

Research

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Results of Using Oxidized Regenerated Cellulose After Surgery in Women Having Cesarean Sections

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ABSTRACT

Introduction: In spite of careful technique, bleeding may continue to occur at time of surgery. Absorbable hemostatic agents have been developed in order to control hemorrhage. However, no study to date has investigated post-operative outcomes when oxidized regenerated cellulose is used routinely at time of cesarean delivery.

Objective: To assess post-operative outcomes associated with routine use of oxidized regenerated cellulose at the time of cesarean delivery

Methods: Retrospective chart review of cesarean deliveries divided into two groups: Those in which oxidized regenerated cellulose was used and those in which it wasn't. Following data were obtained: Maternal baseline characteristics, estimated blood loss, pre- and post-operative complete blood counts and incidence of fever and post-operative abscess. Student *t*-test and Chi-square were used for statistical analysis.

Results: Of 155 patients, oxidized cellulose was used in 77 (50%). Baseline characteristics between groups were similar. Mean estimated blood loss was not significantly different between groups (803 mL vs 800 mL, $p=0.32$). Increase in pre- and post-operative white blood cell count (3.5 vs. 3.3, $p=0.65$) and decreases in pre- and post-operative hemoglobin (1.7 vs. 1.9, $p=0.21$) and hematocrit (4.5 vs. 5.1, $p=0.29$) were not significantly different between groups. However, there was a significantly increased incidence of fever in the group in which oxidized cellulose was used (13.0% vs. 3.9%, $p<0.05$). Abscess formation did not occur in either group.

Conclusion: Oxidized regenerated cellulose use was associated with an increased incidence of post-operative fever without significantly affecting changes in pre- and post-operative hemoglobin and hematocrit.

KEYWORDS: Oxidized regenerated cellulose; Cesarean section; Post-operative outcome.

INTRODUCTION

Cesarean delivery is one of the most commonly performed surgical procedures in women. The national cesarean delivery rate is approximately 30%.¹ At the time of cesarean, careful surgical technique and dissection is essential in avoiding bleeding, a principle that is fundamental to all surgical approaches. However, bleeding may continue to occur in spite of these efforts and has led to the development of absorbable hemostatic agents in order to control hemorrhage. Literature within the hepatic and spinal surgery fields has supported the efficacy of these agents.²⁻³ Oxidized-regenerated cellulose and microfibrillar-collagen have been used at the time of cesarean delivery. The mechanism by which these agents accelerate clotting is not completely understood but it is theorized that a physical effect and/or an alteration of normal physiologic processes may be at play.⁴ These agents are typically placed over the uterine incision closure at the time of cesarean delivery in order to provide hemostasis in addition to conventional methods using suture. In spite of its benefits, use of absorbable hemostatic agents may not necessarily be without risk and may cause a probiotic microenvironment that can contribute to bacterial proliferation.⁵⁻⁶ A study performed by Anderson et al⁷ investigated the association of gelatin-thrombin matrix use and abscess formation in patients undergoing hysterectomy and found that

nine patients developed an abscess with gelatin-thrombin use as opposed to only two patients who developed an abscess in the absence of gelatin-thrombin use. However, no study to date has assessed the association between routine absorbable hemostatic agent use, as a means of preventing post-operative bleeding, and post-operative fever and abscess formation in women undergoing cesarean delivery. Hence, the purpose of this study was to assess post-operative outcomes associated with routine use of oxidized regenerated cellulose at the time of cesarean delivery.

METHODS

This study was an IRB-approved retrospective cohort study. Inclusion criteria consisted of those who underwent cesarean delivery and received their post-operative care at Hofstra University-Northwell Health System-Staten Island University Hospital between 2013 and 2015. Exclusion criteria consisted of those with a documented estimated blood loss of greater than 1000 milliliters and those who underwent procedures in addition to cesarean delivery such as bilateral tubal ligation, myomectomy and lysis of adhesions. Charts of 155 patients were reviewed. The following information were obtained: Age, parity, gestational age at time of cesarean delivery, body mass index, number of prior cesarean deliveries, estimated blood loss, incidence of administration of pre- and post-operative antibiotics, pre- and post-operative complete blood counts and incidence of post-operative fever and abscess. If oxidized regenerated cellulose was used at the time of cesarean, it was placed over the uterine incision after uterine incision closure. All patients received pre-operative antibiotics and received the same pre-operative antibiotic post-operatively for up to 24 hours after surgery, unless the provider determined that the post-operative antibiotic regimen should be changed. Student's *t*-test and Chi square were performed on the relevant data.

RESULTS

No significant differences were noted between the groups with respect to maternal age, parity, gestational age at time of delivery, body mass index and number of prior cesarean deliveries (Table 1). There was no significant difference between the groups with choices of pre-operative and post-operative antibiotic administration.

Mean estimated blood loss did not differ significantly between the group in which oxidized regenerated cellulose and the group in which it wasn't (803 ± 34 mL vs. 800 ± 0 mL, $p=0.32$). There were no significant differences between the groups with respect to preoperative white blood cell count, post-operative white blood cell count, preoperative hemoglobin and hematocrit and post-operative hemoglobin and hematocrit (Table 2). However, 13.0% of those in the group in which oxidized regenerated cellulose was used experienced post-operative fever versus 3.9% in the group in which it was not used. There were no cases of abscess formation.

DISCUSSION

Over the past decade, the use of hemostatic agents to control bleeding has increased significantly. These hemostatic agents can be divided into physical, absorbable, biologic and synthetic agents.⁸ Oxidized cellulose was first introduced in 1942⁹ and oxidized regenerated cellulose was launched in 1960. Oxidized regenerated cellulose is created by decomposing wood pulp and then regenerating the cellulose by manufacturing continuous cellulose fibers. This material has been branded as Surgicel[®] by Johnson & Johnson[®] and is used as a knitted fabric that can be cut to match the size of the area that needs hemostasis. Additionally, it does not stick to instruments, thus facilitating easier handling.

Table 1: Baseline Characteristics.

	Cellulose used (n=77)	Cellulose not used (n= 78)	p value
Age	31.4±6.4	30.6±5.7	0.46
Parity	1.2±1	1.0±1.0	0.23
Gestational Age	39±2.3	38.7±2.3	0.56
Body Mass Index	28.9±6.8	27.6±7.8	0.30
Number of prior cesarean deliveries			
0	30	35	0.46
1	30	28	0.16
2	10	12	0.67
3	5	3	0.46
4	2	0	0.15
Pre-operative antibiotics			
Cefazolin	72	73	0.98
Gentamycin/Clindamycin	5	3	0.46
Vancomycin	0	2	0.16
Post-operative antibiotics			
Cefazolin	70	73	0.53
Gentamycin/Clindamycin	5	3	0.46
Ampicillin/Gentamycin/Clindamycin	2	0	0.15
Vancomycin	0	2	0.16

Age, parity and gestational age are presented as mean±standard deviation. For number of prior cesarean deliveries and antibiotics, the number of patients per patient characteristic is indicated.

	Cellulose used (n= 77)	Cellulose used (n= 78)	p value
Pre-operative white blood cell count	10.4±3.5	10.8±3.5	0.35
Post-operative white blood cell count	13.8±4.9	14.0±4.2	0.72
Change between pre- and post-operative white blood count	3.5±4.0	3.3±3.3	0.65
Pre-operative hemoglobin	12.1±1.2	12.1±1.2	0.80
Post-operative hemoglobin	10.4±1.5	10.2±1.3	0.44
Change between pre- and post-operative hemoglobin	1.7±1.2	1.9±0.9	0.21
Pre-operative hematocrit	36.2±3.1	36.0±3.0	0.69
Post-operative hematocrit	31.6±4.0	30.9±3.4	0.22
Change between pre- and post-operative hematocrit	4.5±3.4	5.1±3.0	0.29
Incidence of post-operative fever	10 (13.0%)	3 (3.9%)	p<0.05

All above are expressed as mean±standard deviation with exception of incidence of post-operative fever which is expressed as number of patients (percentage).

This hemostatic agent is absorbable and belongs to the same category as gelatin thrombin matrix and microfibrillar collagen. It is not completely clear how oxidized regenerated cellulose but several mechanisms have been theorized. As oxidized regenerated cellulose has a low pH, it may cause red blood cell lysis which may trigger hematin formation thus accelerating clotting with the help of normal physiologic processes. However, the acidic nature of oxidized regenerated cellulose may increase inflammation in surrounding tissue and delay wound healing.¹⁰ Oxidized regenerated cellulose absorption typically lasts between two and six weeks but histologic evidence of oxidized cellulose fibers several years after cardiac surgery has been reported.¹¹ Research has been limited in regards to adverse effects of use of this agent but cases have been reported in which oxidized regenerated cellulose was used for hemorrhage control during thoractomy and the cellulose passed through the intervertebral foramen and caused cord compression.¹² No study till now has evaluated the use of oxidized regenerated cellulose in obstetric surgery.

In this study, it was found that the routine use of oxidized regenerated cellulose as a means to prevent hemorrhage was associated with a significantly increased incidence of post-operative fever without significantly attenuating the decrease in hemoglobin and hematocrit that occurs before and after surgery. There were no cases of abscess formation. Given the increase in incidence of post-operative fever, it was expected that there would be an association between use of oxidized regenerated cellulose and increase in white blood cell count before and after surgery. However, it was found that use of oxidized regenerated cellulose did not significantly elevate the increase in white blood cell count that occurs before and after surgery when compared to when oxidized regenerated cellulose wasn't used. Additionally, it was felt that in those instances in which oxidized regenerated cellulose was used and in which post-operative fever occurred that the fever was most likely attributed to use of the hemostatic agent as all other sources of post-operative fever were reliably ruled out. These other sources included deep venous thrombosis, pneumonia, urinary tract infection, mastitis and wound infection and were ruled out on the basis of unremarkable physical exam and imaging findings and negative blood and urine cultures.

There are weaknesses to this study. The retrospective nature and the small sample size diminishes the ability of these results to be generalized. Future directions for the research question at hand would be to perform a randomized, controlled study and to assess for incidence of post-operative fevers between the two groups in the absence of administration of post-operative antibiotics. Administration of post-operative antibiotics is a practice not performed at many institutions. Additionally, this study design would allow one to further clarify the relationship, if one does exist, between abscess formation and routine use of oxidized regenerated cellulose at the time of obstetric surgery and to truly elucidate a source, if any, for the increased incidence in post-operative fever that could have been masked by routine administration of antibiotics post-operatively in our institution. This is of critical importance, from a cost standpoint, as detection of post-operative fevers may trigger additional tests such as performance of chest x-rays, lower extremity Doppler and blood and urine cultures.

Nonetheless, this study does present data indicating that routine use of oxidized regenerated cellulose does not significantly attenuate the decrease in hemoglobin and hematocrit that occurs before and after surgery. Furthermore, routine use of oxidized regenerated cellulose at the time of cesarean delivery may be associated with an increased incidence of post-operative fever.

CONFLICTS OF INTEREST

The author has no conflict of interests to declare.

ETHICAL CONSIDERATION

Ethical approval was obtained for this retrospective chart review from the Institutional Review Board at Hofstra University–Northwell Health System–Staten Island University Hospital.

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