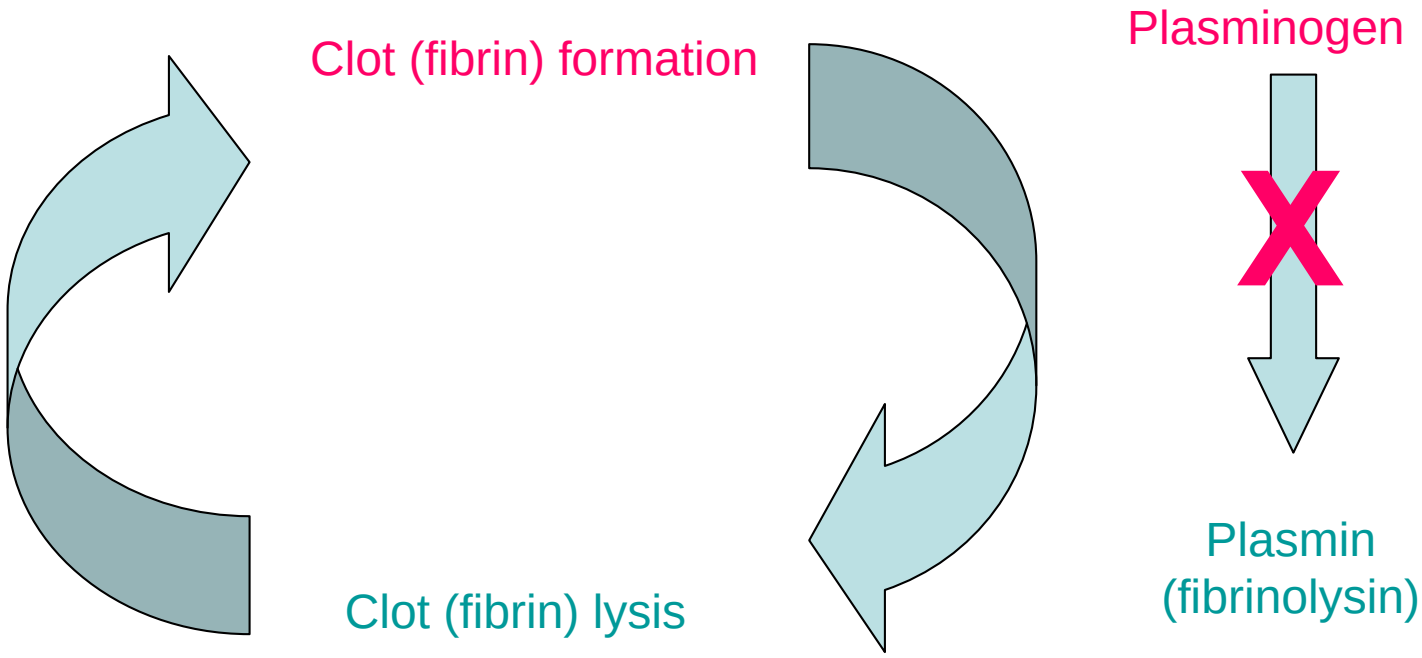
Tranexamic acid and PPH

Mechanism of action

Anti-fibrinolytic agent



Tranexamic acid & PPH

- A drug used when in ‘trouble’
- We do not know if it is an effective primary / secondary agent
- We do not know if it prevents PPH
- If effective, is it better (cheaper, safer) than other drugs?

Tranexamic acid & 3rd stage of labour

Ferrer et al. (2009)
Anti-fibrinolytic agents in post partum haemorrhage: a systematic review

Results

- Identified 3 trials involving 461 participants
- Compared tranexamic acid with no treatment
- In all three trials, allocation concealment was either inadequate or unclear
- Tranexamic acid associated with a reduction in blood loss of 92ml

Active management of 3rd stage

- 5 RCTs, 6500 women
- Reduced risk of PPH > 1000 ml [risk ratio = 0.34]
- Reduced risk of PPH > 500 ml [RR 0.34]
- Reduced blood loss at delivery [**−78.80** ml]
- Reduced risk of blood transfusion [RR 0.35]
- Reduced need for iron therapy in the puerperium [RR 0.59]
- Increased risk of postnatal hypertension [RR 4.10]
- Lower average birth weight [−76.90 g]

Tranexamic acid and PPH

Cochrane review 2010

Tranexamic acid decreases blood loss after vaginal birth and caesarean section based on two RCTs of unclear quality. Further investigations are needed on efficacy and safety of this regimen for preventing PPH

Since 2010

- At least 5 published RCTs
- Different entry criteria
- Different dose regimens
- All show significant reduction in blood loss

The Quiz of Life

Question 1

With respect to air travel, how many passengers die per 100 million passenger miles?

A = 0.001 B = 0.01 C = 1 D = 10 E = 15

B = 0.01

Tranexamic acid & surgical bleeding

Perel et al. (2013)
Tranexamic acid for reducing mortality in emergency and urgent surgery

Results

- Three trials (260 patients)
- Tranexamic acid had no effect on mortality
- Tranexamic acid reduced the need for blood transfusion by 30%
- No increase in risk of DVT or stroke
- Another review of 129 trials

34% reduction in blood loss
38% reduction in risk of receiving blood transfusion

Tranexamic acid & acute traumatic injury

Roberts et al. 2011 (CRASH Trials)

Results

- Two trials with a combined total of 20,451 patients
- Reduced the risk of death by 10%
- Reduced the risk of death from bleeding by 15%
- No increase in the risk of vascular occlusive events
- No substantial difference in the receipt of blood transfusion
- The estimated incremental cost per life year gained is $64
- Paramedics now carry and administer Tranexamic acid

The Quiz of Life

Air travel: Risk of death = 0.01 per 100 million passenger miles

Car travel: Risk of death = 0.72 per 100 million passenger miles

Question 2

With respect to Operation Iraqi Freedom, how many US soldiers died per 100,000 per year?

A = 4 B = 41 C = 410 D = 600 E = 900

Answer = C

416/100,000/year

2,231/100,000/year (Vietnam)

Goldberg 2010. Military Medicine 175;4:220-226

The Quiz of Life

Iraq war: 416/100,000/ year. Vietnam: 2,231/100,000/year

Iraq war: 2.3/100,000/48h. Vietnam: 12/100,000/48h

Question 3

In the UK, how many women die because of pregnancy per 100,000 births?

A = 5 B = 12 C = 22 D = 45 E = 98

Answer = B (12) USA = 21 Afghanistan = 460 Cameroon = 690

- 50% fall in maternal mortality between 1990 and 2010
- 99% of deaths occur in developing countries
- Over 50% of deaths are due to haemorrhage

Source: WHO

The WOMAN Trial

- World Maternal Anti-fibrinolytic Trial

Inclusion criteria

- Blood loss >500 ml (Vaginal) or 1000 ml (CS)
- Blood loss sufficient to cause haemodynamic compromise

Trial treatment

- 1g Tranexamic acid / NaCl by iv injection
- Further dose if bleeding continues after 30 mins or re-bleed within 24h

Primary outcome

- Death or hysterectomy

Sample size

- 15,000 across high, medium & low-income countries
- Newcastle randomised 92 women

The WOMAN Trial

Consent

- Woman has capacity: Reads & signs consent
- Mental capacity impaired: Personal / Professional Rep signs consent
- Mental capacity impaired and no Rep available: Investigator + 1 other randomise

Once capacity restored, obtain written consent to use data

The WOMAN Trial

Patient information leaflet
- All women coming through ANC
- Pre-CS clinic
- IOL suite

X

Face-to-face discussion
- Pre-CS clinic
- IOL suite
- Delivery suite

X

Woman's decision

NO

X

Orange sticker on
Partogram / consent form

- Do not approach again
- Do not randomise

YES

X

Green sticker on
partogram / consent form

Treat with next trial pack if
EBL > 500ml at vaginal birth
EBL > 1000ml at CS

Decision not known

No sticker on
Partogram / consent form

Approach, consent & treat if
EBL > 500 ml at vaginal birth
EBL > 1000 ml at CS

Is Tranexamic acid better?

- ?
- Doing nothing is appropriate in most women
- Effective prophylaxis & treatment
- Potentially fewer side-effects than Ergometrine / Carboprost and ? Oxytocin
- Requires iv injection
- Stored at room temp

PPH – Wonder drug

- Effective for prophylaxis as well as treatment
- Suitable for breastfeeding women
- Stable at room temperature
- Active by oral / rectal / sub-lingual route
- Good side-effect profile

Thank you