented in the obstetric service at National Women’s Hospital, Auckland, using evidence-based individual practices that have been shown to confer patient benefit.

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3. Peripartum complications with caesarean delivery: A review of Maternal-Fetal Medicine Units Network publications. Hammah IA, Chauhan SP, Magann EF, Abuhamad AZ. J maternal, fetal and neonatal medicine. 2014; 27(5):463.
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5. Ministry of Health. 2017. Report on Maternity 2015. Wellington: Ministry of Health.
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7. Carter EB, Temming LA, Fowler S et al. Evidence-based bundles and caesarean delivery surgical site infections: A systematic review and meta-analysis. Obstetrics and Gynecology 2017 Oct; 130(4):735-746.
8. Temming LA, Raghuraman M, Carter EB et al. Impact of evidence-based interventions on wound complications after caesarean delivery. Am J Obstet Gynecol 2017 Oct; 217(4):449.e1-449.e9
9. Haas DM, Morgan S, Contreras K et al (2018) Vaginal preparation with antiseptic solution before caesarean delivery for preventing postoperative infections. Cochrane Database of Systematic Reviews 2020, Issue 4.
10. Berrios-Torres S, Umscheid C, Bratzler D, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA Surg. 2017;152(8):784-791.
11. Davidson C, Enns J, Dempster C et al. Impact of a surgical site infection bundle of cesarean delivery infection rates. American Journal of Infection Control May 2020; 45 (5): 555-559.

Research methods

This study is a pragmatic study including two prospective cohorts. It is also a Quality Improvement study, as described by the SQUIRE criteria. The study involves two cohorts of women in the obstetric population prior to and after the implementation of a peri-operative bundle that aims to reduce the incidence of post-operative wound complications. In the pre-implementation period, information on all women undergoing caesarean section at Auckland DHB will be recorded and entered into a worksheet. Since some of the P-SSICS bundle components are already standard practice within the department we will use the P-SSICS bundle compliance checklist during the pre-implementation period to assess current compliance with departmental recommendations. The pre-implementation period will be of three months duration, anticipating a sample size of around 400 patients. Four components are assessed in theatre, whilst the fifth component (maintenance of normothermia) will be assessed using clinical records by the research team. Checklists will be collected in dedicated closed boxes in the theatre complex. Boxes will be emptied thrice weekly by the study team and checklist information entered into a Microsoft Excel spreadsheet, Compliance scores will be calculated using the completed checklists. Characteristics of each patient will be recorded, including the category of caesarean delivery, booking and most recent BMI, diagnosis of diabetes, presence and duration of ruptured membranes, age, ethnicity and indication for caesarean. These patients will have their medical records remotely followed for four weeks (28 days) during the post-operative period, for readmissions or reviews in hospital and antibiotic prescriptions received in the community. Patients affected by a post-operative complication will have swab and culture results collected where available, however positive cultures are not required to meet criteria for post-operative surgical site complication. Where prescriptions are noted to have been collected on the hospital electronic patient record, which also covers community dispensing, the lead maternity carer or general practitioner may be contacted to confirm the indication for antibiotic prescription, if a review in hospital or readmission has not occurred. Category one caesarean sections will be considered separately as these women are at greatest risk of post-operative complications and are more likely to have components of the P-SSICS bundle omitted during their delivery. This period of data collection will also allow us to assess our current rate of post-operative infectious complications, data which has not been formally collected for several years.

After the three month pre-intervention period, there will be a four-week period during which time the P-SSICS bundle will be implemented but data will not be collected. This is primarily to familiarise practitioners to the bundle and its components. During the post-implementation period, a P-SSICS bundle compliance checklist will be completed for all patients undergoing caesarean delivery whether elective or emergency. The same techniques for electronic remote follow up will be employed for the post-implementation patients. Following implementation of this bundle, we hypothesise that the rate of post-operative surgical site complications will be reduced.

The P-SSICS project and checklist has been presented to departmental theatre staff and their views sought. They are familiar with the checklist concept as this has been a recent project in the gynaecology service. They have indicated satisfaction with the project, its aims and feel that the completion of the relevant components of the checklist can be achieved during cases in theatre.

Bundle components are listed below.

1. Vaginal aseptic cleansing prior to all caesarean sections, including cleaning the vulva and perineum
2. Complete coverage of the incisional area with 2% chlorhexidine gluconate/70% iso-alcohol solution. Minimum of two minutes contact time; must be allowed to air dry, no cloths or towels used to dry the skin
3. Antibiotics given prior to skin incision- weight-based regime. Repeat dose if EBL >1500ml or operating time over three hours
4. Before closing rectus fascia, remove or change one pair of surgical gloves
5. Maintenance of normothermia (i.e avoidance of hypothermia)- 36.5-37.5 degrees celcius

In this study, two areas of care are being evaluated.

1. Women having caesarean section should have all five elements of the perioperative bundle completed (Targeting ≥90% to allow for the category 1 emergency CS where time constraints may limit adherence)
2. The mean rate of post-caesarean surgical site infection should be reduced following implementation of the peri-operative care bundle

The primary outcome will be surgical site infection, a composite of wound infection, cellulitis, haematoma or seroma, endometritis or any deep pelvic space infection, with a need for antibiotic treatment. The diagnosis of surgical site infection will be made clinically.

Secondary outcomes will be readmission, length of hospital stay, need for intravenous antibiotics and need for negative-pressure or additional wound care.

**Rationale and evidence base for the P-SSICS bundle components**

1. **Vaginal aseptic cleansing prior to all caesarean sections, including cleaning the vulva and perineum.**

*Note: a June 2020 TI audit suggests a 60% adherence to this departmental standard*

Rationale: Pre-operative vaginal cleansing with povidone-iodine or chlorhexidine solution immediately before caesarean delivery reduces the risk of post-caesarean endometritis, postoperative fever and post-operative wound infections.

Evidence: Haas DM, Morgan S, Contreras K et al (2018) Vaginal preparation with antiseptic solution before caesarean delivery for preventing postoperative infections. Cochrane Database of Systematic Reviews 2020, Issue 4. Art. No.: CD007892.

1. **Complete coverage of the incisional area with 2% chlorhexidine gluconate/70% iso alcohol solution. Minimum of two minutes contact time; must be allowed to air dry, no cloths or towels used to dry the skin.**

Rationale: Drying of prep by evaporation is equally important for biocidal effect of alcohol in the skin prep solution. Chlorhexidine/Alcohol combination has shown superiority over iodine-based solutions and has a faster drying time. Flammability risk if alcohol if allowed to pool.

Evidence: Health Quality and Safety Commission New Zealand; Surgical Site Infection Improvement Programme, 2014.

Darouiche RO, Wall MJ, Itani KM et al (2010) Chlorhexidine-Alcohol versus Povidone-Iodine for Surgical Site Antisepsis. NEJM 2010, Jan 7; 362(1): 18-26.

1. **Intravenous antibiotics given within 60 minutes prior to skin incision. Standard obstetric regime: 2g Cefazolin if weight <120kg; 3g if weight >120kg.**

Rationale: Pre-operative antibiotics have high quality evidence to support their use, and have been a mainstay of perioperative care for many years. Evidence shows that weight-based dosing for morbidly obese patients reduces the incidence of post-operative infectious morbidity.

Evidence: Ho VP, Nicolau DP, Dakin GF, et al. Cefazolin dosing for surgical prophylaxis in morbidly obese patients. Surg Infect (Larchmt). 2012;13(1):33–37.Mackeen AD, Packard RE, Ota E et al. Timing of intravenous prophylactic antibiotics for preventing postpartum infectious morbidity in women undergoing caesarean delivery. Cochrane Database of Systematic Reviews 2014, Issue 12. Art. No.:CD009516.

1. **Before closing rectus sheath, change one pair of surgical gloves.**

Rationale: Recent evidence suggests that changing surgical gloves prior to closing the abdomen (peritoneum or sheath regarded as commencement of closure) resulted in reduction in the incidence of post-caesarean wound complications- 13.6% versus 6.4%. A 2020 RCT showed a reduction in wound infection from 18.8% to 5% with a practice of intraoperative glove change.

Evidence: Scrafford J, Reddy B, Rivard C, Vogel R. Effect of intra-operative glove-changing during caesarean section on post-operative complications. A randomised controlled trial. Arch Gynecol Obstet 2018 Jun; 297(6); 1449-1454.

Hameed N, Jamshed R, Ali MA, et al. The impact of intraoperative gloves changing by the surgical team on the post-operative wound infection after a Caesarean section, in a tertiary care hospital. *Endocrinol Metab Int J.* 2020;8(4):82‒84

1. **Maintainence of normothermia (i.e avoidance of hypothermia)- Target temperature 36.5-37.5 degrees celsius. Active warming from 36.0 celsius.**

Rationale: Hypothermia intra and post-operatively is associated with significantly increased rates of surgical site infection. Active rewarming reduces the risk of surgical site infection and complications.

Evidence: Reynolds L, Beckmann J, Kurz A. Perioperative complications of hypothermia. Best Pract Res Clin Anaesthesiol. 2008;22(4):645-57.

Cheadle WG. Risk factors for surgical site infection. Surg Infect (Larchmt). 2006;7 Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med. 1996;334(19):1209-15.

Madrid E, Urrútia G, Roqué I Figuls M et al. Active body surface warming systems for preventing complications cause by inadvertent perioperative hypothermia in adults. Cochrane Database of Systematic reviews 2016, Issue 4. Arr. No.: CD009016.

Limitations of design

Incomplete capture of cases: Incomplete capture of cases will be our primary limitation. We anticipate difficulty in following up all patients for the four-week period, particularly as regards infectious morbidity that is managed in the community by general practitioners or lead maternity carers. We plan to limit the research period to four weeks post-operatively, before patients are discharged from their lead maternity carer, thus simplifying access to medical records for individual patients. For patients for whom Auckland DHB is not their domicile DHB, there may also be incomplete data capture, however, the majority of those patients delivering away from their local DHB will be doing so due to a need for paediatric or neonatal intervention that is likely to keep them in the Auckland area for several weeks, allowing their inclusion in the study cohort.

Compliance: We expect a period during which time bundle compliance will be incomplete, as practitioners begin to incorporate the process into their practice. Using a checklist approach, we plan to use a one-month introductory period to increase practitioner awareness and involvement, before we begin to prospectively identify patients for the three-month post-implementation period. We anticipate that adherence may be reduced in category one deliveries due to the time-critical nature of these caesarean deliveries.

Participant selection criteria

A consecutive block sample of pregnant women undergoing elective or emergency caesarean section at Auckland City Hospital will be included in the study cohort. There are no exclusion criteria.

Data collection

Data will be prospectively collected in both the pre and post-intervention period and entered into Microsoft Excel©. Prior to data analysis, patient information will be deidentified. Three-times-weekly review of hospital and community records will be performed by the investigation team to look for presentation or readmission to hospital or the prescription of antibiotics in the community within 28 days of delivery. The peri-operative bundle checklists will also be collected for each patient, and adherence to the bundle assessed. Weighted scores will be calculated for compliance. The best quality evidence exists for pre-operative antibiotics (high quality evidence) and per vagina aseptic preparation (med-low quality evidence) thus they will be weighted with a score of 2 whilst the other three components will be weighted with a score of 1, giving a maximum compliance score of 7.

The majority of demographic data is already routinely collected and recorded in the hospital maternity system and can thus be easily access.

Where prescriptions for antibiotics are noted on electronic health records, without documentation elsewhere on the electronic record as to the indication, the lead maternity carer or prescriber may be contacted for information.

Statistical analysis

This is a pragmatic study designed to assess the value of a peri-operative bundle consisting of multiple evidence-based interventions. Previous studies have reported a reduction in post-caesarean section wound complications of up to two-thirds following the implementation of perioperative bundles. A 50% reduction in the rate of post-operative infection would be considered clinically significant. There is a paucity of recent data in the department regarding post-operative complications after caesarean section. Data on the effect of the introduction of vulvovaginal cleansing on rates of endometritis showed a reduction in incidence from 6% to 2%. Extrapolating this data showing a two-thirds reduction and using a p-value<0.05 for significance, the total sample size required is 752, with 376 patients in each group. Over a three month period, we anticipate that the study can be adequately powered using the current monthly rate of caesarean deliveries within the department. (Approximately 50 per week) The rates of surgical site infection in the pre and post-intervention period will be calculated and statistical analyses performed to look for significance. Adherence to the bundle will also be assessed as a procedural outcome with a compliance score calculated. To assess for quality improvement, data points will be recorded fortnightly to show the incidence of complications meeting primary outcome criteria and how this changes over time as the P-SSICS bundle is implemented.

Dr Helen Winrow

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