CSL Behring

Tranexamic acid (TXA) should be administered prophylactically for every caesarean delivery. Pro-con

Chair: Prof. Carolyn Weiniger

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Postpartum bleeding is a major cause of maternal morbidity and mortality1. So far, uterotonic drugs are the only procedure that has proven to reduce postpartum bleeding after birth[2].

Tranexamic acid (TXA) is an inhibitor of plasminogen activation to plasmin, thus inhibiting fibrinolysis. TXA has proven effective in reducing bleeding in elective surgery and mortality in trauma patients with critical bleeding[3,4]. In obstetrics, the **WOMAN** clinical trial proved the reduction of mortality due to postpartum bleeding, particularly if administered right after birth[5]. **The World Health Organization recommends the administration of TXA in severe postpartum hemorrhage (preferably within three hours after birth), after either vaginal or C-section delivery**.

Several randomized clinical trials have been carried out to determine the role of TXA in postpartum bleeding prevention. Most of them were small trials with methodological issues. However, three of them were large and robust enough[6-8].

PRO: TXA SHOULD BE ADMINISTERED PROPHYLACTICALLY FOR EVERY CAESAREAN DELIVERY

Loic Sentihles, France

ARGUMENTS IN FAVOR OF USING TXA IN C-SECTION BLEEDING PREVENTION

- The safety profile of TXA in bleeding prevention has been proven after birth[6-8].
  - Some fatal cases have been published, but they were due to the mistaken intrathecal administration of TXA[9].
- An effect—mild yet significant—has been shown in bleeding prevention.
- Benefits of tranexamic acid **depending on the type of delivery**[6-8]:

C-section (TRAAP2[7])
- ↓Average blood loss (reduction in hematocrit variation).
- ↓Need for uterotonic drugs.
- Not a higher incidence of thrombotic events.

Vaginal (TRAAP1[6])
- No ↓ in risk of bleeding ≥ 500 mL.
- ↓ Need for uterotonic drugs.
- Not a higher incidence of thrombotic events.

- El TXA is cost-effective ([10], article under review).

The clinical trial by **Pacheco et al.**[8], recently published, did not observe a significantly lower risk in the primary endpoint (maternal mortality or blood transfusion) following the prophylactic use of TXA in C-section postpartum versus placebo.

The effect observed in terms of bleeding reduction, though mild, could end up having an impact on breastfeeding, the mental health of the mother, and the development and behavior of the children, among other outcomes that have not been sufficiently studied so far.

The benefit-risk ratio is favorable to the use of TXA in all C-section deliveries, particularly in low- to medium-income countries.

CON: TXA SHOULD NOT BE ADMINISTERED PROPHYLACTICALLY FOR EVERY CAESAREAN DELIVERY

Catherine Bagot, United Kingdom

ARGUMENTS AGAINST USING TXA IN C-SECTION BLEEDING PREVENTION

- Postpartum hemorrhage is due to the "4Ts" (uterine atony, trauma, retained tissues, and thrombin alteration). However, only 1% of hemorrhage cases are due to coagulopathy (thrombin alteration)[11].
- The coagulopathy can be a consequence of a higher fibrinolytic activity if the postpartum hemorrhage is poorly controlled, hence the benefit of TXA.
- According to the **WOMAN** study, TXA reduces bleeding and death due to bleeding in women suffering from postpartum hemorrhage, with no adverse effects if administered within 1 to 3 hours, probably at the onset of the coagulopathy[12]. Nevertheless, some data should be considered when interpreting the results of the WOMAN study[13]:

WOMAN[5]
- **No changes in all-cause mortality were observed (primary endpoint).**
- The absolute reduction of death due to bleeding was 0.4%.
- The absolute reduction of surgery to stop the bleeding was 0.4%.

- A systematic review by **Ferrari** et al. analyzed 22 publications on the role of TXA to prevent C-section-related bleeding[14]:

FERRARI et al.[5]
- **Out of 22 studies, only three approached bleeding from a subjective standpoint.**
- **All studies presented a high degree of heterogeneity.**

- In the **TRAAP2** study, TXA prophylaxis resulted in a reduction in the estimated blood loss volume > 1000 mL or red blood cell transfusion on day 2. Nevertheless, some data should be considered when interpreting the results of the WOMAN TRAAP2[7].

TRAAP2[7]
- **The benefits were only observed in C-sections performed before labor and in patients not at risk of postpartum hemorrhage.**
- **No significant improvements in hemorrhage-related secondary clinical results were observed.**

The recent Egyptian clinical trial **Shalaby** et al. shows a benefit in high bleeding risk patients requiring a C-section[15]. However, its robustness is low, and so further studies would be needed.

Other risks in prophylactic use of TXA
- **Decrease in the preeclampsia / eclampsia threshold.**
- **Risk of accumulation in renal failure.**
- **Not recommended in case of disseminated intravascular coagulation.**
- **Prothrombotic effect.**
- **Crosses the placental barrier.**

Therefore, in C-section deliveries, the benefits of TXA prophylaxis are minimal.

DISCUSSION-CONCLUSION

In favor of TXA administration in high bleeding risk C-sections.

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