Preventing Postpartum Hemorrhage: Managing the Third Stage of Labor

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Postpartum hemorrhage is a significant cause of maternal morbidity and mortality. Most postpartum hemorrhages are caused by uterine atony and occur in the immediate postpartum period. Expectant or physiologic management of the third stage of labor has been compared with active management in several studies. Active management involves administration of uterotonic medication after the delivery of the baby, early cord clamping and cutting, and controlled traction of the umbilical cord while awaiting placental separation and delivery. Good evidence shows that active management of the third stage of labor provides a better balance of benefits and harms and should be practiced routinely to decrease the risk of postpartum hemorrhage. Oxytocin, ergot alkaloids, and prostaglandins have been compared, as have timing and route of administration of these uterotonic medications. Oxytocin is the uterotonic agent of choice; it can be administered as 10 units intramuscularly or as 20 units diluted in 500 mL normal saline as an intravenous bolus, and can safely and effectively be given to the mother with the delivery of the baby or after the delivery of the placenta.
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The third stage of labor is the time from the delivery of the infant until delivery of the maternal placenta.[1] The natural course of this final stage of childbirth involves cessation of umbilical cord pulsation, separation of the placenta from the uterine wall, and passage of the placenta through the birth canal. Volume of blood loss depends on how long it takes the placenta to separate from the uterine wall and how effectively the uterine muscle contracts in the immediate postpartum period.

Incidence and Risk Factors

Postpartum hemorrhage occurs in approximately 4 percent of vaginal deliveries, and estimates are that it causes significant morbidity and 25 percent of all maternal childbirth-related deaths.[2] The World Health Organization defines postpartum hemorrhage as blood loss of 500 mL or more in the first 24 hours postpartum.[3] Postpartum blood loss is difficult to evaluate[4]; some healthy women tolerate a 500-mL loss of blood, whereas other women become clinically unstable.

Maternal risk factors for postpartum hemorrhage are summarized in *Table 1*.[5] Postpartum hemorrhage often occurs in women with no identifiable risk factors. Uterine atony is the most common cause of postpartum hemorrhage. Uterotonic medications (e.g., oxytocin [Pitocin], ergot alkaloids, and prostaglandins) are widely available in developed countries, are rapidly effective, and have become standard therapy in the treatment of postpartum hemorrhage.

TABLE 1
Risk Factors for Postpartum Hemorrhage

Risk factor	*Odds ratio*
Prolonged third stage of labor	7.6
Preeclampsia	5.0
Mediolateral episiotomy	4.7
Previous postpartum hemorrhage	3.5
Twin pregnancy	3.3
Arrest of descent	2.9
Soft-tissue lacerations	2.0
Asian ethnicity	1.7
Augmented labor	1.7
Forceps or vacuum delivery	1.7
Hispanic ethnicity	1.7
Midline episiotomy	1.6
Nulliparity	1.5

Adapted with permission from Combs CA, Murphy EL, Laros RK Jr. Factors associated with postpartum hemorrhage with vaginal birth. Obstet Gynecol 1991;77:73.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Practice active management of the third stage of labor during obstetrical delivery to prevent postpartum hemorrhage. Active management includes prophylactic administration of uterotonic agent with the delivery of the baby, early clamping and cutting of the umbilical cord, and constant controlled cord traction.	A	6,8,9
For the prevention of postpartum hemorrhage, and in conjunction with the other components of active management of the third stage of labor, oxytocin can be administered with the delivery of the anterior shoulder or after the delivery of the placenta.	B	16
The recommended dose is oxytocin 10 units intramuscularly or 20 units diluted in 500 mL normal saline intravenously to prevent postpartum hemorrhage in the third stage of labor.	B	10
Oral prostaglandins should not be used for the prophylaxis of postpartum hemorrhage.	A	13

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 956 or http://www.aafp.org/afpsort.xml.

Attempts to prevent postpartum hemorrhage have focused on the prophylactic use of uterotonic agents and the active clinical management of the third stage of labor. This article reviews the evidence supporting these approaches in the prevention of postpartum hemorrhage. Key terms are defined in *Table 2*.[1,2,6]

Expectant vs. Active Management

Expectant management of the third stage of labor also is called the physiologic method and is best described as a "hands off" approach. The umbilical cord is not clamped or cut until cessation of pulsating; separation of the placenta occurs without intervention; and the placenta is delivered spontaneously or aided by gravity.[6] In active management, the physician facilitates the separation and delivery of the placenta and enhances the effectiveness of the uterine contractions to shorten the duration of the third stage of labor and reduce the risk of postpartum hemorrhage. Active management of labor incorporates three main interventions: administration of a uterotonic medication after delivery of the baby; early cord clamping and cutting; and controlled traction on the umbilical cord while awaiting placental separation and delivery.[6] The clinical adoption and practice of active management or its individual components varies throughout the world.[7]

A Cochrane systematic review[6] identified five randomized controlled trials (RCTs) comparing active and expectant management that included more than 6,400 women. Compared with expectant management, active management was associated with: a shorter third stage (mean difference, –9.77 minutes); a reduced risk of postpartum hemorrhage (number needed to treat [NNT] = 12) and severe postpartum hemorrhage (NNT = 57); a reduced risk of anemia (NNT = 27); a decreased need for blood transfusion (NNT = 65); and a decreased need for additional uterotonic medications (NNT = 7).[6] Active management also was associated with an increased risk of maternal nausea (number needed to harm [NNH] = 15), vomiting

TABLE 2
Postpartum Hemorrhage: Definitions of Key Terms

Term	*Definition*
Third stage of labor	Time from the delivery of the infant until delivery of the maternal placenta
Active management	Uterotonic medication administered after the delivery of baby; early clamping and cutting of umbilical cord; and controlled umbilical cord traction until separation and delivery of the placenta
Expectant management	No uterotonic medication administered; umbilical cord not cut or clamped until after cessation of pulsating; separation of the placenta without intervention; and placenta delivered by gravity or spontaneously by maternal expulsion
Postpartum hemorrhage	Blood loss of at least 500 mL within 24 hours of delivery
Severe postpartum hemorrhage	Blood loss greater than 1,000 mL within 24 hours of delivery
Uterotonic medication	Any medication causing uterine contraction
Prophylactic use of uterotonic medication	Uterotonic medication used to prevent postpartum hemorrhage
Therapeutic use of uterotonic medication	Uterotonic medication used to treat postpartum hemorrhage

Information from references 1, 2, and 6.

(NNH = 19), and elevated blood pressure (NNH = 99), likely caused by the use of an intramuscular ergot alkaloid as the uterotonic medication in four of the five studies in the systematic review. There were no advantages or disadvantages for the baby with either approach.

The uterotonic agents and the route of administration varied, but the outcomes of active and expectant management of the third stage of labor were similar among the five trials. In one trial,[6] manual removal of the placenta was more common after active management. This trial[6] was the only one that used an intravenous ergot alkaloid as the uterotonic agent. Ergot alkaloids are thought to promote contraction of the lower uterine segment and may thereby increase the risk of an entrapped placenta and the subsequent need for manual removal of the placenta.[8] Of the other four trials, one used intramuscular oxytocin, and three used prophylactic ergometrine-oxytocin (a combination of five units of oxytocin and 0.5 mg of ergometrine, which is not available in the United States).

A second analysis[9] of these data, excluding the trial using intravenous ergonovine and a trial of lesser quality, demonstrated the benefits of active management in preventing postpartum hemorrhage while finding no increased risk of retained placenta or maternal side effects. Together, these two systematic reviews[6,9] provide evidence that active management with uterotonic agents other than an intravenous ergot alkaloid confers important benefits without significant side effects.

Choice of Uterotonic Agent

The evaluation of individual components of the active management of the third stage of labor has focused on the uterotonic medications. A Cochrane systematic review[10] evaluated oxytocin as the prophylactic uterotonic agent in the third stage of labor. In seven RCTs[10] comparing the use of prophylactic oxytocin with no prophylactic uterotonic agent in more than 3,000 women, the use of oxytocin was associated with reduced risk of postpartum hemorrhage (NNT = 8) and reduced need for therapeutic uterotonics (NNT = 15). The trials varied in dose of oxytocin administered, route of administration, and general management (active versus expectant) of the third stage of labor. In the studies using prophylactic oxytocin without the other components of active management (early cord clamping and cutting, controlled cord traction), there was a nonsignificant trend toward increased manual removal of the placenta (4.6 percent of women receiving prophylactic oxytocin versus 3.8 percent of women receiving placebo).The Cochrane review[10] also evaluated six trials that compared the prophylactic use of ergot alkaloids with the use of oxytocin in women in the third stage of labor. The agents were equally effective in preventing postpartum hemorrhage, but the ergot alkaloids were associated with an increased risk of manual removal of the placenta (NNH = 92).

The use of intramuscular ergometrine-oxytocin has been studied in a systematic review including six trials totalling more than 9,000 women.[11] The combination uterotonic agent was found to be more effective than oxytocin alone for preventing postpartum hemorrhage (NNT = 61). No difference was seen for the prevention of severe postpartum hemorrhage, and there was significantly more nausea and vomiting (NNH = 61) and hypertension (NNH = 96) in the women receiving ergometrine-oxytocin.[11]

Overall, the prophylactic use of oxytocin reduces postpartum hemorrhage and the need for therapeutic uterotonics. The ideal dose of oxytocin has not been directly studied. From the available data, the most effective dose appears to be 10 units administered intramuscularly or 20 units diluted in 500 mL of normal saline and given as an intravenous bolus. There seems to be no significant benefit to the prophylactic use of ergot alkaloids alone when compared with oxytocin alone or with the combination of oxytocin and ergometrine-oxytocin.

Carbetocin (not available in the United States) is a synthetic oxytocin analogue with a half-life four to 10 times longer than oxytocin. It can be administered intramuscularly or intravenously as a single injection. An RCT[12] compared 100 mcg of intramuscular carbetocin with 10 units of intravenous oxytocin and found no difference in the number of women requiring additional uterotonic medication.

Misoprostol (Cytotec) is available as a tablet that can be administered by oral, sublingual, rectal, or vaginal route. It is stable at room temperature, inexpensive, and has been studied as prophylactic therapy in the management of the third stage of labor. Neither oral nor rectal administration of misoprostol has been shown to be as effective as injectable uterotonics in preventing postpartum hemorrhage.[13] In a systematic review including 17 studies, there was an increased need for therapeutic uterotonic medications (NNH = 22) among the women receiving prophylactic misoprostol when compared with women receiving other injectable uterotonic agents. Side effects from misoprostol were common and included shivering (NNH = 7), vomiting (NNH = 225), diarrhea (NNH = 258), and elevated body temperature (NNH = 18). Although prostaglandins are an effective treatment of postpartum hemorrhage because of the balance of risks and benefits, they currently have no role in the prevention of postpartum hemorrhage.

Timing for Administration of the Uterotonic Agent

An area of controversy has been whether to administer the uterotonic agent at the time of the delivery of the anterior shoulder or after the delivery of the placenta. There is concern that administration of these agents before the delivery of the placenta may increase the risk for manual removal of the placenta. Results of a prospective cohort study[14] and an RCT[15] indicated that oxytocin administered before the delivery of the placenta decreased the risk of postpartum hemorrhage; however, the studies were not blinded and did not control for nonpharmacologic interventions (e.g., controlled cord traction). A double-blinded RCT[16] of 1,486 women receiving active management of the third stage of labor was performed to more definitively isolate the effect of the timing of the uterotonic agent. The early administration of prophylactic oxytocin did not increase the risk of manual removal of the placenta, and there was equal effectiveness in preventing postpartum hemorrhage; thus, the uterotonic agent can be administered before or after delivery of the placenta.

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