Trauma and Injury Subcommittee

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Defense Health Board
14 June 2011

TACEVAC Discussion

- **MEDEVAC: Red Cross-marked dedicated air ambulance – no guns, no armor**
- **CASEVAC – tactical aircraft - no Red Crosses but HAVE guns and armor**
- **TACEVAC – includes both MEDEVAC and CASEVAC**

Theater TACEVAC Capabilities

- DustOff
  - Army
  - HH-60
  - One EMT-B flight medic
- Pedro
  - USAF
  - HH-60
  - Two PJs (paramedics)
  - Relatively limited in number
- UK MERT

UK Medical Emergency Response Team (MERT)

- CH-47 platform
- EM or Critical Care physician
- 2 EMT-Ps and Crit Care Nurse
- Routine plasma:PRBCs in flight when needed
- Advanced airways and RSI
- Ketamine analgesia
- Chest tubes and thoracotomies with aortic cross-clamping
- Tranexamic acid
- Only one; used for most critical casualties

JTTS VTC Case 1

- 21 y/o male
- Dismounted IED blast
- Injuries: splenic lacerations, transected colon, liver lacerations, pancreatic contusion, diaphragmatic perforation, left 8-11 rib fractures, left scapula fracture, BL upper extremity injuries
- CAT TQ to right arm by ground medic
- Severe pain and agitation in flight
- In shock on admission to ED: BP 70 palpable; Base Excess -8
- Complications: anuric renal failure and mucormycosis infection
- Undergoing dialysis at Walter Reed

JTTS VTC Case 1

- **TACEVAC Flight medic: One EMT-<u>Basic</u> qualified medic**
- **No IV or IO access obtained**
- **No plasma or blood given in flight**
- **No Hextend given in flight**
- **No prehospital analgesia**
- **No documentation of length of flight**
- **No documentation of hypothermia prevention or antibiotics**

JTTS VTC Case 2

- 24 y/o male
- Dismounted IED blast
- Bilateral lower extremity amputations
- Right hand injury
- Soft tissue groin injuries
- Shrapnel peppering of face
- CAT TQ x 2 to right leg on ground

JTTS VTC Case 2

- Flown by MERT
- CAT TQ to left leg in flight
- Rapid sequence intubation
- Sternal IO
- Humeral IOs
- 3 units fresh frozen plasma
- 3 units PRBCs
- TXA 1 gm

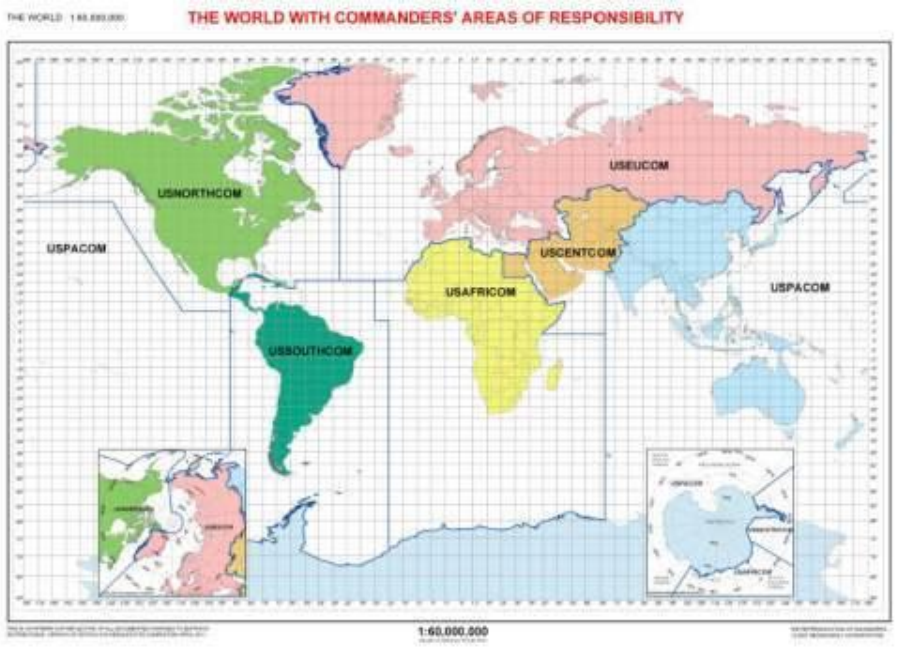
TACEVAC Recommendations

Develop a U.S. Advanced TACEVAC Capability

- Team and equipment structured after the successful MERT model insofar as possible
- Critical-care trained and experienced personnel
- Most capable aircraft available designated for evacs
- Routine PRBCs and plasma in 1:1 ratio – definitive
- resuscitation in flight
- Advanced airways
- IV medications
- Advanced interventions

Advanced TACEVAC Capability

- Field in the near term on a limited basis as pilot
- - Where feasible and there is a high probability
- of critical casualties
- - Use for the most critical casualties
- - Enables a tiered response when needed
- Document the outcomes
- Injury severity subgroups
- Decide about system-wide
- changes based on
- outcomes
- Think beyond Afghanistan



Advanced TACEVAC Capability

More capable platforms when available - MH-47, CH-53, or MV-22 platforms vs HH-60

- Ability to walk around casualty
- Access to both sides of casualty
- Enables better care
- White light capability when possible

Advanced TACEVAC Capability: Concept Support

- USMC Forces forward
  - Urgent UNS submitted to MCCDC
- JTTS Deployed Evacuation Care Director
- OTSG DCBI Task Force
- CoTCCC
- Trauma and Injury Subcommittee

TACEVAC Recommendations

Optimize TACEVAC response time

- **SecDef-directed 60-minute max**
- **Plan for optimized response time**
- **Faster transport to optimal care may be lifesaving for critical casualties**
- **Critical issue in immature theaters**
- **Right patient, right care, right platform, right facility**

TACEVAC Recommendations

Hostile Fire Evacuation Option

- Should be identified in planning phases
- Supplement dedicated MEDEVAC platforms
- Armed, armored aircraft with no Red Crosses
- Avoids evacuation delays due to ground fire
- Modular medical packages
- for aircraft of opportunity
- Concept used in Special
- Operations TF planning
- in 2003

TACEVAC Recommendations

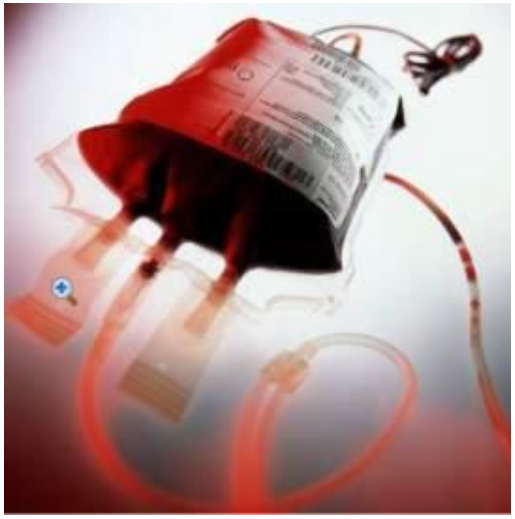
<u>In-flight care providers that meet or exceed the civilian standard</u>

- Critical care flight-trained paramedic, or
- Critical care flight-trained nurse, or
- Critical care flight-trained physician
- CCFT trained PAs also an option
- At least 2 of the <u>above</u> providers per platform when transporting critical casualties
- At least 1 of the <u>above</u> providers per critical casualty

TACEVAC Recommendations

<u>Routine</u> availability of PRBCs and plasma on TACEVAC platforms for critical casualties

- Limit amount of crystalloid infused
- Hypotensive resuscitation with Hextend if no blood is available



TACEVAC Recommendations

Pre-Deployment Trauma Experience for TACEVAC Providers in Evacuation Units

- Ongoing ICU/trauma experience
- Service Trauma Training Center rotations
- Other trauma rotations
- TCCC training
- Primary focus of deployment work-up for designated personnel
- Metric? (as per CCATT)
- Medic skills sustainment on Commander's USR (unit status report)

TACEVAC Recommendations

Standard Protocol for TACEVAC care

- **Outlined in TACEVAC section of TCCC Guidelines**
- **Should be the theater standard for evacuation care**
  - **- Evidence-based**
  - **- Reviewed quarterly and modified as necessary**
  - **- Periodically upgraded along with rest of guidelines**

TACEVAC Recommendations

Oversight of TACEVAC Care in Theater

- Qualified EMS medical direction oversight
- Prehospital cell part of the deployed JTS team
- Prehospital cell as part of JTS home structure

TACEVAC Recommendations

Improve Documentation of TACEVAC Care

- TCCC card from ground medic
- NATO card for flight portion
- Reliable entry into Joint Theater Trauma Registry (JTTR) and Electronic Medical Record
- Enhance prehospital data fields in JTTR
- Integrate with unit-based Prehospital Trauma Registry
- Integrate with Armed Forces Medical Examiner's office data
- Flight care documentation on Commander's USR (unit status report)

TACEVAC Recommendations

Physician oversight in TACEVAC units

- **Medical officer must be trained and experienced in trauma care**
- **Must be trained in TCCC**
- **Trauma skills sustainment on Commander's USR (unit status report)**

TACEVAC Recommendations

<u>Standardized TACEVAC capability</u>

- **Should be <u>joint</u> requirement**
- **Not all services need to provide, but all service casualties should receive same standard of care**

TACEVAC Recommendations

Process Improvement

- Flight reviews of TACEVAC care should
- be part of JTTS QA
- Depends on documentation
- “No prehospital data” should be a trigger
- for follow-up

Summary

All necessary steps should be taken to implement the preceding recommendations in the near term to ensure that our nation's combat casualties receive care that meets or exceeds the civilian standard.

All of the above recommendations were made by the CoTCCC and unanimously endorsed by the Trauma and Injury Subcommittee of the DHB.

Questions?

Dried Plasma

Background

- **Hemorrhage is the leading cause of potentially preventable death in combat**
- Coagulopathy increases the risk of hemorrhagic death
- Crystalloids and colloids dilute existing clotting factors in the blood
- **Plasma replaces clotting factors lost through hemorrhage. PRBCs do not. Crystalloids do not.**

Background

- **Coagulopathy worsens outcomes in TBI casualties as well as those with uncontrolled hemorrhage.**
- **Causes of coagulopathy in combat casualties:**
  - **Hypothermia (especially in shock)**
  - **Large volume crystalloid resuscitation**
  - **Platelet-inhibiting drugs (aspirin and other NSAIDs such as ibuprofen)**
  - **Acidosis (associated with shock)**
  - **Intrinsic**

Background

- **One of the dramatic advances in the care of trauma patients realized from the U.S. experience in Afghanistan has been the use of higher ratios of plasma to red blood cells in casualties requiring massive transfusions.**
- This increased emphasis on in-hospital plasma is now the standard of care for the military and is rapidly being adopted by the civilian sector.

Large Volume Crystalloids: A Fading SOC

- **There is a growing body of evidence that the historical standard of prehospital fluid resuscitation with large volume crystalloid worsens outcomes.**
- **NO RCTs of LR or NS have shown a benefit**
- **Potential mechanisms for worsened outcomes: longer time on scene, dilutional coagulopathy, and restoration of normal blood pressure in the presence of an unrepaired vascular injury with resultant increased blood loss.**
- **Prehospital plasma is an extension of definitive resuscitation in the ED.**

Mortality in Trauma

- 600% increase – with coagulopathy in combat casualties requiring a transfusion (Niles)
- 428% increase – remote location vs urban (Fatovich)
- 291% increase – from blunt head trauma with coagulopathy (Wafaisade)
- 245% increase - early deaths with coagulopathy (Mitra)
- 209% increase – more than 1.5 L of crystalloid (Ley)
- 44% increase - IV or IV fluids in shock patients (Haut)
- 29% increase – IV fluids in shock patients (Bickell)

----------Baseline----------

Coagulopathy and TBI

- 291% increase – in mortality from blunt head trauma with coagulopathy (Wafaisade)
- 285% increase – in Grade III and IV intracranial hemorrhage with antiplatelet agents (Ivascu)
- 270% increase - in intracranial lesions with ASA or ibuprofen (Fabbri)
- 41% increase – in progression of intracranial hemorrhage with coagulopathy (Allard)

----------Baseline----------

Fluid Resuscitation: Summary

- **Large Volume Crystalloids**
  - **<u>Increase</u> mortality**
  - **<u>Worsen</u> coagulopathy of trauma and TBI**
- **Hypotensive Resuscitation with Hextend**
  - Better logistically (less weight) **BUT**
  - Improved survival over LR not well established
  - Does not treat coagulopathy
- **Liquid plasma**
  - The **standard of care** for treating coagulopathy
  - Increases survival as part of DCR

Advocates for Prehospital Plasma

- Mayo Clinic
- Memorial Hermann – Houston
- U. S. Special Operations Command
- US Army Special Operations Command
- Army Surgeon General's DCBI Task Force
- Army Special Missions Unit
- Navy Special Missions Unit
- U.S. Army Institute of Surgical Research
- Committee on TCCC
- DHB Trauma and Injury Subcommittee
- French, German, British militaries

Earlier Thawed Plasma

Placement of thawed plasma in the Emergency Department vs having to request it from the Blood Bank has been done at Memorial Hermann in Houston and has resulted in shorter time to first transfusion (42 min vs 83 min), reduction in subsequent transfusion requirements, and increased 30-day survival (86% vs 75%).

Cotton

ATACCC 2011

Presented at February 2011 CoTCCC Meeting

Pre-Hospital Thawed Plasma: A Preliminary Report

Smoot DL, Park MS, Berns KS,
Osborn JB, Jenkins DH, Zietlow SP

Mayo Clinic
Rochester, MN

MAYO CLINIC

Our Rationale

- Current evidence supports increased ratio of plasma:PRBC and early use of plasma in trauma
- Packed Red Blood Cells (PRBCs) and plasma are optimal resuscitative fluids for patients with serious hemorrhage and/or impairment of coagulation
- Emergency use of Fresh Frozen Plasma is limited by time to thaw (15-30 minutes)

CONCLUSION

- We successfully implemented pre-hospital thawed plasma use into our rural Level-I trauma system
- Initial results (e.g. feasibility, INR reduction), while not conclusive, are promising
- Feasibility studies now underway to see if the protocol can be expanded to other transports in our system

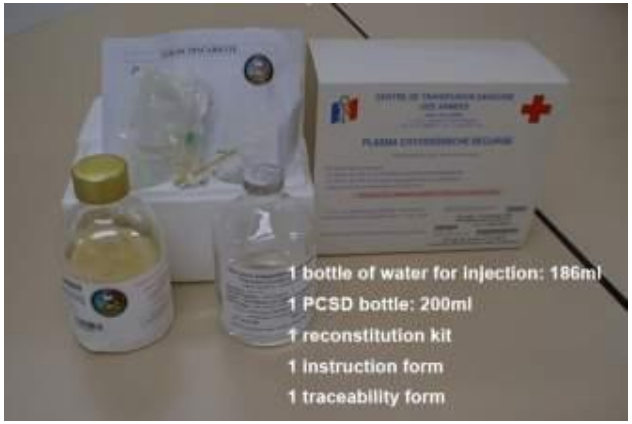
Prehospital Plasma for Ground Medics, Corpsmen, PJs

- Liquid plasma not an option for ground troops
- Dried plasma (freeze-dried or spray-dried) is currently the best option for units not able to utilize liquid plasma
- Dried plasma contain approximately the same levels of clotting proteins as liquid plasma
- **French, German, British militaries are using freeze-dried plasma at present**
- Outcomes data pending

FDA-Approved Dried Plasma Product

- None at present
- HemCon freeze-dried product in Phase I trials
- Entegrion - pooled spray-dried product in development
- Velico – single donor spray-dried plasma system in development
- Arrival of an FDA-approved dried plasma product is not imminent – ETA 2015 or beyond
- A solution is needed now
- Think beyond Afghanistan - especially for SOF and other early entry forces in the next conflict

French FDP - PCSD



- Produced in it's present form since 1994
- Used only by its military; shelf life 2 years
- Universal donor and pH buffered; no adverse events in 8 yrs
- Produced from pools of 5 – 10 donors
- Previously held for 8 weeks prior to re-testing and release
- Now confident of their Cirus pathogen intercept technology and have suspended the quarantine
- $800 per unit

German FDP - LyoPlas

- Each unit of LyoPlas is drawn from only one donor
- Tested for all pertinent bloodborne pathogens; quarantined for 4 months until the donor is re-tested.
- Type specific; shelf life 1.5 years
- Must be reconstituted with buffering solution, since it is alkaline as supplied
- $100 per unit

United States Special Operations Command Memo

UNITED STATES SPECIAL OPERATIONS COMMAND
OFFICE OF THE COMMANDER
7701 TAMPA POINT BOULEVARD
MACDILL AIR FORCE BASE, FLORIDA 33621-5323

July 1, 2010

The Honorable Charles Rice
Assistant Secretary of Defense, Health Affairs
1200 Defense Pentagon
Washington, DC 20301-1200

I am requesting a waiver to the Health Care policy regarding non-Food and Drug Administration approved blood products. The specific product is freeze-dried plasma, currently being fielded and used by German medical units in the existing theaters of operation. I am seeking this waiver as our Special Operations medics are often the sole medical providers in remote and austere locations where SOF frequently operate-many of which are beyond the range of immediate medical evacuation and access to surgical care. Within these environments, German certified freeze-dried plasma would serve as a critical enabler in reconstituting blood in cases of traumatic loss, specifically at the point of injury. Although we are monitoring an American company's development of freeze-dried plasma, the German product offers an immediately-available, modality-proven, clinically tested, and very low-risk interim capability.

U.S. Navy Perspective

UNITED STATES SPECIAL OPERATIONS COMMAND
OFFICE OF THE COMMANDER
7701 TAMPA POINT BOULEVARD
MACDILL AIR FORCE BASE, FLORIDA 33621-5323

July 1, 2010

Thank you for your full consideration. This is a real life saver with very low risk.

Sincerely,

Eric T. Olson
Admiral, U.S. Navy
Commander

Army Surgeon General Perspective

"I have reviewed your request to use non-FDA licensed freeze dried plasma in support of special forces operations which occur in austere environments. I fully support your request from a clinical perspective. However, legal and regulatory concerns prevent the acquisition and use of these non-licensed products for the foreseeable future. General Counsel has stated that the only legal option to use these products is under an Investigational New Drug. Unfortunately, neither of the European manufacturers plan to bring their product to the U.S. and seek FDA licensure." (Schoomaker 2010)

Dried Plasma

“The consensus of discussants at the USAISR-sponsored symposium on prehospital fluid resuscitation overwhelmingly favored the development of a dried plasma product that could expand and maintain blood volume while providing lost coagulation factors resulting from the traumatic injury.“

Dr. Michael Dubick

USAISR

AMEDD Journal 2011

FDA-Approved Dried Plasma Product

"If I had FDP, logistically, we would use that AND I would put it on my ALS ambulances. "

Dr. Don Jenkins

Medical Director, Trauma Clinic

Mayo Clinic

All Necessary Steps to Expedite Fielding of an FDP Product

The Department of Defense should immediately take all necessary steps to expedite the fielding of dried plasma to ground medics and to aeromedical evacuation platforms that do not have liquid plasma and packed red blood cells, to include:

- **Conduct expedited studies in trauma systems using prehospital liquid plasma as the primary resuscitation fluid to determine the effect of this practice on outcomes.**
- **Consider physiologic indicators such as INR normalization (restoring normal coagulation), serum pH, and serum lactate as well as TBI markers as outcome measures in addition to mortality.**
- **Increase support for the development and fielding of an FDA-approved dried plasma product.**

All Necessary Steps to Expedite Fielding of an FDP Product

(Continued from previous slide)

- **Proceed with expedited plans to use a U.S. dried plasma product under a Phase II Military Use IND for treatment of coagulopathy and/or hemorrhagic shock.**
- **Gather data on French and German FDP products.**
- **Discuss other options for use of FDP that may include an exception to policy (ETP) or waiver to DoDI 6200.02 (and 21 CFR Part 312) in order to permit the acquisition and use OCONUS of a well-proven European-manufactured dried plasma.**

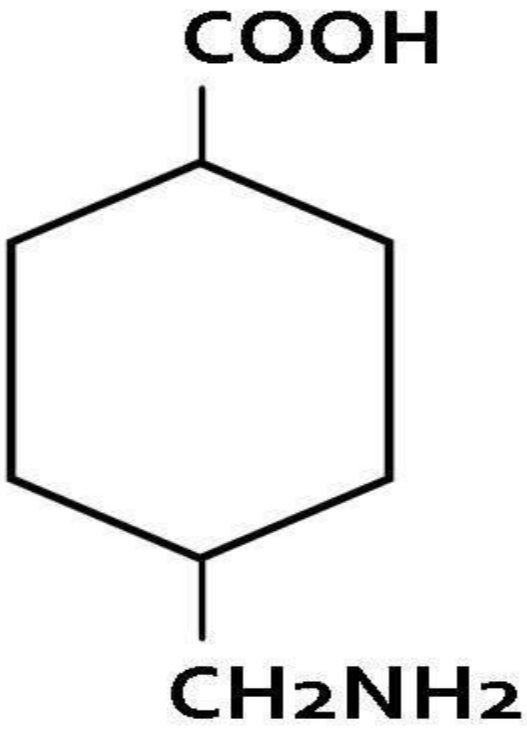
Questions?

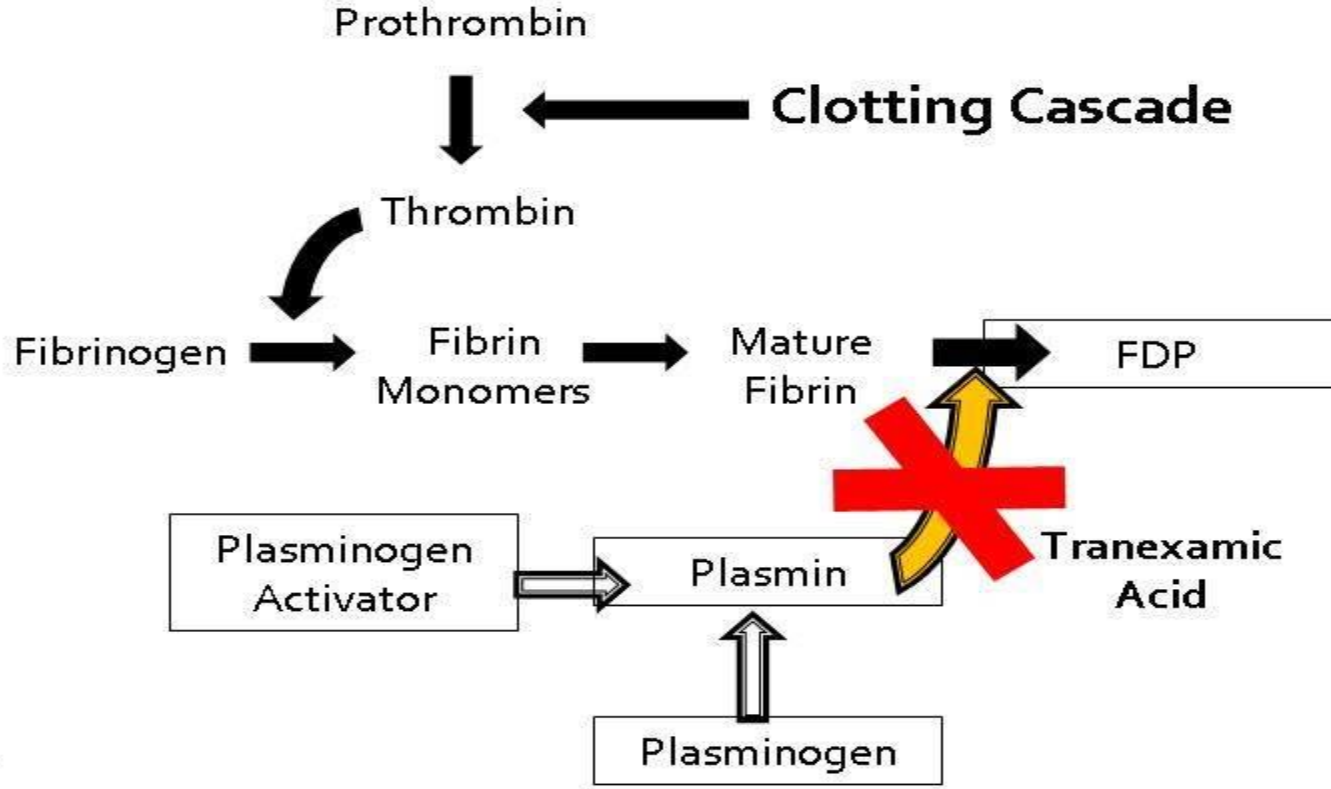
Tranexamic Acid

TXA Background

TXA Background

U.S. AIR FORCE





TXA – CRASH 2 Study Lancet Online Article 2010

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

*CRASH-2 trial collaborators**

- **Prospective, randomized controlled trial**
- **Over 20,000 patients**
- **TXA significantly reduced all causes mortality from 16.0% to 14.5%**
- **TXA significantly reduced death from bleeding from 5.7% to 4.9%**

TXA – CRASH 2 Study Lancet Online Article 2010

USAISR Information Paper:

- **Blocks plasmin activation and clot lysis**
- **Loading dose 1 gram over 10 minutes IV**
- **FDA-approved for dental procedures in hemophiliacs**
- **Noted to increase cerebral ischemia in SAH**
- **Randomized, double-blinded, placebo-controlled trial – highest level of clinical evidence**
- **No subgroup analysis for patients requiring massive transfusion or those with TBI**
- **Cost: $80 for 2-dose regimen used in CRASH 2**
- **Used for the past year by UK forces**
- **Might have saved 23 of 1500 preventable deaths in OIF/OEF**

TXA - CRASH 2 Study Lancet Online Article 2010

Holcomb comments:

- **In a drug that was supposed to decrease bleeding:**
- **50% of the patients did not get any RBCs**
- **The rate of transfusion was the same between groups = 6 units**
- **Only 48% had any surgery**
- **The difference in mortality due to bleeding was 0.8%**
- **Hours 1-3 after injury is where all the benefit was**
- **How do you determine if these was a significant type 1 error?**

TXA - Crash 2 Study Lancet Online Article 2010

Additional comments – Bryan Cotton:

- **It would be interesting to study this drug in patients who actually had "traumatic hemorrhage.“**
- **Not surprised to see that such a drug would not have any effect on the number of units transfused in such a general population.**
- **Sub-group analysis on patients arriving in shock?**
- **Here is a trauma paper without any mention that I can find of ISS, base deficit, lactate.**
- **MOST IMPORTANT: we're talking about a 0.7% absolute reduction in "death due bleeding”**
- **Zero POINT seven**
- **This translates into number needed to treat of 132**

TXA- CRASH 2 Study Lancet Online Article 2010

Additional comments:

- **TXA administered 2.8-2.9 hours after injury**
- **Given to those “at risk” of hemorrhage**
- **68% had SBP > 90 mmHg**
- **What should protocol be in at MTFs?**
- **Prehospital protocol?**
- **JTTS Directors conference 23 July 10 – no decision to add TXA to theater formulary**

CRASH-2: Timing of TXA Dosing – Lancet 2011

The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial

*The CRASH-2 collaborators**

- Subgroup analysis of 20,211 trauma patients based on time of administration of TXA
- Timing; only deaths due to bleeding
- 3076 overall deaths; 1063 due to bleeding
- Risk of death due to bleeding was significantly reduced (5.3% vs 7.7%) if TXA given within 1 hour of injury. At 1-3 hrs after injury, also significant (4.8 vs 6.1%)

CRASH-2: Timing of TXA Dosing – Lancet 2011

The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial

*The CRASH-2 collaborators**

- Cochrane Review 2011: “The review concluded that tranexamic acid safely reduces mortality in bleeding trauma patients without increasing the risk of adverse events.”
- “Our results strongly endorse the importance of early administration of tranexamic acid in bleeding trauma patients and suggest that trauma systems should be configured to facilitate this recommendation.”

The MATTERS Study

The MATTERS Study

U.S. AIR FORCE

Retrospective Study Analysing UK Experience of TXA in CCC

MATTERS Inclusion Criteria
- Combat Injury
- Admitted to Bastion
- Jan 09 to Dec 10 inclusive
- Received ≥ 1 unit PRBC

Received TXA

Did Not Received TXA

- End Points
  - Mortality (<24hr and 28-day)
  - Blood product use within 24hrs of wounding
  - (Coagulation, arterial and venous thrombosis)

Patients

Patients

U.S. AIR FORCE

Point of Wounding

MERT Retrieval
n = 411
(PHB = 182)

FOB Dwyer
n = 8

Other
n = 477

Bastion
n = 896

TXA
n = 293
MT n = 125
Mean dose: 2.3g ± 1.3

No-TXA
n = 603
MT n = 196

Mortality Analysis

Mortality Analysis

U.S. AIR FORCE

Overall	TXA	No-TXA	p Value
< 24 Hr	8.2%	8.5%	0.892
28 Day	16.4%	23.2%	**0.018**

MT	TXA	No-TXA	p Value
<24 Hr	8.8%	9.2%	0.907
28 Day	13.6%	27.6%	**0.003**

Any Questions?