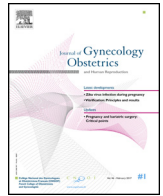




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Case Report

Uses of chitosan for treating different forms of serious obstetrics hemorrhages



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ARTICLE INFO

Historique de l'article :

Received 23 October 2016
 Received in revised form 2 August 2017
 Accepted 18 August 2017
 Available online 31 August 2017

Keywords:

Chitosan
 Postpartum hemorrhage
 Uterovaginal packing

ABSTRACT

Postpartum hemorrhage is a major cause of maternal death worldwide. Many therapeutic strategies have been developed to reduce maternal morbidity and mortality like oxytocin, prostaglandin, and uterine balloons. A new member of the therapeutic arsenal has recently emerged, the chitosan (Celox[®]), used since several years by military doctors to stop bleeding of combat wounds. In 2012, a first study was reported with the successful use of chitosan-coated gauze to treat severe postpartum hemorrhage. We report here four cases of the use of chitosan to treat life-threatening obstetric bleeding. In the first case, a pelvic packing with chitosan gauze after hemostatic hysterectomy with persistent bleeding. In the second case, the use of chitosan powder in a case of severe bleeding from multiple vaginal tears. In the third case, the use of chitosan gauze in uterine packing for postpartum hemorrhage by atonia. In the fourth case, the use of chitosan powder for stop bleeding during a hemorrhagic cesarean section. Postpartum hemorrhage of uterine origin resistant to treatment with prostaglandins can be treated with chitosan-coated gauze. This treatment requires no training and its costs are one fifth those of a Bakri[®] intrauterine balloon. Using these two forms of chitosan, powder and gauze, we have a new therapeutic method at our disposal for dealing with the most serious cases of bleeding.

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Introduction

Postpartum hemorrhage (PPH) is a major cause of maternal death worldwide, causing about 127,000 deaths per year [1]. The WHO defines PPH as the loss of more than 500 mL of blood for a vaginal delivery, and more than 1000 mL of blood after cesarean section, in the first 24 hours after delivery. Many therapeutic strategies have been developed to reduce maternal morbidity and mortality and to avoid the need for radical and invasive procedures, such as hysterectomy. Treatments include oxytocin, prostaglandin analogs, and ergot derivatives. In addition to pharmacological treatments, uterine packing techniques, such as Bakri[®] balloons, are used. A new member of the therapeutic arsenal has recently emerged – chitosan (Celox[®]) – used in two principal forms as a hemostatic agent: a powder and a hemostatic gauze. This product has been used for several years by military doctors, to stop the bleeding of combat wounds. In 2012 and 2013,

Schmid et al. reported the first case of the successful use of chitosan-coated gauze to treat severe PPH [2,3].

We report here four cases of the use of chitosan to treat life-threatening obstetric bleeding.

Clinical case 1: pelvic packing with chitosan hemostatic gauze after cesarean section

Mrs. B. was 35 years old and in her 10th pregnancy. She already had seven live-born children, four of whom were delivered by cesarean section. The monitoring of her pregnancy was poor, with only one ultrasound scan, yielding normal results, at 36 weeks of gestation. This patient presented at the emergency room in early labor at 37 weeks + 4 days of gestation. Hemostasis results were normal and hemoglobin concentration was 10.5 g/100 mL. An emergency cesarean section was performed, resulting after delivery, in the discovery of placenta accreta. The patient displayed extensive bleeding (2,3 liters) and hemodynamic instability, necessitating hysterectomy. Despite the transfusion of 4 packed red blood cells and 4 fresh frozen plasma, the patient continued to bleed from the edge of the cervix and a layer within the pelvic cavity. The bleeding was not stopped by hemostatic sutures, or by the compression of this pelvis displaying multiple adhesions with surgical sheets, and the patient's hemodynamic status worsened. We, therefore, decided to attempt the packing of the pelvic cavity

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with chitosan-coated gauze. The bleeding stopped completely, within five minutes. The gauze was left in place and the wall of the cavity was closed. Postoperative hemoglobin concentration was 4.5 g/100 mL, and the patient presented major hemostatic problems (Quick test 25%, platelet count 24,000/mm³). She received six units of packed red blood cells and four of fresh frozen plasma. The gauze was removed, without difficulty, during a surgical intervention two days later. We observed no specific inflammatory response to contact with the gauze. The biological and clinical progression of the patient was satisfactory, with normal coagulation tests after 24 hours, and she was released from hospital seven days after surgery, following an abdominopelvic CT scan revealing an absence of abnormalities.

Clinical case 2: use of chitosan powder in a case of severe bleeding from multiple vaginal tears

Mrs D. was a young patient (18 years old) in her first pregnancy, with no particular medical or surgical antecedents. Her pregnancy had been monitored correctly and the various obstetric scans were all normal. She presented with preeclampsia in late pregnancy, for which labor was triggered with misoprostol.

Hemoglobin concentration at admission was 11.3 g/100 mL. The patient was treated with a combination of urapidil and magnesium sulfate, due to a worsening of the clinical signs of preeclampsia during labor. During the second stage of labor, the fetus presented an abnormal heart rate, prompting vacuum extraction through the pelvis. Delivery was aided by the intravenous injection of 5 IU of oxytocin during clearance of the shoulders. The placenta was considered to be complete on examination. The immediate postpartum period was normal, but the patient displayed heavy bleeding 2 hours later. We estimated that she had lost more than 2 liters of blood and her hemoglobin concentration fell to 5.7 g/100 mL. A uterine examination was performed under general anesthesia, leading to the removal of an abnormal cotyledon and numerous clots.

Examination of the birth canal revealed several vaginal tears that were bleeding heavily. Hemostatic sutures and manual compression were insufficient to stop the bleeding. Biological tests revealed a hemoglobin concentration of 4.2 g/100 mL and disturbed hemostasis. The patient presented hemodynamic instability with low blood pressure, requiring the transfusion of three units of packed red blood cells and two of fresh frozen plasma. Given the persistent bleeding, chitosan powder was applied to the hemorrhagic vaginal tears, which were then subjected to compression with gauze for five minutes. No further vaginal bleeding was observed after removal of the gauze and hemostatic tests were normal after 2 days. The patient was able to leave the hospital five days later, and vaginal examination showed good healing with no signs of an inflammatory reaction to chitosan. To our knowledge, this is the first case of the use of powdered chitosan on multiple vaginal lesions in context of PPH.

Clinical case 3: uterovaginal packing for PPH

Mrs. P., 25 years of age, fourth pregnancy, with three previous live births and no particular medical or surgical antecedents, presented with spontaneous labor at 40 weeks + 2 days of gestation. Labor was normal, with the spontaneous delivery of the baby and the delivery was aided by the intravenous injection of 10 IU oxytocin.

The patient then displayed abnormal bleeding, with an estimated blood loss of 800 mL. A uterine examination was carried out, including the birth canal and the cervix, and no abnormalities were found.

The bleeding persisted and the patient received another injection of 10 IU oxytocin and a perfusion of one ampoule of sulprostone over the course of an hour. Despite this treatment, the patient continued to bleed heavily, due to uterine atonia. We decided to pack the uterus with chitosan-coated gauze. We introduced the gauze with a clamp inside the uterine cavity. The bleeding stopped immediately. The patient had a hemoglobin concentration of 11.5 g/100 mL on admission, and of 8.6 g/100 mL after the bleeding was stopped. Her total blood loss was estimated at 1.2 L. The gauze was removed the day after delivery, by simply pulling it out of the uterine cavity. The postpartum period was otherwise unremarkable.

Clinical case 4: use of chitosan powder during an hemorrhagic cesarean section

Mrs S., 43 years old, 4 previous cesarean section, current cesarean section planned at forty weeks of gestation.

After a transversal skin and transrectal incision, it has been seen that the anterior uterine wall is welded to the posterior abdominal wall. The careful dissection of the inferior segment will be limited to our needs for a safe delivery. After the fetal extraction, hysterotomy is sewed with stitches. At that time, we were facing a diffuse hemorrhage from the anterior face of the uterus, and we failed to stop it with stitches or electrocoagulation. The total blood loss was estimated at 1,8 liter. It was decided to use chitosan powder, which ends the bleeding after few seconds. Excess powder will be removed with a cautious aspiration. After few minutes, we decided to close abdominal incision without difficulty.

Discussion

Chitosan is a hydrophilic biopolymer obtained by the chemical deacetylation of chitin, the principal component of crustacean shells. Its hemostatic mode of action is independent of the coagulation cascade. Its effects are due to electrostatic interactions with red blood cell membranes [4]. Chitosan coagulates blood, even in the presence of heparin, and has antibacterial properties, reducing the risk of infection [5,6]. It is used by the British and American armies to achieve rapid and efficient hemostasis in the battlefield, mostly to control bleeding due to bullet wounds. Chitosan exists in three forms: granules, gauze, and nasal plugs.

Most studies evaluating the hemostatic activity of chitosan have been carried out on laboratory animals and have yielded spectacular results [7,8]. The few studies performed on humans essentially concerned military personnel in war zones [9–11]. The rapid hemostatic action of chitosan considerably reduces bleeding, facilitating the transport of the wounded to the operating theatre. The largest series of traumatic injuries in civilians treated with chitosan was performed by Hatamabadi et al. It involved 160 patients and concluded that chitosan resulted in faster hemostatic control than a conventional compression bandage, with no adverse effects [12]. Other uses are being developed, including the maintenance of hemostasis during surgery [13] or the prevention of recalcitrant epistaxis [14].

Only one group has evaluated a hemostatic chitosan dressing for PPH [3]. The group of Schmid et al. obtained good results for uterovaginal packing with chitosan in 18 of 19 cases. The rate of hysterectomy in this department has decreased by 75% in 18 months (OR 4.27; *P* = 0.044).

PPH of uterine origin resistant to treatment with prostaglandins can be treated with chitosan-coated gauze. This treatment requires no training and its costs are one fifth those of a Bakri[®] intrauterine balloon (50 euros/250 euros). We report here four types of life-threatening obstetric hemorrhage for which chitosan rapidly stopped the bleeding. Using these two forms — powder and gauze —, we have a new therapeutic arsenal at our disposal for

dealing with the most serious cases of bleeding. Chitosan-coated gauze could also be used to treat extensive vulvar hematomas, which are often difficult to treat surgically.

Conclusion

We report four cases of severe obstetric hemorrhage resolved by the use of chitosan. Chitosan thus constitutes a new alternative for the treatment of all forms of severe bleeding. It is inexpensive, its use requires no training, and could be made available in developing countries. Larger comparative studies are required to determine the place of chitosan treatment among the resources already at our disposal.

Disclosure of interest

The authors declare that they have no competing interest.

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