Q: Following cesarean delivery, what is the optimal oxytocin infusion duration to prevent postpartum bleeding?

A: High-reliability cesarean delivery requires a postoperative oxytocin infusion of 4 to 8 hours to reduce the risks of uterine atony and excessive postpartum bleeding

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CASE Discontinued oxytocin leads to postpartum hemorrhage

You have just completed a repeat cesarean delivery for a 41-year-old woman, now G2P2. You order an infusion of oxytocin, 20 U in 1 L lactated Ringer's solution, to run at a rate of 125 mL/hr for 8 hours. Without informing you, the recovery room nurse discontinues the bag with the oxytocin solution and starts an infusion of lactated Ringer's solution without oxytocin.

One hour later, you are called to the recovery room because your patient is having a postpartum hemorrhage (PPH). Physical examination shows that the uterus is boggy and above the level of the umbilicus. On bedside ultrasonography, the uterine cavity is demonstrated to contain minimal blood, and Doppler sonography does not demonstrate any vascular tissue within the uterine cavity. You diagnose uterine atony and initiate treatment. You massage the uterus, rapidly infuse 1 L crystalloid solution, place misoprostol 800 µg in the rectum, and reinitiate the oxytocin infusion. The uterine bleeding slows and then stops.

The following morning, the patient's hematocrit has decreased from a preoperative value of 37% to 21%.

Could this case of PPH have been prevented?

Instant Poll

How many hours following cesarean delivery do you think that an oxytocin infusion should be maintained to reduce the risk of uterine atony and postpartum hemorrhage?

If the patient is a Jehovah's Witness and refuses the transfusion of all blood products, how many hours following cesarean delivery do you think that an oxytocin infusion should be maintained to reduce the risk of uterine atony and postpartum hemorrhage?

Tell us—at **rbarbieri@frontlinemedcom.com**
Please include your name and city and state.

Cesarean delivery is one of the most commonly performed major operations in developed countries. More than 1,250,000 cesarean deliveries are performed annually in the United States. In 2012, there were 3,952,937 births and a cesarean delivery rate of 32.8%.[1] It is an important goal of obstetric care providers to continuously improve

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our approach to cesarean delivery in order to minimize the surgical risks of this procedure. Evidence-based, standardized protocols for cesarean delivery are critical to ensuring high-reliability surgical outcomes.

A key gap in cesarean delivery protocols is the lack of a nationwide, standardized approach to reducing the risk of postoperative bleeding by maintaining a continuous infusion of oxytocin in the hours immediately following cesarean delivery.

Oxytocin: A critical intervention to prevent PPH

More than half of all maternal deaths occur in the 24 hours following delivery, with the most common cause being PPH.[2] In addition to death, serious complications of PPH include coagulopathy, shock, emergency hysterectomy, transfusion complications, respiratory distress, and pituitary necrosis. Most cases of PPH that occur within 24 hours of delivery are caused by uterine atony.[3] Other causes include retained products of conception, placenta accreta, infection, coagulation defects, and amniotic fluid embolism.

Administering a uterotonic such as oxytocin at the time of delivery reduces the risk of PPH by approximately 66% and the risk of maternal blood transfusion by about 65%.[4] In order to prevent uterine atony and PPH, oxytocin should be routinely administered following birth of the baby or after delivery of the placenta. Appropriate doses following vaginal delivery are oxytocin 10 U administered intramuscularly or 10 U administered as a slow intravenous (IV) infusion.[5] The onset of action of oxytocin is approximately 2 to 5 minutes after an intramuscular dose and 1 minute after an IV dose.[6]

PHOTO: SHUTTERSTOCK

Oxytocin and cesarean delivery

Many clinical trials have reported that during a cesarean delivery, the routine administration of a uterotonic agent following birth of the baby reduces the risk of uterine atony and excessive bleeding. Three uterotonics: oxytocin, misoprostol, and carbetocin (a long-acting oxytocin analogue, see sidebar on page 14), have been reported to reduce the risk of excessive bleeding during cesarean delivery.[7] Oxytocin is the uterotonic most commonly used during cesarean delivery in developed countries.

In the United States, there is no standardized oxytocin regimen for prevention of uterine atony and hemorrhage at cesarean delivery. The most common regimen is to add 10–40 U of oxytocin in 1 L crystalloid solution and initiate the oxytocin infusion following delivery of the baby. Initially, the infusion is run at a rapid rate. Once the obstetrician reports that there is adequate uterine tone, the infusion rate is slowed to one that maintains uterine tone.

Some clinicians administer a single bolus of oxytocin following birth of the baby. However, a bolus of oxytocin commonly causes hypotension and, less commonly, ST segment changes on the electrocardiogram (EKG) suggestive of cardiac ischemia.[8–10] **Many experts recommend against administering one large bolus of oxytocin over a short period of time and favor a continuous infusion.**

At cesarean delivery, the minimum infusion rate of oxytocin that has been reported to avoid most cases of uterine atony, as reported by the obstetrician immediately following delivery, is approximately oxytocin 0.3 U/min.[11] Oxytocin infusion rates of 0.2 U/min and 0.1 U/min were associated with uterine atony rates of 21% and 40%, respectively. An infusion rate of oxytocin 0.3 U/min can be achieved by the administration of 20 U of oxytocin in 1 L crystalloid solution at a rate of 15 mL/min until uterine tone is achieved. The oxytocin

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Alternatives to oxytocin to prevent postpartum hemorrhage: Carbetocin, tranexamic acid, and nipple stimulation

Carbetocin

Oxytocin has a short half-life of 4 to 15 minutes.[1] Because of the short half-life, a single bolus of oxytocin has a limited duration of efficacy. Following the bolus, rapid clearance of oxytocin from the circulation can result in uterine atony and excessive bleeding. Therefore, a continuous oxytocin infusion is more likely to maintain uterine tone following cesarean delivery.

In Canada and the United Kingdom, carbetocin, a long-acting analogue of oxytocin, is available. Carbetocin has a half-life of 85 to 100 minutes.[2] A single bolus of carbetocin has a long duration of action, thereby maintaining uterine tone and preventing uterine atony.

In one randomized trial, 377 women undergoing a cesarean delivery were randomly assigned to a bolus of oxytocin (5 U administered intravenously over 30 to 60 seconds) or to a bolus of carbetocin (100 µg administered intravenously over 30 to 60 seconds).[3] In this study, uterine atony requiring additional uterotonic treatment occurred in 46% of the oxytocin group and 34% of the carbetocin group (P <.023). There was no difference in the rate of PPH between the two groups.

Carbetocin costs approximately $35 for the standard 100-µg dose, making it more expensive than oxytocin.

Tranexamic acid

Tranexamic acid is an antifibrinolytic drug that is approved by the US Food and Drug Administration for the treatment of heavy uterine bleeding[4] and for the treatment of hemophilia. Tranexamic acid is not an uterotonic agent; it prevents the degradation of a developing clot, thereby reducing bleeding. It is commonly used, off-label, for the treatment of massive hemorrhage caused by trauma or surgery.[5]

A few clinical trials have reported that, at cesarean delivery, IV administration of tranexamic acid (10 mg/kg of body weight) 10 minutes prior to the skin incision modestly reduced mean blood loss compared with a placebo infusion.[6–8] In two of these studies, tranexamic acid reduced mean blood loss by 63 mL[7] and 216 mL.[8] In these studies, oxytocin was administered to all the study participants.

One gram of tranexamic acid costs approximately $80.

Some experts are concerned that tranexamic acid may be associated with an increased risk of deep venous thrombosis (DVT). However, there is no strong evidence from large surgical trials that tranexamic acid causes a significant increase in postoperative DVT.[9]

Nipple stimulation

Nipple stimulation and suckling cause the release of oxytocin from the posterior pituitary and modestly increase uterine tone.[10] There are no clinical trial data demonstrating that nipple stimulation or suckling are superior to oxytocin administration for reducing the risk of postpartum hemorrhage following cesarean delivery. However, if a cesarean birth occurs in a setting where no uterotonic agent is available, it is advisable to initiate nipple stimulation or suckling as soon after birth as possible in order to stimulate the release of oxytocin and increase uterine tone.

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dose then can be titrated to maintain adequate uterine tone. Following completion of surgery, uterine tone can be maintained with a low-dose continuous infusion of oxytocin.

4- to 8-hour oxytocin rule

A key gap in our cesarean delivery protocols is a standardized recommendation concerning the duration of the oxytocin infusion following cesarean delivery. To my knowledge, no national organization has made a firm recommendation concerning the duration of oxytocin infusion following cesarean delivery.

One recent clinical trial studied PPH following cesarean delivery utilizing two oxytocin regimens: a bolus of oxytocin following delivery of the baby versus a bolus of oxytocin followed by a 4-hour IV infusion of oxytocin.[12] In this trial, 2,058 women undergoing a scheduled cesarean delivery with a singleton pregnancy were randomly assigned to an oxytocin bolus alone, oxytocin 5 U administered intravenously over 1 minute, or an oxytocin

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bolus *plus* a 4-hour oxytocin infusion at a rate of 10 U/hr. The 4-hour postoperative oxytocin infusion was formulated by adding 40 U of oxytocin to 500 mL saline and infusing the solution at 125 mL/hr, equivalent to 0.167 U of oxytocin per minute. In this trial, 65% of the women were undergoing a repeat cesarean delivery and 35% were undergoing a primary cesarean delivery.

The authors reported that women who received the oxytocin bolus alone were significantly more likely to be diagnosed with uterine atony requiring additional uterotonic treatment than women who received both the bolus and the 4-hour postoperative infusion (18.4% versus 12.2%, respectively; P <.001). There was no difference in the rate of PPH between the two groups.

The rate of PPH was 16% in women receiving an oxytocin bolus alone and 15.7% in women receiving both an oxytocin bolus and the continuous oxytocin infusion. However, among less experienced surgeons, the rate of PPH was significantly greater in the group that received the oxytocin bolus alone compared with the women receiving the bolus and continuous infusion (22.2% versus 17.3%, respectively). The authors concluded that obstetricians should consider using a 4-hour infusion of oxytocin following cesarean delivery to reduce the risk of uterine atony.

In a recent evidence-based review of optimal interventions in cesarean delivery, the authors recommended an IV infusion of 10 to 40 U of oxytocin administered over 4 to 8 hours after cesarean delivery.[7] Following cesarean, an IV infusion of crystalloid solution is typically maintained for at least 4 to 8 hours. Consequently, adding oxytocin (which costs approximately $1 for 10 units) to the crystalloid infusion does not add substantially to the cost of the patient's postoperative care and may reduce the risk of uterine atony and PPH.

My bottom-line recommendation. In the United States, we should adopt a policy of maintaining a continuous infusion of oxytocin for 4 to 8 hours following a cesarean delivery. Following a 4- to 8-hour rule will decrease the rate of uterine atony and excessive bleeding, thereby improving the safety of our cesarean delivery surgery.

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Correction: Reference citation, Editorial, March 2014

The following sentence on page 20, Volume 26, No. 3, should have been cited as follows: "When the uterus is too large for a standard approach, vaginal coring using a scalpel is often utilized (Video 2, page 11).[11]" The correct reference for citation is: 11. Wong WS, Lee TC, Lim CE. Novel vaginal "paper roll" uterine morcellation technique for removal of large (>50 gm) uterus. J Minim Invasive Gynecol. 2009;17(3):374–378.