We Don’t Know How It Works, But It Works!

TRANscending a new EXAMination & understanding of an old ACID:

The Role of Tranexamic Acid in EMS

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1,100 square miles
Population
– 1.6 million day
– 1.2 million night
209,029 calls (2012)
142,467 transports (2012)
68% transports
Difference Makers
High-Force Abdominal Trauma

- BP 90/40
- P 130
- R 22
- Pulse ox 92%
- ETA to trauma center is 20+ mins
Tranexamic Acid?

By EMS?
What is TXA?

• Antifibrinolytic
• Anti – “Clot buster”
• Clot stabilizer (inhibits clot breakdown)
• Likely more... Anti-inflammatory modulator?
Is TXA New?

- Old player in cardiovascular surgery
- Written about 40+ years ago
- Re-discovery is not novel to TXA (or EMS)
  - IO
  - Tourniquets
Does the FDA approve?

• Approved to decrease bleeding
  – Hemophilia
  – Uterine bleeding
CRASH-2

Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage 2

Lancet. 2010 Jul 3;376(9734):23-32
CRASH-2 Study Design

• Prospective civilian trauma patients
• Randomized controlled trial
• 274 hospitals in 40 countries
• 20,211 adult trauma patients
  – With, or risk of, significant bleeding
    – HR >110, SBP <90 mmHg, clinical judgment
• Treatment within 8 hours of injury
  – TXA or placebo
CRASH-2 Study Outcome Points

• Death in hospital within 4 weeks of injury
  – Bleeding
  – Vascular occlusion (MI, stroke, PE)
  – Multiorgan failure
  – Head injury
  – “Other”

• Vascular occlusive events

• Need for blood transfusion/surgery
CRASH-2 Study Results

• All cause mortality (TXA)
  - 14.5% v 16.0%
  - RR 0.91
  - 95% CI 0.85 - 0.97
  - p = 0.0035

• Death due to bleeding (TXA)
  - 4.9% v 5.7%
  - RR 0.85
  - 95% CI 0.76 - 0.96
  - p = 0.0077
CRASH-2 Study Results

NNT = 67
TXA – Is there harm?

- No difference in rate of MI/Stroke/DVT/PE
- 1.7% v 2.0% (168 v 201)
- \( p = 0.084 \)
TXA – Treatment Course Effects?

- Did NOT reduce need for blood
- Did NOT reduce need for surgery

- ........BUT, it did increase survival!
MATTERs

Military Application of Tranexamic Acid in Trauma Emergency Resuscitation Study

MATTERs Study Design

• Retrospective combat casualties
  – British helo physicians in Afghanistan
• TXA v no TXA if receiving 1+ uPRBC
  – Subgroup massive transfusion (10+)
• 896 consecutive admissions
  – 293 received TXA (IV bolus only)
MATTERs Study Outcome Points

- Characterize TXA use in combat injury care
- Effect of TXA on
  - Total blood product use
  - Thromboembolic complications
  - Mortality (24 hr, 48 hr, 30 days)
MATTERs Study Results

• TXA lower mortality - overall
  – 17.4% v 23.9% (p = 0.03)
  – Mean ISS higher in TXA group (25.2 v 22.5; p<0.001)

• TXA lower mortality – massive transfusion
  – 14.4% v 28.1% (p = 0.004)
  – Survival odds ratio 7.228 (95% CI 3.0 – 17.3)
MATTERs Study Results

NNT = 7
What about DVT/PE?
Matters (of Concern?) in MATTERs

• DVT – Overall
  – TXA 7 (2.4%) v no TXA 1 (0.2%) p=.001
• DVT – Massive Transfusion
  – TXA 2 (1.6%) v no TXA 1 (0.5%) no sig difference
Matters (of Concern?) in MATTERs

• PE – Overall
  – TXA 8 (2.7%) v no TXA 2 (0.3%) p = .001
• PE – Massive Transfusion
  – TXA 4 (3.2%) v no TXA none p = .01
MATTERs TXA Group

• Higher injury burden = More thrombotic event
• ? Military theater – penetrating/ortho
• ? Survival allows for DVT/PE to be diagnosed
• ? Retrospective design limitations
  – Screening/diagnostic approaches
  – DVT/PE clinical significance
MATTERS Take-Aways

• Survival benefit to any patient getting blood
• Massive transfusion? (10u PRBC + / 24 hrs)
  – TXA independent predictor of survival
• Benefit not really shown until 48 hrs
  – Can’t be clot function alone
  – ? Anti-inflammatory component
• Earlier the better….as in first hour post trauma
TCCC = Tactical Combat Casualty Care

- TXA if anticipated significant blood transfusion
  - Hemorrhagic Shock
  - Major amputation(s)
  - Penetrating torso trauma
  - Severe bleeding
- Class I Recommendation
Who should get TXA?

• Serious trauma (think neck to mid-thigh)
  – Not isolated head injury
• Likely to need massive transfusion
  • Sustained tachycardia
  • Sustained hypotension
How do we give TXA?

- 1 gram in 100 mL NS or LR over 10 mins
- First dose must be within 3 hours of injury
  - Better within 1 hour of injury
- Second dose
  - 1 gram over 8 hours IVPB
What does TXA cost?

- Military $1.50 a dose ($10 - 100/life)
- Civilian $55 a dose ($385 – 3,685/life)

- Military considers shelf life in years
- Manufacturer likely doesn’t
- Advised temps 59-86 degrees F
- Viewed very heat stable in Middle East
TXA – Where do we go?

• “Early adopters”
  – OKC & TUL effective 4/1/13 (est. 60+ pts/year)
  – London Ambulance Service 4/1/13

• Ongoing study - ?DVT/PE risk
  – No evidence in CRASH-2
  – Mostly transfusion ratios + TXA

• Likely won’t see scope of CRASH-2 again
Take Home Points

• No current EMS answer for all bleeding
• Should EMS administer TXA?
  – Good clinical benefit shown in EBM
  – Must administer early (within 3 hrs of injury)
  – Good safety profile (vasoocclusive events)
  – Fits in operational/fiscal realities
• Discussion with trauma surgeons essential
Protocol Resources

okctulomd.com

“Training & Protocols” tab

MCB Pre-Hospital Operational Standards

2013 State of Oklahoma EMS Protocols
Field & Reference Editions