"STOP USING RECTAL MISOPROSTOL FOR THE TREATMENT OF POSTPARTUM HEMORRHAGE CAUSED BY UTERINE ATONY"
ROBERT L. BARBIERI, MD
(EDITORIAL; JULY 2016)

The BEPCOP strategy for uterine atony

I appreciated Dr. Barbieri's editorial about oxytocics for postpartum uterine atony and have personally noted the poor effectiveness of rectal misoprostol. I was reminded of his previous editorial that recommended administering intravenous (IV) oxytocin to postcesarean delivery patients for about 6 to 8 hours to reduce the risk of postoperative hemorrhage.

At my current hospital we usually use postpartum oxytocin, 30 units in 500 mL of 5% dextrose in water (D5W) for vaginal deliveries, and that infusion typically is administered for only 1 to 2 hours. Cesarean delivery patients receive oxytocin, 20 units in 1,000 mL of Ringer's lactate, over the first 1 to 2 hours postoperatively. As an OB hospitalist I have been summoned occasionally to the bedside of patients who have uterine atony and hemorrhage, which usually occurs several hours after their oxytocin infusion has finished.

With this in mind I developed a proactive protocol that I call BEPCOP, an acronym for "Barnes' Excellent Post Cesarean Oxytocin Protocol." This involves simply running a 500-mL bag of oxytocin (30 units in 500 mL of D5W) at a constant rate of 50 mL/hour, which provides 50 mU/min oxytocin over the first 10 hours postdelivery.

I recommend BEPCOP for every cesarean delivery patient, as well as for any vaginally delivered patients who are at increased risk for atony, such as those with prolonged labor, large babies, polyhydramnios,

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multifetal gestation, chorioamnionitis, and history of hemorrhage after a previous delivery, and for patients who are Jehovah's Witnesses. It is important to reduce the rate of the mainline IV bag while the oxytocin is infusing to reduce the risk of fluid overload.

Since starting this routine I have seen a noticeable decrease in postpartum and postcesarean uterine atony.

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Nondissolving misoprostol is ineffective

There is something about misoprostol that is not mentioned in Dr. Barbieri's editorial. There are 2 types of misoprostol: the proprietary formulation (Cytotec, Pfizer) and the generic form (probably the one used in most hospitals, and possibly also the one used in the randomized studies alluded to).

The generic form, manufactured overseas, is literally insoluble. In my experience, these undissolved tablets are expelled *intact* from the rectum 5 hours after insertion and they therefore do nothing. The proprietary brand of misoprostol dissolves instantly in the rectum, and the results are dramatic to say the least.

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Bundles of care protocols useful in critical events

We often assume the etiology of the postpartum hemorrhage (PPH) is purely and exclusively uterine atony. A frequent clinical scenario is as follows: A hospital birth is conducted by a trained attendant, in a US learning hospital, on a parturient assessed as being at low risk; the single circulating nurse is busy at the keyboard complying with the data entry requirements; the just-delivered patient is enjoying skin-to-skin contact as recommended; and the new father is obtaining all the appropriate pictorial material when a massive vaginal bleed ensues, diagnosed as due to uterine atony. There is little time to remember the results of the randomized controlled trials condemning the use of misoprostol, or the effectiveness of the individual components of the AMTSL (active management of the third stage of labor). The IV oxytocin at the prescribed dose is running wide open, extra personnel are summoned to help, the first doses of methylergonovine are given, and the misoprostol tablets are stored in the nearby drawer as prescribed by the institution's protocol.

Currently, a multi-state, multi-institutional initiative spearheaded by the American College of Obstetricians and Gynecologists and known as AIM (Alliance for Innovation in Maternity Care) supports the use of "bundles of care" to standardize obstetric care as recommended by the Joint Commission and the

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Society for Maternal-Fetal Medicine. One of the "bundles" addresses PPH. It is understood that each institution may adjust the steps in accord with its individual capabilities. Included in the algorithm is the use of rectal misoprostol 800 to 1,000 µg.[1–5]

The International Federation of Gynecology and Obstetrics, in referencing the Blum trial,[6] states that the results indicated misoprostol was noninferior to oxytocin at controlling bleeding (90% vs 89%) and preventing additional blood loss (31% vs 34%).[7] Misoprostol's contraindications and side effects are recognized by all investigators. In the field of obstetrics, changes are slow in permeating into daily practice.[8] Dr. Barbieri's recommendation, originating from an influential academic institution, opens the door to continue the dialog on a critical clinical event.

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Rectal misoprostol has merit

It is well established in medicine that IV medications have a rapid onset

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of action. Therefore, IV uterotonics would be the first choice to control PPH. Most likely they will control the majority of uterine atony.

However, the causes of uterine atony are numerous, and they most commonly include prolonged labor and/or infection. Like any fatigued muscle, there is rebound relaxation. IV uterotonics have a very short half-life and have a maximum total dose. Repeating oxytocin 40 U in a 1,000-mL infusion over 15 minutes carries the risk of water intoxication due to the antidiuretic effect.

Misoprostol 800 to 1,000 mg when used rectally will have a longer effect—up to 4 hours—and fewer side effects. It should be used in combination with other parenteral uterotonics to act in synergistic way. This way the more serious cases of PPH can be reduced or even prevented.

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›› Dr. Barbieri responds

I deeply appreciate the perspectives provided by Drs. Barnes, Zapata, Mariona, and Michael. The obstetricians and gynecologists who read OBG MANAGEMENT have vast clinical experience, expertise, and exceptional insights. By sharing our knowledge with each other we best advance the care provided to women and their families.

As a hospitalist, Dr. Barnes is privileged to care for women at the highest-risk time of their pregnancy. I think his BEPCOP proactive protocol to reduce the rate of PPH is superb and urge him to publish his experience. I appreciate Dr. Zapata's insight that misoprostol tablets from different manufacturers have markedly different rates of dissolution. I agree with him that I have seen entire, undissolved misoprostol tablets expelled from the rectum many hours after they were administered for the treatment of PPH. If the tablet does not dissolve, it certainly cannot work. Dr. Mariona's guidance to adhere to protocol bundles and continuously improve and update the bundles is absolutely critical to advancing health care for pregnant women. Dr. Michael rightly points out that one advantage of misoprostol is that it has a longer half-life than many parenteral uterotonics. However, in my practice I prefer Dr. Barnes' BEPCOP protocol involving the multi-hour administration of oxytocin to prevent and treat a PPH.