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Tranexamic Acid for Postpartum Hemorrhage

Postpartum hemorrhage (PPH) occurs in 2–3% of U.S. births and is the fourth most frequent cause of maternal mortality (Centers for Disease Control and Prevention, 2017). Although the incidence of PPH is higher in some other countries, the incidence of PPH in the United States appears to be on the rise: a 26% increase occurred from 1994–2006 primarily due to uterine atony (Callaghan, Kuklina, & Berg, 2010). Recent efforts to reduce PPH in the United States have focused on risk assessment, more timely recognition of hemorrhage, better coordination of health care teams, and optimized use of uterotonics (Association of Women's Health, Obstetric and Neonatal Nurses, 2017). These national efforts are aligned with recommendations from the World Health Organization (WHO; 2012) for the prevention and treatment of PPH. However, despite these efforts, 11.4% of pregnancy-related maternal deaths in the United States 2011–2013 were caused by hemorrhage (Centers for Disease Control and Prevention, 2017).

Results of a new trial are likely to cause a major shift in the way health care providers around the world approach PPH. The World Maternal Antifibrinolytic (WOMAN) trial is an international, randomized, double-blind, placebo-controlled trial to test tranexamic acid to treat PPH (WOMAN Trial Collaborators, 2017). Tranexamic acid is an anti-fibrinolytic medication that blocks the trauma-activated enzymatic breakdown of fibrinogen and fibrin and allows blood to clot more efficiently (Kruithof et al., 1987; Sawamura et al., 2009). Before the WOMAN trial, tranexamic acid was already known as a useful treatment for bleeding in surgical or emergency room settings. When infused intravenously within three hours of trauma, tranexamic acid reduced deaths caused by bleeding by one third with no increase in vascular occlusive events (Shakur et al., 2010). These findings with trauma patients prompted the WHO (2012) to recommend that women's health care providers use tranexamic acid to treat PPH. However, because evidence on the use of tranexamic acid in pregnant women was lacking at that time, the WHO specified that providers should use this agent as a secondary treatment only if uterotonics failed to control bleeding or if the bleeding was thought to be caused by trauma. The WOMAN trial was conducted to test the use of tranexamic acid as a primary treatment in women with PPH (WOMAN Trial Collaborators, 2017).

The WOMAN trial included participants from 193 hospitals among 21 countries (N = 20,021; WOMAN Trial Collaborators, 2017). Investigators found that women diagnosed with PPH (>500 ml blood loss following vaginal birth, >1,000 ml blood loss following cesarean birth, or any blood loss sufficient to cause hemodynamic instability) who received tranexamic acid were 19% less likely to die from bleeding (Risk Ratio [RR] 0.81, 95% Confidence Interval [CI] [0.65, 1.00]) than women who received placebo. This reduction in the death rate was even greater when treatment with tranexamic acid was initiated within 3 hours of birth (RR 0.69, 95% CI [0.52, 0.91]). The 3-hour window for best results was also seen in the earlier trials involving traumatic injuries and is thought to relate to the early activation of fibrinolysis following trauma and childbirth (Kruithof et al., 1987; WOMAN Trial Collaborators, 2017).

The WOMAN Trial Collaborators (2017) also found that the use of tranexamic acid reduced the need for abdominal surgery (laparotomy) following PPH by 36% (RR 0.64, 95% CI [0.49, 0.85]). Initially there was concern that use of tranexamic acid in pregnant women might cause thromboembolic events; however, the WOMAN Trial Collaborators (2017) found no evidence of

these complications. Tranexamic acid is typically given intravenously (1gm dose, infused as 10ml of a 100mg/mL solution; Shakur et al., 2010). If bleeding persists after 30 min, the dose can be repeated. Furthermore, tranexamic acid is very inexpensive and costs approximately $6.00 per dose.

In response to these results, the WHO (2017) outlined efforts to fast-track an update to the existing Cochrane systematic review on treatment of primary PPH with priority given to the use of antifibrinolytics to treat PPH. Women's health care providers can expect to see the new Cochrane review and new recommendations by the third quarter of 2017. However, given the strength of the design and compelling results of the WOMAN trial, now is the time for health care providers across the United States to prepare to incorporate tranexamic acid in PPH response plans. With the addition of antifibrinolytics to the tools available to treat PPH, the United States can begin to make real headway towards reducing the number of women who die from PPH.

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From Cochrane Database of Systematic Reviews (CDSR) Issue 5–6 (2017)

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