ONLINE EXCLUSIVE

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Q/ Does tranexamic acid reduce mortality in women with postpartum hemorrhage?

EVIDENCE-BASED ANSWER

A/ **Yes.** When used in conjunction with the standard of care, 1 g intravenous (IV) tranexamic acid given 1 to 3 hours after delivery is associated with a significant reduction in maternal mortality from postpartum hemorrhage (PPH) (strength of recommendation: **A**, randomized controlled trial [RCT] and Cochrane review).

No known significant risks are associated with the use of tranexamic acid to treat PPH.

Evidence summary

A 2017 double-blind RCT that included 20,060 women with PPH from 21 countries (the WOMAN trial) found that the risk of maternal mortality was significantly lower among women who received tranexamic acid as part of their PPH treatment compared with placebo (1.5% [N = 155] vs 1.9% [N = 191]; *P* = .045; relative risk [RR] = 0.81; 95% confidence interval [CI], 0.65-1; number needed to treat [NNT] = 250).[1]

Inclusion criteria were age 16 years or older, postpartum course complicated by hemorrhage of known or unknown etiology, and a case in which the clinician considered using tranexamic acid in addition to the standard of care. PPH was defined as > 500 mL blood loss after vaginal delivery, > 1000 mL blood loss after cesarean section, or blood loss sufficient to produce hemodynamic compromise.

Researchers randomized 10,051 women to the tranexamic acid group and 10,009 to the placebo group. Women in the experimental group received a 1-g IV injection of tranexamic acid over 10 to 20 minutes. A second dose was given if bleeding restarted after 30 minutes and within 24 hours of the first dose.

To reduce mortality give tranexamic acid promptly

Tranexamic acid reduced mortality most effectively compared with placebo when given within 3 hours of delivery (1.2% [N = 89] vs 1.7% [N = 127]; *P* = .008; RR = 0.69; 95% CI 0.52-0.91; NNT = 200). After 3 hours, no significant decrease in mortality occurred. No significant difference in effect was noted between vaginal and cesarean deliveries nor between uterine atony as the primary cause of hemorrhage and other causes.

Administering tranexamic acid didn't reduce the composite primary endpoint of hysterectomy or death from all causes. Nor did it reduce the secondary endpoints of intrauterine tamponade, embolization, manual placental extraction, arterial ligation, blood transfusions, or number of units of packed red blood cells. The tranexamic acid group showed a significant decrease in cases of laparotomy for PPH (0.8% vs 1.3%; *P* = .002; RR = 0.64; 95% CI, 0.49-0.85; NNT = 200).

Women who received tranexamic acid vs placebo showed no significant difference in mortality from pulmonary embolism (0.1% [N = 10] vs 0.1% [N = 11]; *P* = .82; RR = .9; 95% CI, 0.38-2.13), organ fail-

ure (0.3% [N = 25] vs 0.2% [N = 18]; *P* = .29; RR = 1.38; 95% CI, 0.75-2.53), sepsis (0.2% [N = 15] vs 0.1% [N = 8]; *P* = .15; RR = 1.87; 95% CI, 0.79-4.4), eclampsia (0.02% [N = 2] vs 0.1% [N = 8]; *P* = .057; RR = .25; 95% CI, 0.05-1.17), or other causes (0.2% [N = 20] vs 0.2% [N = 20]; *P* = .99; RR = 0.99; 95% CI, 0.54-1.85).

Tranexamic acid doesn't increase the risk of thromboembolism

A 2018 Cochrane review sought more broadly to determine the general effectiveness and safety of antifibrinolytic drugs in treating primary PPH.[2] Of 15 RCTs identified, only 3 met the inclusion criteria for the review, 1 of which was the WOMAN trial (which contributed most of the data in the review).

The other trials were a study conducted in France that recruited 152 women and a study of 200 women in Iran that contributed only 1 primary outcome—estimated blood loss—to the review. The former study didn't report any maternal deaths, and the latter study didn't look at maternal deaths.

The Cochrane review concluded, based on data from the WOMAN trial, that IV tranexamic acid, if given as early as possible, reduced mortality from bleeding in women with primary PPH after both vaginal and cesarean delivery and didn't increase the risk of thromboembolic events.[2]

Recommendations

The newest practice guidelines on the management of postpartum hemorrhage published by the American College of Obstetricians and Gynecologists recommends considering tranexamic acid as an additional agent in managing PPH when initial standard-of-care treatments fail.[3]

Editor's takeaway

The large international double-blind, randomized placebo-controlled trial provides convincing evidence that tranexamic acid should be administered readily in cases of PPH. JFP

References

1. WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. *Lancet*. 2017;389:2105–2116.
2. Shakur H, Beaumont D, Pavord S, et al. Antifibrinolytic drugs for treating primary postpartum haemorrhage. *Cochrane Database Syst Rev*. 2018;2:CD012964.
3. Committee on Practice Bulletins-Obstetrics (American College of Obstetricians and Gynecologists). Practice Bulletin No. 183: Postpartum Hemorrhage. *Obstet Gynecol*. 2017;130:e168-e186.