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Expecting two, delivering three: A case of tranexamic acid and the hidden triplet

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Introduction

We describe a clinical case where a pregnant woman with twin gestation was given Tranexamic Acid (TXA) after delivery of her two neonates but was found to have a third fetus during placenta removal. Tranexamic acid is an antifibrinolytic agent that has been widely studied for its potential in reducing Postpartum Hemorrhage (PPH) [1]. Postpartum hemorrhage, defined as bleeding ≥500 mL in the first 24 hours after delivery, is responsible for 25% of all maternal deaths worldwide [1]. Despite advances in obstetric care, PPH remains a significant concern. Several studies, including the WOMAN Randomized Controlled Trial (RCT), have investigated the effects of TXA in women with PPH [2]. Results demonstrate that the use of TXA significantly reduces maternal death due to bleeding, without any increase in maternal adverse events. These benefits were particularly pronounced when TXA was administered within three hours of birth. Few studies, however, have thoroughly investigated the effects of TXA on neonates in utero.

Drugs that are lipid soluble, smaller (<500 Da), non-protein bound, and have a low ionized fraction have greater placental transfer. Tranexamic acid is a class B pregnancy drug that can pass through the placental barrier, with its concentration in cord blood matching that in maternal blood. Other classes of drugs known to cross the placenta include opiates, benzodiazepines, local anesthetics, beta blockers and barbiturates. When considering the administration of any medication during pregnancy or labor, it is important to weigh the potential benefits against the risks to both mother and fetus.

Case presentation

A 37-year-old G3P1101 woman at 34 weeks and 6 days of dichorionic twin gestation dated by fetal ultrasound with a history of preeclampsia without severe features, Wolff-Parkinson White syndrome treated with ablation, endometriosis, and rheumatoid arthritis on hydroxychloroquine presented to our Labor and Delivery floor. In triage, her systolic blood pressure

was in the 150s and diastolic pressures were in the 100s. She also reported daily headaches for the past 4 months and worsened lower extremity edema. Her Aspartate Aminotransferase level (AST) was elevated to 45 units/L, and her protein to creatinine ratio increased to 3 from 0.89. Given the worsening features of her preeclampsia, magnesium was started and a plan for repeat Cesarean Delivery (CD) with tubal sterilization was established.

The patient's most recent fetal ultrasound demonstrated dichorionic diamniotic twin gestation at 14 weeks. Growth charts of the two known fetuses were within normal limits based on transabdominal ultrasound at 27 weeks (Figure 1). Prior to delivery, a combined spinal epidural was placed. Amniotomies for the first and second neonate were performed for clear fluid. Following their deliveries, an attempt was made to deliver the placentas. With gentle traction on the umbilical cords, a bulging bag was noted at the hysterotomy. Thought to be a residual membrane sac, the bag was ruptured, revealing the back and shoulders of the third neonate. Prior to this third delivery, oxytocin and tranexamic acid had been started for PPH. The patient's blood loss was estimated to be 1.5 L. After being told the news, the patient described the experience as a "miracle" and is happy with the arrival of her third newborn.

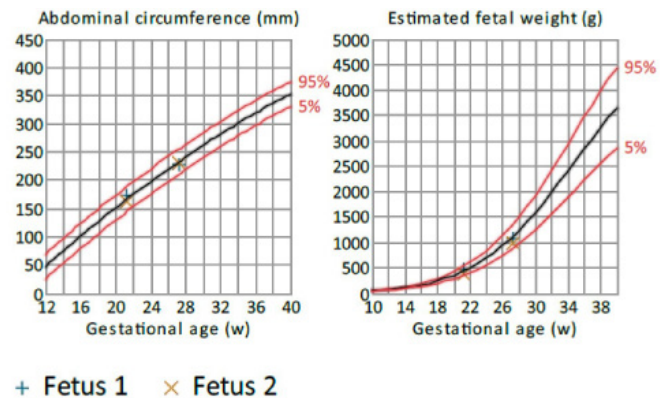

Figure 1: Growth charts of the two known fetuses based on transabdominal ultrasound at 27 weeks.

Discussion

The effect of TXA on neonatal outcomes has been sparsely studied. Tranexamic acid may cause serious side effects in neonates before cord clamping [3-5]. Several published studies and case reports have described fetal and neonatal functional issues such as low Apgar score, neonatal sepsis, cephalohematoma, low birth weight, and preterm birth in fetuses and infants exposed to TXA in utero [6]. However, no RCTs examining TXA administration for women undergoing CD have clearly demonstrated that these risks are associated with TXA. Tetruashvili et al. 2007 used TXA to stop bleeding in women with recurrent and threatened miscarriages [7]. Although two neonates passed away, their deaths were attributed to the severe bleeding complications from placental abruption, rather than the administration of TXA. In another RCT investigating TXA for reducing intraoperative blood loss after high-risk CD, there were no significant differences in neonatal APGAR scores or NICU admission rates [8]. Additionally, the WOMAN trial did not find any significant difference in neonatal deaths, stillbirths, or other adverse neonatal outcomes [2].

While evidence suggests TXA does not appear to be associated with increased risks to neonates, robust RCTs are still lacking [2,7,8]. Plus, in this case of a third undetected fetus, additional medications other than TXA were administered around the time of delivery including fentanyl, acetaminophen, ropivacaine, phenylephrine and oxytocin, all of which cross the placenta. Physiologic changes during pregnancy alter maternal pharmacokinetics, which in turn affect the amount of drug reaching the placenta and fetus. One study found no increased risk of thrombosis or seizures in neonates administered TXA at these doses [9]. Nonetheless, even if TXA and other drugs are safe in neonates, we do not know the impact of delivering postpartum dosages of medications to an undelivered fetus.

Declarations

Conflicts of interest: None.

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