

Introduction

- Tranexamic acid (TXA) is a widely used antifibrinolytic that reduces bleeding by binding to plasminogen and inhibiting breakdown of fibrinogen and fibrin
- The World Maternal Antifibrinolytic trial (WOMAN, 2017) found that TXA reduces death due to bleeding in women with post-partum haemorrhage, and TXA has been increasingly used in obstetrics since
- The first case report of anaphylaxis to TXA was described in 2004, by 2021 this had risen to seven¹
- Here we report the first case report to anaphylaxis in an obstetrics patient

Background

35 year-old female, P3 G4, presented for elective caesarean section

Past medical history: Gestational diabetes, alpha-thalassaemia trait, BMI 27

Drug history: Metformin, insulatard, ferrous sulphate
No known drug allergies, no history of atopy

Previous surgical history: Three previous caesarean sections

Pre-operative concerns:

- Fourth caesarean section
- High risk of bleeding:
 - Discussed in team brief
 - Starting Hb 125
 - 2 units of red blood cells crossmatched
 - Consented for cell saver and blood transfusion

Intra-operative events

08:50 Patient in theatre

- IV access
- **09:02** Routine antibiotic prophylaxis given
- **09:10** Combined spinal and epidural with 1.8mls 0.5% hyperbaric bupivacaine and 25mcg fentanyl: uneventful



09:31 Knife to skin

- Significant adhesions
- Second obstetric consultant to help
- Team informed that the patient is oozing
- Asked to administer prophylactic TXA 1g prior to delivery of baby



09:45 Tranexamic acid 1g IV administered

- **09:50** Patient complains of itchy eyes
- **09:55** Patient develops hoarse voice, significant facial angioedema and widespread rash
- BP 67/40 HR 95 O₂Sats 88%



09:55 Anaphylaxis

- Obstetric team asked to deliver baby urgently
- Partner reluctant to leave
- Resuscitation of mother
- Adrenaline 0.5mg 1:1000 IM, hydrocortisone 200mg IV, chlorphenamine 10mg IV



09:57 Baby delivered in good condition

- Repeat IM adrenaline for significant angioedema
- 4L of IV crystalloids given
- BP stabilised
- **10:05** IV Carbetocin 100 mcg administered
- Estimated blood loss: 700mls

Postoperative management

- Epidural left in situ for pain relief until able to swallow oral medications
- Patient in monitored area for close observation 24 hours following reaction
- Symptoms continued to improve and had completely resolved by 5pm the same day
- Patient and partner informed of suspected reaction to TXA, letter written to GP and patient referred to drug allergy clinic

Follow-up

Mast cell tryptase levels

1st level at 10:30am: 16.7 ng/ml

2nd level at 12:30pm: 28.6 ng/ml

3rd level at 11:00am (>24hrs later): 4 ng/ml

Drug allergy clinic results

- POSITIVE intradermal test to TXA
- Negative skin prick test to TXA
- Negative skin prick and intradermal tests to:
Lidocaine 1%
Bupivacaine 0.25%
Fentanyl
Metronidazole
Cefuroxime
Povidone iodine
Chlorhexidine 0.05%
Latex

Diagnosis: Anaphylaxis to TXA

Discussion

- Anaphylaxis to TXA confirmed in our patient
- Significance of human factors when managing anaphylaxis during elective caesarean section
- A rare reaction to a commonly used drug in obstetrics – as TXA is increasingly used the number of anaphylaxis reactions is likely to rise
- Side effects of TXA: gastrointestinal disturbance, allergic dermatitis, venous thromboembolism, seizures, visual disturbance
- TXA is neurotoxic – safety alert following accidental intrathecal administration
- Possible rare long-term renal complications following TXA administration together with other drugs in women with severe post-partum haemorrhage²
- Recent systematic review and meta-analysis found no particular safety concern of TXA use for prevention of obstetric haemorrhage³, but many studies underpowered to detect adverse drug reactions and high risk groups excluded

Conclusion

- TXA forms part of guidelines for major obstetric haemorrhage worldwide
- Always consider risk/benefit before administering TXA
- Particular caution prior to delivery of baby in view of anaphylaxis risk

References:

1. El Hanache H , Verdaguer M, Collin L, Babin M, Favrelière S, et al. Two Cases of Anaphylaxis to Tranexamic Acid Confirmed by Drug Provocation Test: What About Skin Tests? *J Investig Allergol Clin Immunol* 2021 31(4): 351-353 doi: 10.18176/jiaci.0651
2. Stämpfli D, Weiler S, Weiniger CF, Burden AM, Heesen M. Renal ischemic adverse drug events related to tranexamic acid in women of child-bearing age: an analysis of pharmacovigilance data. *Eur J Clin Pharmacol* 2021 77(6):913-919 doi: 10.1007/s00228-020-03064-y
3. Franchini M, Mengoli C, Cruciani M, et al. Safety and efficacy of tranexamic acid for prevention of obstetric haemorrhage: an updated systematic review and meta-analysis. *Blood Transfus* 2018 16(4):329-337 doi:10.2450/2018.0026-18