TRIUMA YEAR IN REVIEW

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Disclosure

- I have no conflicts of interest to disclose.

Background

- Trauma = #1 cause of death persons <40 yo
- Hemorrhage cause of death in 30% pts
  - exacerbated by Acute Coagulopathy of Trauma (ACoT)
- ACoT: endogenous impairment of all components of homeostasis after injury
- Potential preventable mortality 40% civilian & 80% military trauma

**Acute Coagulopathy of Trauma**

- ACoT: develops rapidly after trauma
  - 56% pts with abnormal coagulation within 25 min of injury
- Associated with 4-fold increase mortality & significant increase transfusion requirements
- Requires combination severe tissue trauma and systemic hypoperfusion


**Acute Coagulopathy of Trauma**

- ACoT characterized by:
  - Dysfibrinogenemia
  - Systemic anticoagulation
  - Impaired platelet function
  - Hyperfibrinolysis (clot breakdown)

- Tranexamic acid used to treat fibrinolytic component of ACoT

**Tranexamic Acid**

- Synthetic lysine derivative
- Initially used for dental procedures in hemophilia patients (1972)
- Used commonly for:
  - Hyperfibrinolysis of cardiopulmonary bypass & liver transplant
  - Hip replacement & total knee arthroplasty
- Reduces blood loss & transfusion requirements

**Tranexamic Acid**

- Occupies lysine binding sites on plasminogen
  - Inhibits plasminogen activation & plasmin activity
  - Prevents binding to fibrin
  - Prevents clot breakdown

**Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial**

- Randomized prospective clinical trial
- 20,211 adult trauma pts
- 274 hospitals, 40 countries

Eligibility:
- Clinical evidence hemorrhage (SBP<90 or HR>110)
- Significant risk of hemorrhage
- Presentation within 8 hrs of injury

*Lancet. 2010; 376: 23-32*
**CRASH-2 Study**

- Loading dose 1 gm TXA over 10 min, followed by 1 gm infusion over 8 hrs
- Primary outcome: death in hospital at 4 weeks
  - Bleeding
  - Vascular occlusion (MI, stroke, PE)
  - Multi-organ failure
  - Head Injury
- Secondary outcomes: vascular occlusive events, surgical intervention, need for blood transfusion, amount blood transfused

**Military Application of Tranexamic Acid in Trauma Emergency Resuscitation (MATTERs) Study**

- Retrospective observational study
- Surgical hospital in southern Afghanistan
- 896 patients, 293 received TXA
- Eligibility: patients receiving at least 1 U PRBC

**MATTERs Study**

- Dose: 1 gm TXA, repeated per clinician discretion
- Primary outcome measures: 24 hr, 48 hr, in-hospital mortality
- Secondary outcome:
  - Transfusion requirements
  - Coagulation parameters (PT, PTT)

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All cause mortality significantly reduced with TXA (14.5% vs 16.0%)

Risk of death due to bleeding significantly reduced (4.9% vs 5.7%)

-Treatment after 3 hrs increased risk of death from bleeding (4.4% vs 3.1%)

No difference in secondary outcome measures


Jonathan J. Morrison; MB, BCh, MRCs; Joseph J. Delene, MD; Todd E. Ramser, MD;
Mark J. Mahovlic, JMedSci, MD, FRCs
MATTERs Study

- Lower mortality (17.4% vs 23.9%)
  - TXA group more severely injured
  - No benefit until 48 hrs
  - Possible anti-inflammatory effect
- Benefit most significant among MTP patients
  - 14.4% vs 28.1%
  - TXA group independently associated with survival (OR 7.28) & less coagulopathy

TXA Complications

- Significant increase in mortality if administered after 3 hrs (CRASH-2)
  - Development/exacerbation DIC
- Increased incidence non-fatal thromboembolic events (MATTERs)
  - Greater injury severity

TXA Complications

- (?)Increased seizure risk
  - GABA antagonist lowers seizure threshold
  - Increased incidence in cardiac surgery pts
  - Dose effect (?)
  - No evidence in trauma

TXA Indications

- Incorporation into worldwide trauma protocols
  - World Health Organization Essential Drug
- Criteria for Treatment (?)
  - Empiric therapy
  - Mechanism
  - Clinical criteria
  - Physician discretion

Criteria for empiric treatment of hyperfibrinolysis after trauma

Matthew E. Kutcher, MD, Michael W. Cripps, MD, Ryan C. McCrary, BS, Ian M. Cusack, BS, Molly D. Greenberg, BS, Leslie M. Castello, BA, Brittany J. Bedick, BA, Mary F. Nelson, RN, MPA, and Mitchell Jie Cohen, MD, San Francisco, California

- 115 pts at Level I trauma center
- Blood samples collected on arrival
- 20% hyperfibrinolysis based on ROTEM
- Pts with hyperfibrinolysis:
  - Higher ISS, INR, PTT
  - Lower temperature, pH, platelet counts
  - Multi-organ failure (63.2% vs 24.6%)
  - Mortality (52.2% vs 12.9%)

TXA Indications

- Hyperfibrinolysis identified with any of following:
  - Hypothermia (T < 36)
  - Acidosis (pH < 7.2)
  - Relative coagulopathy (INR > 1.3, PTT > 30)
  - Relative thrombocytopenia (platelets < 200)
- 100% sensitivity, 55.4% specificity
  - Eliminated 46.6% of inappropriate therapy
  - Access to thromboelastography not necessary

TXA Benefits

- Mortality benefit:
  - Less severely injured: NNT = 67
  - More severe: NNT = 7
- Cost effective across all countries
  - Life yrs saved per 1000 trauma pts
    - 372 in Tanzania, 755 in UK
  - Cost per life yr gained
    - $48 in Tanzania, $64 in UK

Roberts I, et al. The CRASH-2 trial: a randomized controlled trial and economic evaluation of the effects of tranexamic acid. Health Technology Assessment. 2013; 17(10)

Future Research

- Mechanism of action
  - Effect on inflammatory pathway
- Thrombotic risk
  - MI
  - DVT, PE
- Seizure risk
  - Safety in TBI patients
Future Research

- Interactions with transfusion regimens & other hemostatic drugs
- Ideal dosing regimen, timing
  - avg dose 27 mg/kg (incl. 1 gm loading dose)
- Effect of renal trauma & dysfunction on drug clearance

TXA Summary

- Mortality benefit if given within 3 hrs of injury
- Dose:
  - 1 gm loading dose, (?) 1 gm over 8 hrs
  - Average 27 mg/kg
- Cost effective (1 g = $2.57 - $23)
- Maintain high suspicion
  - Thromboembolic events
  - Seizures

Background

- Vascular disruption with hemorrhage leading cause of preventable trauma deaths
- Difficult to achieve rapid vascular control in torso & pelvis
- Aortic cross-clamping via resuscitative thoracotomy traditionally used
- Intra-aortic balloon occlusion (IABO) suggested as alternative
Intra-Aortic Balloon Occlusion

- First reported in the Korean War
- Recently adapted for use in rapid control ruptured aortic aneurysms
  - Significant improvement in survival
- Not been widely introduced for trauma
  - Technologic limitations
  - Inadequate skill set
  - (?) Effectiveness


Proposed indications
- Hemorrhagic shock with refractory hemodynamic status
- Penetrating abdominal trauma
- Pelvic fracture causing hemorrhage
- (?) Loss of vital signs

Technique

- 5 steps
  - Arterial access
  - Balloon selection & positioning
  - Balloon inflation
  - Balloon deflation
  - Sheath removal


- Arterial access
  - Femoral artery
  - Percutaneous or open exposure
  - Sheath 5-8 Fr, 8-15 cm length

- Balloon selection & positioning
  - Soft, compliant large diameter balloon
  - Select zone of occlusion
  - Position using fluoroscopic guidance
**Aortic occlusion zones**
- Zone I: distal to left SC to celiac
- Zone II: celiac to lowest renal artery
- Zone III: infra-renal aorta to bifurcation

- Zone II: **NEVER** occlude
  - Mesenteric ischemia

**Balloon positioning:**
- Wire advanced to distal aortic arch under fluoroscopic guidance
- Appropriate sheath & balloon advanced to desired position

**Balloon inflation**
- 30-60 ml of 50:50 saline & contrast
- Inflate until edges change from convex to parallel
- Secure balloon/wire position

**Balloon deflation**
- Perform slowly in coordination with team

**Sheath removal**
- Balloon & wire removed
- Sheath flushed heparinized saline (1000 U/1 L)
- Remove sheath via open surgical exposure
  - Proximal & distal control
  - Flush w/heparinized saline
  - Repair arteriotomy
Multiple studies swine hemorrhagic shock model
- Significantly improved survival compared to controls (40 min occlusion)
- Increased MAP & cerebral perfusion, decreased bleeding & fluid resuscitation
- Tolerated up to 90 min of occlusion with adequate resuscitation
- No evidence cerebral or spinal ischemia

Comparison IABO vs aortic cross clamping
- IABO: less acidosis, lower fluid & pressor requirements
- Equivalent aortic pressure, carotid blood flow, brain oxygenation
- No histologic difference brain or cardiac tissue

Limited data in humans

- 21 hemodynamically unstable pts isolated penetrating abdominal trauma
- Successful occlusion in 20 pts
- 11 pts with successful operative control
- 7 pts survived to discharge
- Complications: ischemic lower extremity, catheter exit thru aortic injury (2)

Balloon occlusion infra-renal aorta shown to be effective at controlling hemorrhage in swine model and humans
Intra-Aortic Balloon Occlusion to Salvage Patients With Life-Threatening Hemorrhagic Shocks From Pelvic Fractures

- 13 pts with pelvic fx & hemorrhage
  - Too unstable for transfer from ER to IR suite
- Infra-renal occlusion without fluoroscopy
- Significant increase in SBP (70 mm Hg, p = 0.001)
- 12 pts became stable enough for transfer
  - 6 pts survived (46%)
  - 2 died after balloon deflation


References


Future Directions

- Unclear role in current trauma algorithms
- Increasing interest due to:
  - Improved technology
  - Greater angio availability (hybrid OR)
  - Development of new training courses
- More research needed

References