Emergency Medicine PRN Focus Session—High-Risk, High-Reward Interventions in Emergency Medicine

Activity Number: 0217-0000-15-120-L01-P, 1.50 hours of CPE credit; Activity Type: An Application-Based Activity

Monday, October 19, 2015
1:30 p.m. to 3:00 p.m.
Continental Ballroom 5

Note: This session is being recorded for future playback. A complimentary copy of these recordings will be available to all 2015 ACCP Global Conference on Clinical Pharmacy registrants approximately two weeks after the conclusion of the conference.

Agenda

1:30 p.m.
Push-dose Vasopressors for Low Blood Pressure--This is a pro/con debate.
Megan E. Musselman, Pharm.D., MS, BCPS
Clinical Pharmacist Specialist, Emergency Medicine/Critical Care, North Kansas City Hospital, Kansas City, Missouri

Meghan E. Groth, Pharm.D., BCPS
Emergency Medicine Pharmacy Clinician, The University of Vermont Medical Center, Burlington, Vermont

2:15 p.m.
Tranexamic Acid and Prothrombin Complex Concentrate for Traumatic Hemorrhage—This is a pro/con debate.
William E. Dager, Pharm.D., FCCP, BCPS
Pharmacist Specialist, Department of Pharmaceutical Services, University of California Davis Medical Center, Sacramento, California

Kelly Killius, Pharm.D., BCPS
Clinical Specialist - Emergency Medicine, Boston Medical Center, Boston, Massachusetts

Conflict of Interest Disclosures
William E. Dager: no conflicts to disclose.
Meghan E. Groth: no conflicts to disclose.
Kelly Killius: no conflicts to disclose.
Megan E. Musselman: no conflicts to disclose.

Learning Objectives

1. Evaluate evidence to support or refute the use of push-dose vasopressors in the emergency department.
2. Identify patient specific circumstances when the use of push-dose vasopressors would be appropriate or inappropriate.
3. Discuss dosing strategies for the use of push-dose vasopressors.
4. Explain potential adverse effects and safety issues with use push-dose vasopressors.
5. Evaluate evidence to support or refute the use of prothrombin complex concentrate in patients with traumatic hemorrhage.
6. Identify patient specific circumstances when the use prothrombin complex concentrate in patients with traumatic hemorrhage would be appropriate or inappropriate.
7. Evaluate evidence to support or refute the use of tranexamic acid in patients with traumatic hemorrhage.
8. Identify patient specific circumstances when the use tranexamic acid in patients with traumatic hemorrhage would be appropriate or inappropriate.

Self-Assessment Questions

Self-assessment questions are available online at www.accp.com/gc15.
Learning Objectives

- Evaluate evidence to support or refute the use of push-dose vasopressors in the emergency department
- Identify patient specific circumstances when the use of push-dose vasopressors would be appropriate or inappropriate
- Discuss dosing strategies for the use of push-dose vasopressors
- Explain potential adverse effects and safety issues with use push-dose vasopressors

Conflict of Interest

- Megan Musselman and Meghan Groth have no conflicts of interest to disclose

Audience Poll #1

- How many have used or currently use push-dose vasopressors in their practice?

Audience Poll #2

- How many support the use of push-dose vasopressors in their practice?

Megan Musselman, PharmD, MS, BCPS

Self-Assessment Question

Which of the following sequelae is the most appropriate reason to avoid hypotension in the peri-intubation period?

- A) Increased hospital days
- B) Increased mortality
- C) Reduced neurologic function
- D) Reduced mechanical ventilation days

Push-Dose Vasopressors

- Increase blood pressure and contractility
  - ↑ cardiac output, ↑ tissue perfusion
- Transient hypotension
  - Reversible cause
    - Atrial fibrillation, procedural sedation, hypoxemia
  - Reduce post-intubation hypotension
  - Increased mortality and ICU LOS
- Temporizing measure
  - Placement of central line

Self-Assessment Question

What receptors does phenylephrine act on to increase blood pressure?

- A) Alpha
- B) Beta
- C) Dopamine
- D) Vasopressin

Self-Assessment Question

Which of the following represents the recommended final concentration of phenylephrine, if push-dose phenylephrine is to be used?

- A) 10 mcg/mL
- B) 10 mg/mL
- C) 100 mcg/mL
- D) 100 mg/mL
**Push Dose Phenylephrine**

- **MOA:**
  - Pure alpha agent
- **Onset:**
  - < 1 minute
- **Duration:**
  - 5-20 minutes
- **Dosing:**
  - 0.5-2 mL (50-200 mcg) every 1-5 minutes

- **Preparation:**
  - Take 100 mL IVPB bag of normal saline (NS) and withdraw and waste 10 mL
  - Add 1 mL of phenylephrine 10 mg/mL
  - Final concentration: 100 mcg/mL
  - Affix a label to the bag

**Self-Assessment Question**

- Cardiac epinephrine syringes are used to prepare push-dose epinephrine. What is the concentration of epinephrine in these pre-made cardiac syringes?
  - A) 1:100
  - B) 1:1,000
  - C) 1:10,000
  - D) 1:100,000

**Push Dose Epinephrine**

- **MOA:**
  - alpha1, alpha2, beta1, beta2 effects
- **Onset:**
  - < 1 minute
- **Duration:**
  - 5-10 minutes
- **Dosing:**
  - 0.5-2 mL every 1-5 minutes

- **Preparation:**
  - Take 10 mL syringe and fill with 9 mL of NS
  - In the syringe with 9 mL of NS, draw up 1 mL of epinephrine from the cardiac epinephrine amp (1:10,000)
  - Final concentration: 10 mcg/mL (1:100,000)
  - Affix a label to the bag

**Self-Assessment Question**

- A 40-year-old male presents to the ED in rapid atrial fibrillation. Patient's vitals are heart rate 156 bpm, blood pressure 72/56 mmHg, O2 saturation 97%. The emergency medicine physician wants to administer a push-dose pressor to increase the patient's blood pressure prior to pharmacological cardioversion. Which one of the following options is best to be administered as a push-dose pressor for this patient?
  - A) Norepinephrine
  - B) Phenylephrine
  - C) Vasopressin
  - D) Dopamine

**Evidence**

- OR
  - Agents:
    - Phenylephrine
    - Ephedrine
  - EMCrit
    - "Used for > 13 years in 100s of patients with no negative outcomes," Scott Weingart, MD
- EMRAP

**Evidence in the ED**

- **Study participants:**
  - N = 119
- **Design:**
  - Retrospective study
- **Methods:**
  - Chart review of hypotensive, adult patients requiring intubation in an academic ED from February 2011 to February 2012
Data collection

- Demographics
- Admitting diagnosis, comorbidities, reason for intubation and intubation medications
- Utilization of push-dose pressors or vasopressors in the peri-intubation period
  - Defined as 30 minutes before or after intubation

Results

- 17% (20/119) received push-dose phenylephrine
  - 65% received multiple doses
  - 70% received continuous infusion vasopressor therapy

<table>
<thead>
<tr>
<th>Heart Rate (beats/min)</th>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-PE 114 (99-130)</td>
<td>73 (67-78)</td>
<td>42 (35-48)</td>
</tr>
<tr>
<td>Post-PE 115 (101-130)</td>
<td>93 (80-105)*</td>
<td>52 (44-58)*</td>
</tr>
</tbody>
</table>

Table I. Effect of Peri-intubation Phenylephrine Push-dose Treatment

Side-by-Side Assessment of Time to Administration

Study participants:
- N = 11; 4 pharmacists, 5 nurses and 2 pharmacy students

Design:
- Multi-center, observational, crossover study

Methods:
- Instructions were provided describing how to make push dose epinephrine and IVPB epinephrine
- Participants were timed from beginning of preparation until delivery of medication to patient

Preparation and administration instructions

Epinephrine 1:100,000 / 10 mcg/mL Push Dose Pressor
- Take 10 mL syringe and fill with 9 mL of NS
- In the syringe with 9 mL of NS, draw up 1 mL of epinephrine from the cardiac epinephrine amp (1:10,000)

Epinephrine 4mg/250mL Continuous Infusion
- Withdraw 4mg from the 1mg/mL epinephrine multi-dose vial
- Inject 4mg of epinephrine into a 250mL NS bag
- Attach IV primary tubing to the epinephrine continuous infusion
- Attach medication to the IV pump to be administered at a rate of 1 mcg/min.

Push vs. Pump

- Quicker delivery and onset
- Less time consuming to administer
- Rapid stabilization allowing patient to receive necessary procedure
  - i.e., intubation, pharmacological cardioversion
- Less risk of extravasation

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Meghan Groth, PharmD, BCPS

Fresh Out of Residency

- Meet Hector

Meet @EMCrit

Learning From the Master

EPINEPHRINE
Has alpha and beta1 effects so it is an inosprror
Do not give cardiac arrest doses (1 mg) to patients with a pulse

Mixing Instructions:
- Take a 10 ml syringe with 9 ml of normal saline
- Into this syringe, draw up 1 ml of epinephrine from the cardiac amp (Cardia amp contains Epinephrine 100 mcg/ml)
- Now you have 10 ml of Epinephrine 10 mcg/ml

Onset: 1 minute
Duration: 5-10 minutes
Dose: 0.5-2 ml every 2-5 minutes (5-20 mcg)

Where’s the Evidence?

- Can you extrapolate?

ED ≠ OR

Why Not?
Many Responsibilities

- Secure ABCs
- Airway
- Maintain circulation
- Teaching students/residents
- Team leader
- Delegation of tasks
- Algebra?

Self-Assessment Question

- A syringe labeled epinephrine 0.1 mg/mL is using which of the following to express strength?
  - A) Ratio strength
  - B) Specific gravity
  - C) Percentage strength (w/v)
  - D) Mass concentration

Epinephrine is Confusing!

- Ratio strength
  - 1:1,000 or 1:10,000
- Mass concentration
  - mcg/mL or mg/L

- Physicians mess up too!
  - RCT of sim lab w/ physicians
  - 13X more likely to err if ratio strength used

Self-Assessment Question

- Which of the following represents the recommended final concentration of epinephrine if “push dose epi” is to be used?
  - A) 1:100
  - B) 1:1000
  - C) 1:10,000
  - D) 1:100,000

Unnecessary Complexity

- Example
  - RSI meds
    - Etomidate and succinylcholine
    - Push-dose pressors
What Could Go Wrong?

- In patients with a pulse:
  - MI
  - Dysrhythmias
  - Intubation
  - AKI → transplant
  - ICU admission

Any Other Options?

- Alternative agents for RSI
- Smart pump technology + vasopressor infusions

Self-Assessment Question

- Which of the following is the most concerning adverse effect that has been associated with inappropriate IV epinephrine administration?
  - A) Extravasation
  - B) Cardiac dysrhythmias
  - C) Acute kidney injury
  - D) Endotracheal intubation

ROUND #2
Not straying too far off the beaten path
- Extrapolation
  - Animal studies
  - Pediatrics
- Study participants
  - Hemodynamically unstable, adult patients

Avoidance of Errors
- Pre-made syringes
- Pre-defined mixing instructions
  - Laminated cards, education
- Pharmacists at bedside

Any Data From the ED?
- Retrospective chart review
  - Intubated, hypotensive adults
  - 20 patients received PE peri-intubation
  - 70% received vasopressor infusion
- “To treat general hypotension without focused interventions on specific disease processes”

Audience Poll #3
- How many will still use or start using push dose pressors in their practice?

Audience Poll #4
- How many will stop using or still won’t use push dose pressors in their practice?

2015 ACCP Global Conference on Clinical Pharmacy
Emergency Medicine PRN Focus Session—High-Risk, High-Reward Interventions in Emergency Medicine
October 19, 2015
Tranexamic acid and prothrombin complex concentrates for traumatic hemorrhage: PRO
William Dager
Date: Monday, October 19th

Learning Objectives

Tranexamic acid and prothrombin complex concentrates for traumatic hemorrhage: PRO
William Dager, Pharm.D., BCPS (AQ Cardiology)
FCSHP, FCCP, FCCM, FASHP, MCCM
Pharmacist Specialist: U C Davis Medical Center
Clinical Professor of Pharmacy, UC San Francisco School of Pharmacy
Clinical Professor of Medicine, UC Davis School of Medicine
Clinical Professor of Pharmacy, Touro School of Pharmacy

No conflicts to disclose.

Conflict of Interests

- No Conflicts of Interest

Assess the Situation

- Bleeding? Scan patient
  - Site: risk of a complication
- Assess Urgency of Situation
  - Eminent life threatening vs some time
- Contributors for bleeding
  - Bleeding Complication Risks
    - Ability to Manage/Treat Agents: Anticoagulants or Antiplatelet
      - Laboratory assay
      - Level of effect present
      - Need to restart

Assessing Risk

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Consider the Patients Entire Needs

- Stop Bleeding
  - Surgery/Stitches etc, Fresh Frozen Plasma (FFP), Platelets, Fibrinogen, Recombinant activated Factor VII (rFVIIa)/Prothrombin Complex Concentrates (PCC), Tranexamic Acid (TXA)
- Replace losses (Calcium too)
  - Transfusion Reaction Risks
- Optimize management of co-morbid situations
- Create a plan and request necessary follow up
- Evaluate risks for therapy complications

Tranexamic Acid

- Inhibits Enzymatic breakdown of fibrin
  - Blocks lysine binding sites on plasminogen
  - Prevents plasminogen ability to bind to fibrin
  - Inhibits plasminogen conversion to plasmin
- Surgery: Commonly used as proven to decrease surgical bleeding and transfusion requirements

CRASH-2 Trial

<table>
<thead>
<tr>
<th>Mortality Outcomes</th>
<th>TXA</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any cause of Death</td>
<td>14.5%</td>
<td>16%</td>
<td>0.0035</td>
</tr>
<tr>
<td>Bleeding</td>
<td>4.9%</td>
<td>5.7%</td>
<td>0.0077</td>
</tr>
<tr>
<td>Vascular Occlusion</td>
<td>0.3%</td>
<td>0.5%</td>
<td>0.096</td>
</tr>
<tr>
<td>Multiorgan Failure</td>
<td>2.1%</td>
<td>2.3%</td>
<td>0.25</td>
</tr>
<tr>
<td>Head Injury</td>
<td>6.0%</td>
<td>6.2%</td>
<td>0.60</td>
</tr>
<tr>
<td>Other Causes</td>
<td>1.3%</td>
<td>1.4%</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Timing to therapy is a issue: CI ≤ 1.0 if administered within 3 hours
- Penetrating Injury slightly better than blunt trauma

Other Trauma Experiences with TXA

- CRASH-2 - Assessment based on baseline risk for death
  - Benefit with TXA within 3 hrs greatest in the higher risk groups, but also seen in lower risk groups.
- CRASH-2 – Intracranial Bleeding Study (n=270)
  - Traumatic brain injury: Hemorrhage growth lower with TXA.
  - Wide CI noted but TXA was not associated with any harm.
- MATTERs - Combat related injury in Afghanistan (n=896)
  - TXA within 1 hr of injury part of major hemorrhage protocol in 2010
  - PT > 18 sec or aPTT > 55 sec
  - Reduction in: Mortality – 6.5%, Massive Transfusion 13.7%; RR = 49%

TXA Trials: 187 trials

- CRASH 3/STOP-AUST/Univ. Washington Pre-Hospital Use:
  - Use in traumatic head injury/ICH underway: (Target N > 10,000)
- PATCH: Pre-hospital administration using CRASH II dosing (Australia)

The question that TXA is overall beneficial in bleeding patients is YES

Now we are exploring earlier administration and specific bleeding situations

CRASH-2 trial collaborates Lancet 2010;376:23-32

CRASH-2 trial collaborates Lancet 2010;376:23-32


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Concentrated Blood Factor Products in USA

<table>
<thead>
<tr>
<th>Brand Names</th>
<th>rFVIIa</th>
<th>3-Factor PCC (PCC3)</th>
<th>4-Factor PCC (PCC4)</th>
<th>aPCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>NovoSeven®</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Bebulin VH®</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Profliline SD®</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Kcentra®</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>FEIBA®</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Factors Provided

- VIIa II, IX, X (Some VII)
- II, VII, IX, X (VIIa)

Activated?

- Yes
- No

Some PCC’s (Kcentra) contain Heparin

Other Considerations

**General** use of PCC in Trauma remains Controversial.

How would you know:
- Congenital or acquired clotting factor deficiency
- Presence of a anticoagulant


PCC 4 for Warfarin Reversal (Kcentra®)

Phase III Prospective Open label, Randomized – n=212 – On VKA with Acute major bleeding

- 25 units/kg (INR > 2 – <4); 35 units/kg (INR 4-6); 50 units/kg INR >6

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Initial INR</th>
<th>INR 30 min</th>
<th>1% event</th>
<th>Effective Hemostasis (24hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCC4</td>
<td>3.9 (1.8 – 2.0)</td>
<td>1.2 (0.9-6.7)</td>
<td>8.7%</td>
<td>72%</td>
</tr>
<tr>
<td>Plasma</td>
<td>3.6 (1.9 – 3.9)</td>
<td>2.4 (1.4 – 1.1)</td>
<td>5.5%</td>
<td>65%</td>
</tr>
</tbody>
</table>

- Hemostatic efficacy similar to plasma at 24 hr
  - PCC4 superior 62% vs 9.6% in achieving INR < 1.3 within 30 min
  - Risk circulatory overload vs plasma (8.7% vs 19.3%)

NOTE: Delay for Consent and Randomization

Prescribing Information Kcentra

Managing Warfarin Related ICH: Reversal, Blood Pressure and Resumption

- INR Reversal (N=1004); Follow Up Imaging – N=853
- PCC 2,000 (1200 – 2400) Units given (3/4 received Vit K)
  - INR < 1.3 within 4 hours of admission → Hematoma Enlargement

- INR:
  - PCC 2.79 → 1.27
  - FFP 2.2 → 1.66

- Hematoma Enlargement: PCC - 36%; FFP - 45%
- Insufficient power for significance – Low FFP numbers

Kuramatsu JB et al JAMA 2015;313:824-36

ICH in geriatric patients with life threatening bleed

- New Protocol (n=29): 3 Factor PCC 25 units/kg for INR > 1.5
  - FFP if follow-up INR is > 1.5
- Historical Control (n=31)

- Protocol:
  - Faster INR reversal – (p < 0.001)
  - Less FFP required – (p < 0.001)
  - Time to INR < 1.5 (p = 0.036)
  - Decreased incidence or ICH progression (p = 0.031)

Edavettal Am Surg 2014;80:372-4

Concentrated Clotting Factors with non-Vitamin K related oral anticoagulants

- In-Vitro Data observations vary and depends on parameter measured.
  - Results inconsistent.
  - May not mimic bleeding patient
  - Many very high doses explored
  - Independently drives hemostasis – does not remove the anticoagulant
  - Unclear what dose should be used, or need to be repeated if anticoagulant effects persist

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PCC and Bleeding with New Oral Anticoagulants

- PCC: Case with some success, Thromboembolic Events rare.
- aPCC: Several case reports/series suggesting potential ability to rapidly stop major bleeding without complications. Also low dose (8-14 units/kg) for dialysis catheter insertion with dabigatran and stopping massive GI Bleeds on rivaroxaban. Guidelines available suggest using a PCC or aPCC if available
- Dose unclear, but PCC/aPCC may be a option until antidotes are available


Getting Drug to the patient

Patient Arrives
- Situation assessed, Medication History, Labs
- Treatment decided
- Medications Ordered
- Pharmacy Processes Order
- Ordered Medications sent to patient
- Medication Infused

Management Considerations

- Establish a standard approach
  - Choose what agents and tests should be used
  - Adaptable to severity of situation
  - Re-assess and adjust therapy
  - Avoid Delays
- Urgency of situation
  - Is their time to use lower doses and titrate to effect ?
  - Manage comorbid conditions
- Think of long term consequences
  - VTE risk and need for prophylaxis
  - Re-initiating anticoagulation therapy

Closing Statement

- Early TXA is a beneficial cost effective therapy for large traumatic hemorrhage, especially if given early.
- PCC’s for general traumatic bleeding has not been established and use is controversial.
- PCC may have a place in selected traumatic bleeding situations: Hemophilia (rare) and presence of oral anticoagulation (common).
Rebuttal

- Matters Trial: Increased PE and DVT with TXA
  - However, Mortality rate was 6.5% lower (p=0.03)
- Of note: Risk for thromboembolism will increase over time post injury, and benefits of TXA will decline. That is for those who survive or don’t have additional bleeding related co-morbid complications.

Literature supporting the “CON”

Valle EJ et al: J Trauma Acute Care Surgery 2014;76:1371-1378

- Ryder Trauma Center: No TXA Benefit - However, they have...
  - Fast Transport
  - Higher elderly population
  - Early surgical intervention
  - Earlier fluid/blood products
- Commentary for Dr. Dudaryk MD from Ryder Trauma notes the lack of differences in the PROPPR trial on transfusion ratios may have been influenced by the use of TXA (http://www.asahq.org/resources/publications/newsletter-articles/2015/june-2015/a-proppr-answer)

Literature supporting the “CON”

Harvin JA et al: J Trauma Acute Care Surgery 2015;78:905-9

- Trauma patients with hyperfibrinolysis
- TXA group was slightly Older (37 vs 32 yo), Higher ISS (29 vs 14), lower SBP (103mmHg vs 125 mmHg), more likely in shock. All P < 0.05
- No differences in VTE; TXA higher unadjusted mortality, but not significant post logistic regression analysis.

Literature supporting the “CON”


- TXA patients had > injury severity, in shock and coagulopathic.
  - TXA associated with reduction in Multisystem Organ Failure (p=0.01)
  - “TXA as part of a major hemorrhage protocol within a mature civilian trauma system provides outcome benefits specifically for severely injured shocked patients.”

Rebuttal

- Low Fibrinogen associated with increased blood loss/transfusions requirements, increased injury severity score, dilution and shock
- Cryoprecipitate or FFP are options used, but must be thawed and can’t be given as easy pre-hospital
- Fibrinogen Concentrates: Can be given rapidly, but data is limited
- Trauma Bleeding Guidelines include PCC for emergency reversal of Vitamin K antagonists and PCC or aPCC for non-Vialmin K oral antagonists

So what occurs at Boston Medical Center


- TXA was considered in MTP …within 8 hours of traumatic injury, were 15 years of age or older, weigh at least 40 kg
- Conclusion: “Multidisciplinary collaboration and standardization of tranexamic acid use in conjunction with an MTP promoted use of the drug within a trauma population.”
OK - Lets see what you would do

Please Raise Your Hand if your Hospital (If it had a Product):

- No – I Would NOT Administer Tranexamic Acid to a patient with major traumatic bleeding!

- Yes – I Would Administer Tranexamic Acid to a patient with major traumatic bleeding!

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Tranexamic acid and prothrombin complex concentrate for traumatic hemorrhage: CON
Kelly Killius, PharmD, BCPS
10/19/15

Learning Objectives
- Evaluate evidence to refute the use of tranexamic acid (TXA) in patients with traumatic hemorrhage
- Identify patient specific circumstances when the use tranexamic acid in patients with traumatic hemorrhage would be inappropriate
- Evaluate evidence to refute the use of prothrombin complex concentrate (PCC) in patients with traumatic hemorrhage
- Identify patient specific circumstances when the use prothrombin complex concentrate in patients with traumatic hemorrhage would be inappropriate

CRASH II
- Largest trial
  - Variety of patients included
- Mortality benefit with TXA, RR 0.91
  - Due to hemorrhage, RR 0.85
- No difference in rate of VTE

Why CRASH II is not perfect
- Severity of Injury
  - Lack of assessment
  - 68% included had SBP 90 or higher
  - Low blood requirements
- Lack of fibrinolysis/coagulopathy assessment
  - Role of TEG, ROTEM?
  - MATTERs utilized PT/INR
  - Area for more research

MATTERs and II
- Mortality benefit in overall and MT cohort
  - Military
  - Penetrating trauma
  - Treated within 1 hour of injury
- Higher VTE risk
  - Injury severity + blood requirements
  - State of coagulopathy
- Use of Cryoprecipitate (Cryo)
  - Should we be using more and earlier?
Real World Experience

- Mortality benefits not seen
- Similar criteria for use but those included were different
  - Older (mean age 40s)
  - High injury severity
  - Low GCS
  - Higher transfusion requirements
- Varying VTE incidence

Anticoagulants

- Warfarin
- Dabigatran
- Apixaban
- Rivaroxaban

PCC in Trauma

- Given with fibrinogen
- TEG/ROTEM guided initiation and continuation
- Dose variability
  - 20 – 30 units/kg
  - 1000 – 1500 units

PCC Questions

- Limited evidence in non-anticoagulated patients
- Safety of co-administration with TXA
- Time from injury

Remaining Unknowns

- TXA
  - Current anticoagulation
  - Severity of injury
  - Objective fibrinolysis testing
  - Age extremes
- PCC
  - Immediate use
  - Without blood products
  - With TXA