OBSTETRICS

Uterine packing with chitosan-covered gauze for control of postpartum hemorrhage

Bernd C. Schmid, MD; Günther A. Rezniczek, PhD; Norbert Rolf, MD; George Saade, MD; Gerhard Gebauer, MD; Holger Maul, MD

OBJECTIVE: To describe the use of gauze covered with chitosan, a potent hemostatic agent derived from chitin, in the treatment of postpartum hemorrhage (PPH).

STUDY DESIGN: Patients suffering from postpartum hemorrhage were treated by uterine packing with chitosan-covered gauze, either through the hysterotomy in case of cesarean delivery or transvaginally, for up to 24 hours.

RESULTS: Chitosan-covered gauze was used in 19 cases of postpartum hemorrhage due to uterine atony, placenta accreta/increta, or anticoagulation, including 5 severe cases where a hysterectomy seemed inevitable otherwise. In all but one case, the bleeding stopped and further interventions were avoided. Over comparable periods of time (18 months) and births (3822 vs 4077) before and after the introduction of the chitosan gauze in our clinic, the rate of peripartum hysterectomies was reduced by 75% (8 vs 2; odds ratio, 4.27; $P = .044$).

CONCLUSION: Chitosan-covered gauze is a viable option in the treatment of (severe) postpartum hemorrhage. It is easy to use and requires no special training. It can be used after both vaginal and cesarean deliveries, and there are no adverse side effects. Furthermore, it is very inexpensive compared with other treatment options, making it suitable for use also in low resource-countries, where the death toll due to postpartum hemorrhage is especially high.

Key words: chitosan, postpartum hemorrhage, utero-vaginal packing

Cite this article as: Schmid BC, Rezniczek GA, Rolf N, et al. Uterine packing with chitosan-covered gauze for control of postpartum hemorrhage Am J Obstet Gynecol 2013;209:225.e1-5.

Obstetric hemorrhage is the leading cause of maternal mortality, accounting for approximately 25% of the more than 500,000 pregnancy-related deaths worldwide in 2000.[1] The most common type of obstetric hemorrhage is postpartum hemorrhage (PPH), which accounts for the majority of the 14 million cases of obstetric hemorrhage that occur each year[1] and is mostly caused by uterine atony. Management of PPH resulting from uterine atony includes the administration of uterotonics, selective devascularization (either by angiographic embolization or suture ligation), the application of uterine compression sutures, and intrauterine packing. In cases of severe PPH, a hysterectomy remains the last option if conservative treatments fail.[2] Recently, the rate of peripartum hysterectomy has increased considerably.[3] Because it is associated with substantial maternal morbidity and results in the loss of fertility, avoiding peripartum hysterectomy improves patient safety and quality of care.[4] Although the control of PPH by uterine packing is not new,[5] the addition of a local hemostatic agent to the packing may improve the control of the bleeding and allows uterotonics more time to take action.[6] The need for hemostasis on the battlefield, where hemorrhage remains the leading cause of mortality, led to the development of chitosan as a hemostatic substance.[7-8] Chitosan, a hydrophilic biopolymer obtained through the deacetylation of chitin (a major component of crustacean shells such as from crab or shrimp)[9] was found to exhibit excellent hemostatic properties. Electrostatic interaction between chitosan and the cell membranes of erythrocytes leads to coagulation of blood independent of the classical clotting cascade, and thus works under hypothermic conditions and even in the presence of heparin. This interaction is not exothermic and thus does not burn or alter the tissue surface in other ways. Furthermore, chitosan is fully biologically degradable and additionally exhibits antibacterial properties, likely reducing the risk of infection.[8,10-12] In this study, we describe a case series of PPH successfully treated through the application of commercially available chitosan-covered gauze.

From the Departments of Obstetrics and Gynecology (Drs Schmid, Gebauer, and Maul) and Anesthesiology (Dr Rolf), Marienkrankenhaus Hamburg, Hamburg, and the Department of Obstetrics and Gynecology (Dr Rezniczek), Ruhr-Universität Bochum (Marienhospital Herne), Herne, Germany, and the Department of Obstetrics and Gynecology (Dr Saade), The University of Texas Medical Branch, Galveston, TX.

Received Nov. 30, 2012; revised Jan. 30, 2013; accepted May 28, 2013.

The authors report no conflict of interest.

Reprints will not be available.

0002-9378/$36.00

http://dx.doi.org/10.1016/j.ajog.2013.05.055

Materials and Methods

Between May 2011 and November 2012, 19 patients were treated with chitosan-covered gauze at the Marienkrankenhaus Hamburg. Patients delivering spontaneously or by cesarean and experiencing persistent bleeding despite uterotonic medication and/or curettage were candidates for treatment with chitosan-covered gauze (CELOX Gauze; Medtrade Products

Ltd., Crewe, UK). CELOX is a CE marked class III medical device in the EU and is FDA approved for bleeding control. One complete gauze (3 meters long) was used for each patient with 1 exception where it was shortened to about half (case 7). All cases were managed by an experienced senior obstetrician, and the head of department was informed before the use of chitosan and/or the decision to perform a hysterectomy. In case of cesarean deliveries, the uterine cavity was packed with the gauze through the hysterotomy, with 1 end of the gauze passed through the cervix into the vagina for subsequent removal. In case of spontaneous deliveries, the gauze was inserted through the vagina and the uterus was compressed bimanually for several minutes. The gauze was usually removed after 24 hours by simply pulling the end left in the vagina. Treatment with sulprostone was continued during this time. Patient and treatment details are listed in Table 1. All patients gave written consent for inclusion of their case data in this report.

Results

Chitosan-covered gauze was used in 19 consecutive cases of PPH (Table 1). Patients were 21-42 years old (median, 35), gravida 1-5 (median, 2), and para 0-3 (median, 1). Delivery was vaginal (8 cases) or through cesarean section (11 cases). Uterine atony was the cause of PPH in 13 cases (1, 3, 6, 9, 10, 12-19). In 3 cases, PPH was caused by placenta percreta (case 4), increta (case 7), or accreta (case 8). In 1 case (2), the reasons were initially unknown. In 2 cases, bleeding occurred 11 days (case 5) and 6 weeks (case 11) after delivery because of a high dose of low molecular weight heparin and curettage to remove placental residues, respectively. Patients received 10 or more units of packaged red blood cells in 5 cases, and less (2-4 units) in 7 cases. In the other cases, no blood transfusions were necessary. After delivery, all patients prophylactically received 3 international units of oxytocin to prevent uterine atony. In each case, a total dose of 40 units of oxytocin was administered as a first measure, which was unsuccessful in stopping the bleeding. Second line measures varied from case to case depending on the treating physician and suspected cause of PPH and included sulprostone infusion (500 μg/h), curettage, bimanual compression, B-Lynch sutures and/or Pereira stitches (Table 1). Tight uterine packing with chitosan-covered gauze was performed in all cases, either through the hysterotomy in the case of cesarean delivery (regularly followed by B-Lynch sutures) or transvaginally in the case of vaginal delivery, leaving one end of the gauze in the vagina; we found that 1 full length gauze (3 m) is adequate. In one case (2), indications of severe bleeding persisted after application of the gauze. A laparotomy revealed that rupture of the lateral posterior uterine wall had occurred, causing severe bleeding into the abdominal cavity, and because of wide lacerations it was decided to perform a hysterectomy. This patient had undergone 2 prior abortions that were not disclosed initially. In all other cases bleeding had stopped immediately after the application of the chitosan-covered gauze, which usually remained in the uterus for a maximum of 24 hours (>30 hours in cases, 1 and 3). During this time, patients were monitored in our intensive care unit, and treatment with uterotonics (sulprostone, 500 μg) was continued. All patients also received broad-spectrum antibiotics. Serum levels of C-reactive protein increased in all women, some beyond the upper detection limit. Both patients in whom the gauze had been left for >30 hours showed rising levels of procalcitonin. However, none of the patients showed any clinical signs of sepsis. Nevertheless, the treatment regime was changed to leaving the gauze for a maximum of 24 hours and to remove it as soon as clinically feasibly. In one case (9), the patient developed high postoperative fever (39-8°C) and the chitosan gauze was removed 7 hours after application, after which the fever subsided. Bleeding did not recur in any of the patients. Two patients (cases 7 and 14) presented with persistent spotting 3 months and 6 weeks postoperatively, respectively, which was attributed to residual chitosan gauze that was identified and removed with hysteroscopy, followed by uterine curettage. One patient (case 14) suffered from a lung edema as a complication, likely as a consequence of mass transfusion.

Figure 1 shows the number of births and PPH-related hysterectomies in our clinic over 18 months before (3822) and 18 months after (4077) the introduction of use of chitosan-covered gauze in the management of PPH. One of the 2 cases where a hysterectomy was performed after introduction of the gauze is described in this report (case 2); in the other case chitosan-covered gauze was not used. Up to the end of the observation period there had been no cases of peripartum hysterectomies for 1 year. Thus, the rate of peripartum hysterectomies was reduced by 75% (8 vs 2; odds ratio, 4.27; Fisher exact text, 1 tailed $P = .044$).

Comment

PPH is a major health problem worldwide, and effective options for prevention or treatment can have significant impact on maternal mortality and morbidity. It is difficult to design randomized controlled trials on the management of potentially life-threatening PPH because the endpoint hysterectomy and/or excessive blood loss in such a trial would be unethical. Therefore, case series are important. In this study, we describe the use of chitosan-covered gauze in the treatment of a series of cases of PPH where in some severe cases a hysterectomy as the ultimate option was considered. In all but 1 case, uterine bleeding stopped immediately after intrauterine application of the gauze and compression for 1-2 minutes. Combination with B-Lynch sutures or Pereira stitches remained possible. The gauze was also used after vaginal birth and it was found that transvaginal insertion is also effective and that uterine compression sutures are not required for successful treatment. Chitosan-covered gauze is available as various brands from several manufacturers, differing in size and specific composition of the hemostatic agent. In one product, the whole gauze is made of chitosan. The decision to use the CELOX brand in this study was based on the physical format of the gauze (3 m long) and available