



Case Report

Uses of FloSeal[®] in obstetric hemorrhage: Case series and literature reviewJacqueline Pui-Wah Chung^{*}, Tak-Yeung Leung

Department of Obstetrics and Gynecology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, N. T., Hong Kong

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ABSTRACT

Objective: FloSeal[®] has been shown to be an alternative and effective method of hemostasis. The current study examines the various uses of FloSeal[®] in obstetric hemorrhage and gives an overview of the literature.

Case reports: In this retrospective case review, a total of 11 cases with obstetric hemorrhage were reviewed throughout a period of one year. All but one case was successful in using FloSeal[®] in arresting the bleeding with hysterectomy avoided. FloSeal[®] can be considered when bleeding occurs locally at the placental bed, bladder base, adhesiolysis site, vaginal tears or at suture holes.

Conclusion: FloSeal[®] was a quick and effective alternative for hemostasis and should be considered when conventional hemostatic techniques fails or is impractical.

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Introduction

Obstetric hemorrhage remains a leading cause for maternal mortality. It can be caused by uterine atony, genital tract laceration, uterine rupture, abnormal placentation, infection, or coagulation defects. Majority of the cases occurs during the postpartum period and during caesarean section. A variety of methods have been employed in dealing with obstetric hemorrhage including uterotonic drugs like oxytocin or prostaglandins, hemostatic sutures like B-lynch sutures, balloon tamponade, ligation of selective vasculature, embolization of the uterine arteries or hysterectomy as ultimate life-saving procedure [1]. However, up to 50% of the cases of peri-partum hysterectomy can, in fact, be avoidable [2].

The use of topical hemostatic agents has been recently widely employed in different specialties including urology, neurosurgery, otorhinolaryngology, orthopedics and traumatology and recently in gynecology [3]. FloSeal[®] hemostatic matrix (Baxter, Deerfield, IL) has been shown to be an alternative and effective method of hemostasis [4–7]. Our unit reported a case report of using FloSeal[®] in controlling bleeding at the placental site due to placenta praevia previously [8]. Yet, since then, the use of FloSeal[®] in obstetric cases in the literature remains limited.

In this paper, we would like to report a case series of our experience on the use of FloSeal[®] in arresting obstetric hemorrhage in different clinical scenarios. A review of the current literature was also performed.

Case reports

We report a retrospective case series carried out in a university affiliated tertiary hospital in Hong Kong throughout August 2015 to August 2016. All women with the use of FloSeal[®] attempted in arresting the obstetric hemorrhage within the study period were retrieved. The medical notes of these patients were reviewed manually in details. All the basic clinical characteristics of the patients including demographic data, obstetric history, operation record, blood loss, hemostatic interventions and treatment outcome were obtained.

FloSeal[®] matrix was only available as a 5 ml product in Hong Kong. The kit consists of a bovine-derived gelatin matrix component, a human-derived thrombin component, applicator tips and mixing accessories (including a syringe with connector, a thrombin bowl, a pre-filled sodium chloride solution syringe and a vial adapter for needle-free reconstitution). The product was prepared each time according to the manufacturer's instruction to add the thrombin solution into the gelatin matrix before its use [9]. The two substances were mixed thoroughly together by pushing the plungers of the syringes back and forth for at least 20 times to produce a viscous hemostatic gel. The mixing procedure took

^{*} Corresponding author. 1/F, Block E, Special Block, Prince of Wales Hospital, Shatin, N. T., Hong Kong. Fax: +852 2636 0008.

E-mail address: jacquelinechung@cuhk.edu.hk (J.P.-W. Chung).

2 min. Before the application, the bleeding site was cleared with suction catheter and the gel was dispensed directly to the bleeding site and pressure was applied using moist gauze to keep the FloSeal® gel in place as shown by us previously [8]. Hemostasis was checked after at least 2 min after the application. In case bleeding continues, additional FloSeal® may be re-applied or further surgical intervention was considered if it failed.

We attempted to arrest obstetric hemorrhage with FloSeal® in a total of 11 cases during the study period. A summary of each case

and the reason why FloSeal® was used has been provided in Table 1. All but one case was successful in using FloSeal® in arresting the bleeding without the need for hysterectomy.

Up to half of the cases attempting the use of FloSeal® was due to bleeding at the placental bed, followed by local bleeding at the raw areas of the vaginal tear or vault, bladder base, adhesiolysis site and suture holes. The average blood loss was 3200 ml. Eighty two percent of the cases required blood transfusion. Case 11 had documented disseminated intravascular coagulopathy and case

Table 1

Clinical summary of the patients with the use of FloSeal® in arresting bleeding.

Case	Age	Parity	Gestation (weeks)	Mode of delivery	Case scenario	Hemostatic methods used	Reason for FloSeal® use	Successful?	Blood transfusion required?	Total blood loss (ml)
1	33	G2P1	38	Elective LSCS	Previous CS, refuse TOS Dense adhesion encountered intraoperatively	40 units syntocinon infusion Hemostatic stitches	Continuous bleeding over uterine serosa after adhesiolysis	Yes	No	500
2	29	G1P0	37	Elective LSCS	Type III placenta praevia with antepartum hemorrhage	40 units syntocinon infusion Carboprost injection Vertical compression sutures	Persistent bleeding from lower segment	Yes	No	600
3	38	G1P0	38	Elective LSCS	Type III placenta praevia	40 unit syntocinon infusion, hemostatic stitches	Persistent bleeding over placental bed despite hemostatic sutures	Yes	Yes 1 u PC	1200
4	38	G1P0	36	Emergency LSCS	Severe pre-eclampsia Uterine atony and bleeding from bladder base	40 unit syntocinon infusion, PR 1 mg cytotec Carboprost injection B-lymph sutures	Persistent bleeding over bladder base	Yes	Yes 4 u PC 4 u FFP 4 u platelets	1800
5	34	G2P0 ⁺¹	35	Emergency LSCS	Type II placenta praevia with antepartum hemorrhage	40 units syntocinon infusion, carboprost injection Compression sutures	Persistent bleeding from placental bed	Yes	Yes 2 u PC	2100
6	31	G1P0	30	NSD	MCDA twins (with one twin IUD at 22 weeks) preterm vaginal delivery PPH due to bleeding from vaginal tear	Hemostatic stitches	Persistent bleeding from raw area of vaginal tear	Yes	Yes 4 u PC 3 u FFP 3 u platelets	2500
7	40	G4P0 ⁺³	35	Emergency LSCS	Type III placenta praevia with antepartum hemorrhage	40 units syntocinon infusion, hemostatic stitches, carboprost injection	Persistent bleeding at placental base, morbid adhesion of placenta with 3 × 2 cm placenta left in-situ	Yes	Yes, 4 u PC 4 u FFP 3 u platelets	3100
8	36	G2P1	37	Elective classical CS	Previous history of classical CS due to large 12 cm lower segment fibroid	40 unit syntocinon infusion, carboprost injection	Persistent bleeding over hemostatic stitch holes	Yes	Yes 5 u PC 4 u FFP 4 u platelets	3500
9	32	G3P0 ⁺²	40	Emergency LSCS	Known thrombocytopenia (platelet 83) Failed IOL	Hemostatic stitches	Persistent bleeding at placental bed	Yes	Yes 4 u PC 4 u FFP 8 u platelets	3900
10	29	G1P0	38	Emergency LSCS	Abruptio placentae with antepartum hemorrhage, ruptured 4 cm left ovarian cyst intraoperatively	40 unit syntocinon infusion Hemostatic stitches	Ruptured endometriotic cyst during manipulation with active bleeding at ovarian base uncontrolled by hemostatic stitches	Yes	Yes 4 u PC 4 u FFP 4 u platelets	4000
11	35	G3P2	37	NSD	Extensive tear from vagina to broad ligament with hematoma and uterine atony	40 units syntocinon infusion, carboprost injection Gelfoam Surgicel® Adrenaline gauze B-lymph sutures TAH	Bleeding over vaginal tear and vaginal vault	No	Yes 34 u PC 27 u FFP 26 u platelets 14 u cryo-ppt	12,000

CS = caesarean section, cryo-ppt = cryoprecipitate, FFP = fresh frozen plasma, IOL = induction of labor, IUD = intrauterine death, LSCS = lower-segment caesarean section, MCDA = monochorionic diamniotic, NSD = normal spontaneous delivery, PC = packed cell, PR = per-rectal, TAH = total abdominal hysterectomy, TOS = trial of scar.

four, eight and 11 required monitoring in the intensive care unit post-operatively. Syntocinon infusion (40 units) was usually the first-line treatment, then carboprost injection either intramuscularly or intramyometrially and followed by hemostatic sutures. All of the cases only required the use of one vial of 5 ml FloSeal® for hemostasis. There were no major complications in terms of allergic reaction, infection, bowel obstruction or thromboembolism from the use of FloSeal®. All of the patients were well during the six weeks postnatal follow-up except for case six who is still under follow-up due to her placenta in-situ.

Discussion

Obstetric hemorrhage remains a challenging condition to obstetricians, especially during caesarean section. Various strategies have been employed in dealing with active bleeding from the placental bed including the use of hemostatic sutures, balloon tamponade or a combined 'uterine sandwich' technique [8]. Preserving the uterus is important especially in those with future fertility wish.

In our paper, we reviewed the different uses of FloSeal® in our obstetric cases and all but one case had the bleeding can be arrested almost instantly with no further intervention required. FloSeal® has been marketed as a surgical device indicated in surgical procedures, apart from ophthalmic surgeries, as an adjunct for hemostasis when sutures or conventional methods has been proven ineffective or impractical [9]. It consists of a bovine-derived gelatin matrix component, a human-derived thrombin component. It is biocompatible and is reabsorbed within six to eight weeks, which is consistent with normal wound healing [10].

The prepared product may be used up to 8 h after mixing with the thrombin solution. It comes with an applicator to facilitate application over the bleeding site and in laparoscopic cases, a longer laparoscopic applicator can be used. After the applying to the bleeding site, the special particles of the FloSeal® Matrix will swell approximately 10–20% upon contact of blood and provides additional compression effect [10]. The maximum swell volume is achieved within 10 min. It also conforms to irregular wound surfaces and thus is ideal for areas where it may be difficult to apply sutures. Its action is quick and able to achieve bleeding within 2 min at the site of action. It works well in both wounds with

capillary oozing or arterial spurting. Its hemostatic action in arterial spurting wounds is better than traditional gelatin cellulose as it contains thrombin which converts fibrinogen into a stable fibrin clot. It must be remembered that FloSeal® should never be injected directly into vessels due to the risk of thromboembolism [10].

In cases where bleeding occurred at the placental bed (cases 3, 5, 7 & 9), there were persistent oozing despite multiple attempts of hemostatic sutures, and thus FloSeal® was decided. While waiting for the nurse to prepare the FloSeal® for use, the oozing was controlled by manual pressure using a gauze, or by pressing the anterior and posterior uterine wall against each other. Once the FloSeal® is ready for application, manual compression was released so that FloSeal® was applied over the placental bed immediately. The oozing area was then compressed manually as before for a few minutes, to allow the hemostatic action of FloSeal® to take place as described previously [reference 8, see video 2: <http://links.lww.com/AOG/A184>]. Hemostasis was achieved in minutes [reference 8, see video 3: <http://links.lww.com/AOG/A185>]. In case 11, there was active oozing over the raw area of the vaginal tear after delivery and FloSeal® was attempted after Surgicel® and adrenaline gauze compression failed. However, in view of persistent uterine atony despite multiple medication and B-lynch sutures, caesarean hysterectomy was decided. There was again bleeding from the vaginal vault after hysterectomy in which the remaining FloSeal® was used and hemostasis was achieved.

Reported uses of FloSeal® in obstetric cases in the literature are shown in Table 2. Apart from using FloSeal® where there is continuous oozing from the placental bed as we have reported before, we suggest FloSeal® can be considered when bleeding occurs locally over the bladder base, raw areas over adhesiolysis site, suture holes or vaginal tears where hemostatic stitches have failed or is difficult to apply. In such situation, it is wise to apply adequate FloSeal® directly over the site of site of active bleeding. A moist wet gauze should be used for gentle approximation to allow the FloSeal® to act. After 2 min, the bleeding site should be inspected. Once the bleeding has ceased, excess FloSeal® matrix, which is not incorporated into the hemostatic clot should be removed by gentle irrigation and not by physical manipulation. In cases of persistent local bleeding, reapplication of the FloSeal® matrix can be tried again. If still failed, other hemostatic method should be considered.

Table 2
Previous case reports in literature using FloSeal® in Obstetric cases.

Authors	Year	Age	Gestation (weeks)	Cause for bleeding	Mode of delivery	Hemostatic methods used	Reason for FloSeal® use	Successful?
Moriarty et al. [11]	2007	35	26 ⁺⁶	Placenta abruptio with uterine atony	Emergency CS	Syntocinon intravenous infusion Carboprost injection PR misoprostol, B-lynch suture Sengstaken balloon tamponade TAH Cell-saver Recombinant factor VII	Despite re-laparotomy and total abdominal hysterectomy difficulty with bleeding from vascular venous plexuses over the vault of vagina and oozing from suture holes	Yes
Law et al. [8]	2010	35	37	Type III Placenta praevia	Elective CS	Syntometrine syntocinon infusion Hemostatic sutures Conservative techniques	Persistent bleeding from placental bed despite hemostatic sutures	Yes
Wohlmuth et al. [12]	2011	28	Unknown	Complete placenta praevia	Elective CS		Profuse bleeding occurred over the placental implantation site	Yes
Nandi et al. [10]	2012	32	Term	Two previous CS	Elective CS	Continuous pressure for 30 min, hemostatic sutures and diathermy	Constant diffuse bleeding from ends of ligated fibrous bands and around the closed uterine wound where bladder were initially adhered, failure to achieve hemostasis despite adopting hemostatic measures	Yes

CS = caesarean section, PR = per rectal, TAH = total abdominal hysterectomy.

Although the use of FloSeal® in pregnant woman is still unclear, increasing evidence of its use in postpartum hemorrhage seems promising. Of course, it should be remembered that the thrombin solution is made from human plasma and thus it may carry a risk of transmitting infectious agents, viruses, and Creutzfeldt-Jakob disease (CJD). Moreover, it should not be used in those with known allergic to bovine products and Factor V deficiency [9,10]. Further studies are required to explore its effectiveness in cases of disseminated intravascular coagulation which commonly occurs after postpartum hemorrhage. FloSeal® matrix may also serve as a nidus for infection and abscess formation and thus is contraindicated in cases with active infection. The cost of FloSeal® may also be another consideration. One vial of 5 ml FloSeal® costs USD\$260 around but it is considered to be less expensive than the use of recombinant factor VII or uterine artery embolization.

Apart from its use in the obstetrics, further studies are required to explore its use in gynecology. There is increasing evidence with using FloSeal® as an alternative hemostatic agent during laparoscopic ovarian cystectomies [13]. In case 10, there was active oozing at the ovarian base despite hemostatic suturing and the use of FloSeal® saved her ovary. Moreover, FloSeal® has also been attempted during the transabdominal repair of supra-trigonal and complex vesico-vaginal fistulas [14] and also after laparoscopic salpingostomies [15].

Conclusion

In conclusion, we believe FloSeal® should be considered in arresting obstetric hemorrhage especially in those cases with active bleeding occurring locally at the placental bed, bladder or ovarian base, suture holes or areas where conventional surgical hemostatic techniques rendered impractical or ineffective. Further studies are required to determine the use to ensure the safety of gelatin-thrombin matrix and explore its use in the field of Obstetrics and Gynecology.

Conflicts of interest

The authors have no conflict of interest relevant to this article.

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