60th Medical Group (AMC), Travis AFB, CA

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

FINAL REPORT SUMMARY

(Please type all information. Use additional pages if necessary.)

PROTOCOL #: FDG20180023A **DATE:** 07June2019

PROTOCOL TITLE: Analysis of Serum Concentrations of Tranexamic Acid Given by the Intramuscular Route in a Swine (*Sus scrofa*) Hemorrhage Model.

PRINCIPAL INVESTIGATOR (PI): Capt. Marguerite Spruce

DEPARTMENT: Surgery **PHONE #:** (314) 620-4808

INITIAL APPROVAL DATE: 19 July 2018 **LAST TRIENNIAL REVISION DATE:** N/A

FUNDING SOURCE: Air Force Surgeon General

1. **RECORD OF ANIMAL USAGE:**

Animal Species:	Total # Approved	# Used this FY	Total # Used to Date
Yorkshire-cross	18	13	13

2. **PROTOCOL TYPE / CHARACTERISTICS:** (Check all applicable terms in **EACH** column)

___ Training: Live Animal	___ Medical Readiness	___ Prolonged Restraint
___ Training: non-Live Animal	___ Health Promotion	___ Multiple Survival Surgery
___ Research: Survival (chronic)	___ Prevention	___ Behavioral Study
_X__ Research: non-Survival (acute)	___ Utilization Mgt.	___ Adjuvant Use
___ Other ( )	_X__ Other (Treatment)	___ Biohazard

3. **PROTOCOL PAIN CATEGORY (USDA):** (Check applicable) ___ C _X__ D ___ E

4. **PROTOCOL STATUS:**

***Request Protocol Closure:**

___ Inactive, protocol never initiated

___ Inactive, protocol initiated but has not/will not be completed

_X__ Completed, all approved procedures/animal uses have been completed

5. **Previous Amendments:**
List all amendments made to the protocol. **IF none occurred, state NONE. Do not use N/A.**

For the Entire Study Chronologically

Amendment Number	Date of Approval	Summary of the Change

6. **FUNDING STATUS:** Funding allocated: $ 34,463.00 Funds remaining: $ 0.00

7. **PROTOCOL PERSONNEL CHANGES:**

Have there been any personnel/staffing changes (PI/CI/AI/TC/Instructor) since the last IACUC approval of protocol, or annual review? ___ Yes _X__ No

If yes, complete the following sections (Additions/Deletions). For additions, indicate whether or not the IACUC has approved this addition.

ADDITIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, IACUC approval - Yes/No)

NAME	PROTOCOL FUNCTION	IACUC APPROVAL

DELETIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, Effective date of deletion)

NAME	PROTOCOL FUNCTION	DATE OF DELETION

8. **PROBLEMS / ADVERSE EVENTS:** Identify any problems or adverse events that have affected study progress. Itemize adverse events that have led to unanticipated animal illness, distress, injury, or death; and indicate whether or not these events were reported to the IACUC.

None

9. **REDUCTION, REFINEMENT, OR REPLACEMENT OF ANIMAL USE:**

REPLACEMENT (ALTERNATIVES): Since the last IACUC approval, have alternatives to animal use become available that could be substituted in this protocol without adversely affecting study or training objectives?

No

REFINEMENT: Since the last IACUC approval, have any study refinements been implemented to reduce the degree of pain or distress experienced by study animals, or have animals of lower phylogenetic status or sentience been identified as potential study/training models in this protocol?

No

REDUCTION: Since the last IACUC approval, have any methods been identified to reduce the number of live animals used in this protocol?

No

10. **PUBLICATIONS / PRESENTATIONS:** (List any scientific publications and/or presentations that have resulted from this protocol. Include pending/scheduled publications or presentations).

Poster presentations:

1. 2019 UC Davis Resident Research Symposium, 23Apr2019
2. 42nd Annual Conference on Shock, San Diego, CA, 10Jun2019

3. 2019 DGMC Research Symposium, 17June 2019
4. 2019 Military Health System Research Symposium, Kissimmee, FL, 19-22Aug2019

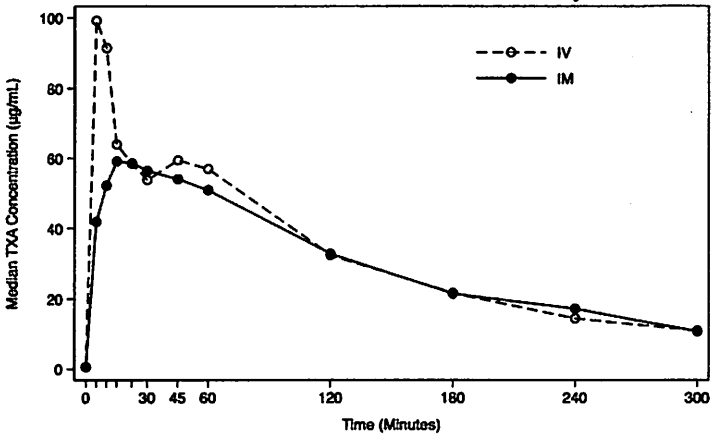
Publication: Manuscript under review after initial revision by the journal "Shock"

11. PROTOCOL OBJECTIVES: (Were the protocol objectives met, and how will the outcome or training benefit the DoD/USAF?)

The protocol objectives were met and demonstrated that intramuscular (IM) injection of Tranexamic acid (TXA) resulted in similar pharmacokinetics to intravenous (IV) infusion even during the shock state. This outcome demonstrates that IM injection could be considered as an alternative to IV when IV access is limited, which is often the case in austere environments. Further investigation is required before equivalence is proven. If proven, the DoD/USAF would benefit significantly from the ability to more expediently administer this life-saving medication to wounded warriors, particularly in austere environments when medical personnel, resources and time are limited.

12. PROTOCOL OUTCOME SUMMARY: (Please provide, in "ABSTRACT" format, a summary of the protocol objectives, materials and methods, results - include tables/figures, and conclusions/applications.)

Introduction:
Tranexamic acid (TXA) improves survival in traumatic hemorrhage, but difficulty obtaining intravenous (IV) access may limit its use in austere environments, given its incompatibility with blood products. The bioavailability of intramuscular (IM) TXA in a shock state is unknown. We hypothesized that IM and IV administration have similar pharmacokinetics and ability to reverse in vitro hyperfibrinolysis in a swine controlled-hemorrhage model.
Methods:
Twelve Yorkshire cross swine were anesthetized, instrumented, and subjected to a 35% controlled hemorrhage, followed by resuscitation. During hemorrhage, they were randomized to receive a 1 g IV TXA infusion over 10 minutes, 1 g IM TXA in two 5 mL injections, or 10 mL normal saline IM injection as a placebo group to assess model adequacy. Serum TXA concentrations were determined using liquid chromatography-mass spectrometry, and plasma samples supplemented with tissue plasminogen activator (tPA) were analyzed by rotational thromboelastometry (ROTEM).
Results:
All animals achieved class III shock. There was no difference in the concentration-time areas under the curve (AUC) between TXA given by either route. The absolute bioavailability of IM TXA was 97%. IV TXA resulted in a higher peak serum concentration during the infusion, with no subsequent differences. Both IV and IM TXA administration caused complete reversal of in vitro tPA-induced hyperfibrinolysis.
Conclusion:
The pharmacokinetics of IM TXA were similar to IV TXA during hemorrhagic shock in our swine model. IV administration resulted in a higher serum concentration only during the infusion, but all levels were able to successfully correct in vitro hyperfibrinolysis. There was no difference in total body exposure to equal doses of TXA between the two routes of administration. IM TXA may prove beneficial in scenarios where difficulty establishing dedicated IV access could otherwise limit or delay its use.



(PI / TC Signature)

7 Jun 19
(Date)

Attachments:
Attachment 1: Defense Technical Information Center (DTIC) Abstract Submission **(Mandatory)**

Attachment 1
Defense Technical Information Center (DTIC) Abstract Submission
This abstract requires a brief (no more than 200 words) factual summary of the most significant information in the following format: Objectives, Methods, Results, and Conclusion.

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