Prehospital Use of Kcentra for Traumatic Bleeding & Shock

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Traumatic Injuries

Trauma is the leading cause death for persons between the ages of 1 and 44 years.

Severe bleeding, head and spinal cord injuries, or a combination of these result in 80% of trauma deaths.

More than half of trauma deaths occur within the first 12 hours after the injury.

Mortality is highest within the first hour after a traumatic injury.

New treatments are needed to prevent early death and ensure that the patient arrives alive to the hospital for definitive care.

Hemorrhage

The most preventable death after trauma is exsanguinating hemorrhage– ***severe bleeding*** that leads to ***shock***.

Signs of shock - low blood pressure, fast heart beat, confusion, pale skin, feeling cold

Hemorrhage

2 types of bleeding- internal and external

External bleeding is managed with pressure dressings, tourniquets, and other methods.

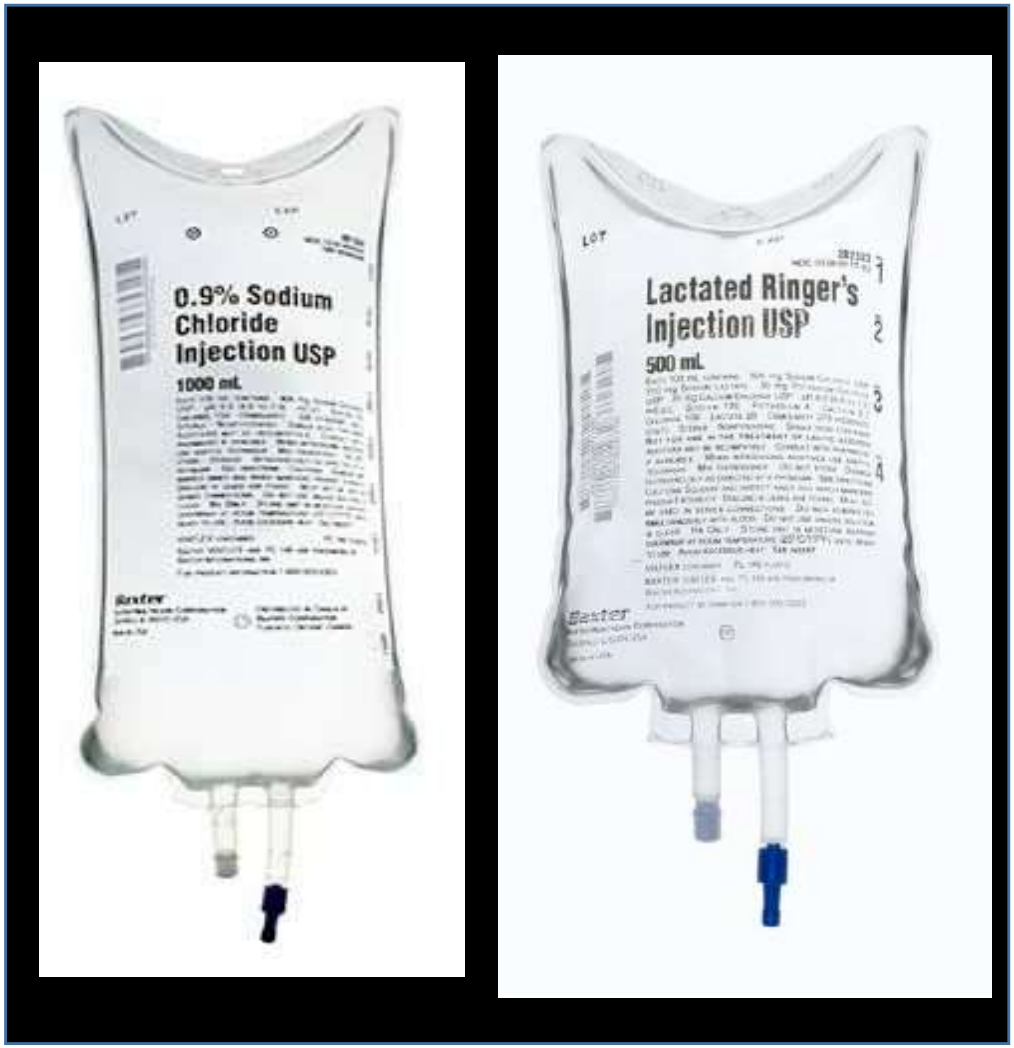
There are currently *no* direct methods for controlling bleeding resulting from internal injuries in the prehospital setting.

Prehospital Treatment of Severe Hemorrhage

IV fluid administration

Purpose: restore blood volume lost due to bleeding

Types: Normal Saline (salt solution) or Lactated Ringers (balanced solution)



Current Science & Studies

Studies have shown that….

1) High IV fluid administration is associated with poor outcomes
2) Delayed and low IV fluid is beneficial until bleeding is controlled
3) Low IV fluid resuscitation has the potential to improve survival in patients with blunt trauma

Significance of Research Study

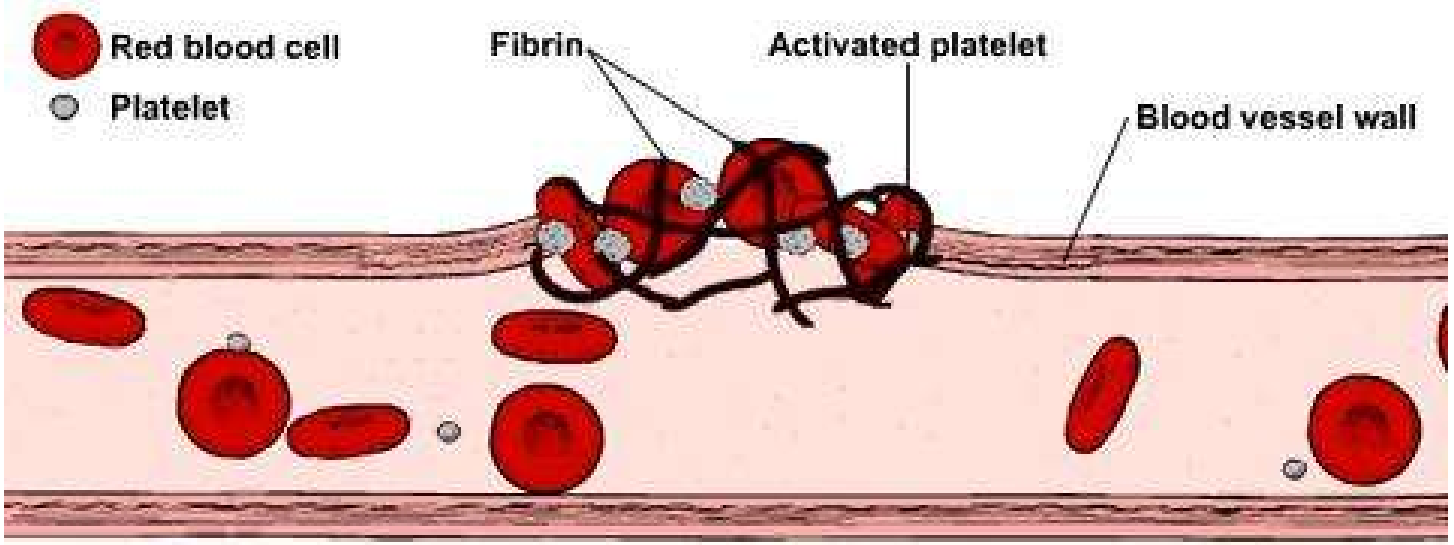
When internal bleeding occurs, the body attempts to stop the flow by forming a clot.

Giving patients large amounts of IV fluid can minimize clot formation by:

Diluting the blood

“Pop” open the holes plugged by clots

Damage the structural integrity of blood vessels



Significance of Research Study

Kcentra is an FDA-approved drug containing four components that help blood clot.

Kcentra is currently approved to reverse warfarin (a “blood thinner”) in bleeding patients, so some trauma patients receive Kcentra in the hospital already.

In addition to blood clotting, studies have shown that Kcentra can also help repair the blood vessel following hemorrhagic shock.

It is quickly reconstituted with water in a vial and given in a very small volume (40ml).

Goal of the Research Study

The primary goal of the trial will be:

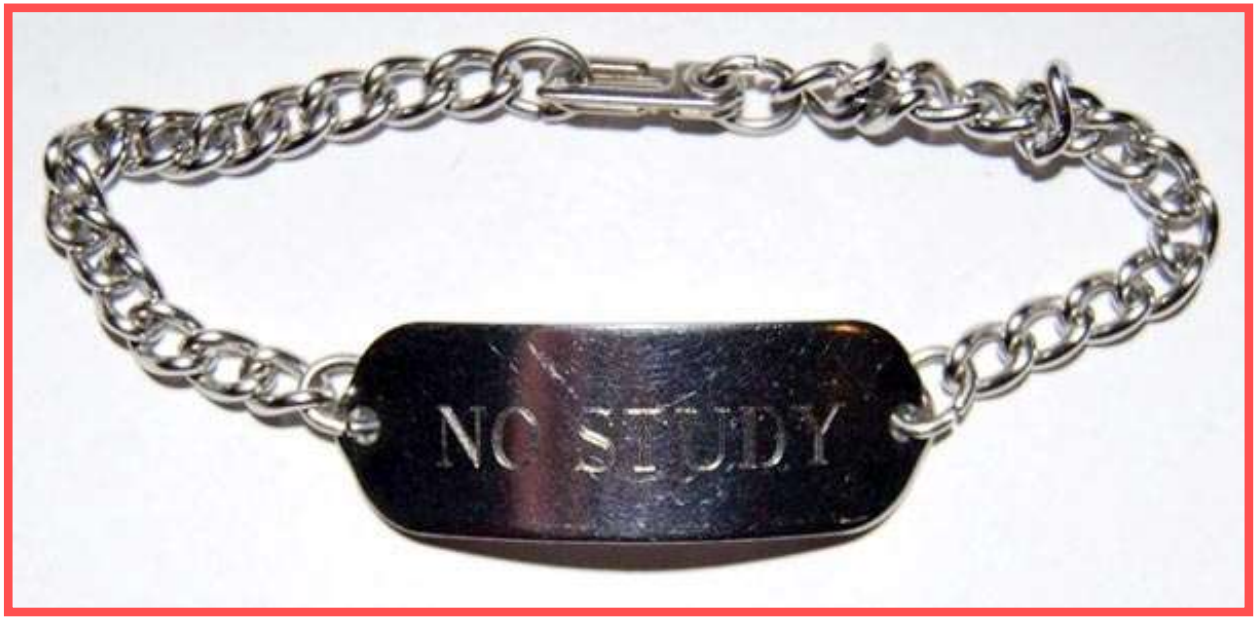
To determine the feasibility and safety of *Kcentra administration* for the early treatment of patients with traumatic shock, compared to *placebo*

Study Trial Design

- Randomized controlled trial
  - Eligibility
    - Adult (age 18+)
    - Trauma patients in hemorrhagic shock (blood pressure <70 or blood pressure <90 and heart rate >108) transported by HFD
  - Treatments randomized: **Kcentra + IV fluids** vs. **placebo + IV fluids**
  - All eligible patients will receive IV fluids as standard of care (SOC), and some will be randomized to receive Kcentra in addition to SOC
- EMS personnel (HFD) will identify eligible patients and administer the randomized treatment during transportation to either MH-TMC or Ben Taub
- Outcomes include
  - Feasibility of giving the drug in the prehospital setting
  - Mortality within 30 days
  - Complications

‘Opt-out’ Option

A “No Study” bracelet will be provided for those who request one.



**To request a bracelet or ask additional questions, call 713-500-7298 or email clinicaltrials@uth.tmc.edu*

Notification and Consent

Will be obtained soon as possible after enrollment from the patient and/or Legally Authorized Representative (LAR).

The patient can withdraw at any time.

Consent is obtained for research blood draws and continued review of your medical record, and only related to the current admission.

Safety Monitoring

The study will be monitored for safety by:

- Data Safety Monitoring Board (DSMB)—an independent group contracted by the lead site
- Institutional Review Board (IRB)
- Food & Drug Administration (FDA)

Exception From Informed Consent (EFIC)

Eligible patients for this study require immediate resuscitation, since *without* intervention, patients in shock face imminent death.

Traditional informed consent is impossible because:

- Patients with severe traumatic injury are unconscious or in shock and not capable of providing consent.
- Resuscitation has to be started immediately, and next of kin may not be immediately available, or are likely to be too distraught to understand an explanation of the study.

A federal regulation (21 CFR 50.24), allows certain studies that meet the following criteria to use this exception:

- Patients' lives must be at risk
- Available treatments are not satisfactory
- Patients are unable to give consent
- Potential risks are reasonable
- Participation in the research could provide a direct benefit (increased survival) to the patient
- The research could not be carried out practically without this exception

Exception From Informed Consent (EFIC)

Requires community input and commentary for the proposed research

- Public disclosure (press releases, ads, social media, websites, etc)
- Community consultation (meeting with community members and asking about their opinions of the research)

EFIC studies are approved in a multistage process by the following:

- US FDA reviews the scientific validity and ethics of the trial (NCT04019015)
- Institutional Review Boards (IRBs) of each institution that will perform the research review human subjects protection
  - This study has already been approved by the FDA, Oregon Health and Science University (the lead site), and University of Washington (another site)
  - UTHealth Houston and BCM IRBs have given preliminary approval to conduct community consultation and public disclosure (CC/PD). Full approval will occur when the CC/PD results are submitted

Community Consultation/ Public Disclosure Activities To Date

- Study staff presented at 4 community meetings
  - 200 attendees and 61 surveys were returned
  - 91.8% agreed that the study was important to perform in the community
  - 95.1% would agree to be enrolled in this or a similar study
  - 95.1% would want their family to be enrolled in this or a similar study

- Social media- a Facebook ad about the study ran for 3.5 months and targeted adult users who live within 150 miles of the Texas Medical Center
  - The ad was shown 312,144 times, reached 89,139 people and 2,329 clicked on the ad to learn more

- Website- a public webpage is posted (https://www.uth.edu/ctrc/participants/efic/KCentra)
  - To date the page has 1,817 views with an average of 1.22 minutes spent on the page

- Public Release- next step
  - Joint public release will go out from UTHealth Houston, BCM, and HFD

Questions?

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