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TITLE: Randomized Trial of Fresh Frozen Plasma Versus Albumin in Acute Burn Resuscitation

PRINCIPAL INVESTIGATOR: Arek Wiktor, MD FACS

CONTRACTING ORGANIZATION: Regents of the University of Colorado, Aurora, CO

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6. AUTHOR(S)
Arek Wiktor, MD; Blaire Balstad; Jaimielyn Burke, CCRC

5d. PROJECT NUMBER

5e. TASK NUMBER

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Regents of the University of Colorado
13001 E 17th Place F428
Aurora, CO 80045

8. PERFORMING ORGANIZATION REPORT NUMBER

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Severe burn injury results in an inflammatory response requiring proper fluid resuscitation due to increased capillary permeability. Colloid (fresh frozen plasma [FFP] and albumin) infusion during resuscitation appears to be beneficial, however the optimal dose, duration, and timing of these fluids are unknown. Our overall goal is to determine the efficacy, safety, and microvascular effect of colloids in critically injured burn patients. We hypothesize that FFP administration in burn resuscitation is as safe as albumin and is more efficacious in both reducing the total fluid volume required and correcting burn endotheliopathy.

This research study is a single-center, prospective, randomized, controlled trial in critically injured burn patients admitted to our American Burn Association (ABA)-verified burn center, directly comparing FFP and albumin. We will enroll a maximum of 100 patients with a goal of 60, and have enrolled 10 to date. 5 participants have been randomized to the FFP arm, and 5 have been randomized to the albumin arm.

This study is still currently in data collection and therefore has no significant or major findings to date. However, we are planning to analyze our first batch of patient samples for endothelial markers within the next month. These results will build the foundation for safe and effective colloid resuscitation strategies in burn injury and subsequent work on freeze-dried plasma therapy in the combat setting, which is capable of revolutionizing combat burn care.

15. SUBJECT TERMS
Burn resuscitation, colloid, albumin, fresh frozen plasma, endotheliopathy, endothelial markers, continuing enrollment

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRDC
U	U	U	UU	9	**19b. TELEPHONE NUMBER** *(include area code)*

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1. INTRODUCTION

Severe burn injury results in an inflammatory response requiring proper fluid resuscitation due to increased capillary permeability. Colloid (fresh frozen plasma [FFP] and albumin) treatment is without consensus regarding optimal component and volume for burn resuscitation. Our overall goal is to determine the efficacy, safety, and microvascular effect of FFP in critically injured burn patients. We hypothesize that FFP administration in burn resuscitation is as safe as albumin and is more efficacious in both reducing the total fluid volume required and correcting burn endotheliopathy. Our research proposal will elucidate safe and effective colloid resuscitation strategies in burn injury to significantly benefit the warfighter. These results build the foundation for subsequent work on freeze-dried plasma therapy in the combat setting, which is capable of revolutionizing combat burn care. We will conduct a single-center prospective randomized trial in critically injured burn patients admitted to our American Burn Association (ABA)-verified burn center. We will enroll a total of 100 patients and randomly assign into one of two (2) fluid resuscitation groups during the trial: FFP or albumin. We anticipate an equal number of patients (n=50) for each group.

2. KEYWORDS

Burn resuscitation, colloid, albumin, fresh frozen plasma, endotheliopathy, glycocalyx

3. ACCOMPLISHMENTS

a. What were the major goals of the project? (Goals to be accomplished and status.)

Primary Objective: To determine the efficacy, safety, and microvascular effect of FFP in critically injured burn patients compared to albumin.

Secondary Objectives: To characterize the effects of FFP and albumin administration on endothelial dysfunction

- *Major Task 1: Preparatory Work (approvals, data collection infrastructure, site materials, training) (months 1-6).*
    - STATUS: completed Y1Q2
- *Major Task 2: Implementation (enrollment with goal of 100 patients) (months 6-33).*
    - STATUS: started Y1Q2
- *Major Task 3: Data Collection/Analysis (data collection, cleaning, dissemination, and reporting) (months 6-36).*
    - STATUS: started Y1Q2

b. What was accomplished under these goals? (Detailed progress and results.)

PRECLINICAL RESEARCH FORMAT EXAMPLE

Primary Objective: To determine the efficacy, safety, and microvascular effect of FFP in critically injured burn patients compared to albumin.

Secondary Objectives: To characterize the effects of FFP and albumin administration on endothelial dysfunction

Major Task 1: Preparatory Work (approvals, data collection infrastructure, site materials, training) (months 1-6).
HRPO Initial Approval was received 02/08/2022. The protocol was locally given the status of “Open to Accrual” within our clinical trial management system (CTMS). This designation is given to those protocols which have received IRB as well as all additional institutional and hospital-level approvals, marking the final task needed to complete Major Task 1 and proceed to Major Task 2: Implementation.

Major Task 2: Implementation (enrollment with goal of 100 patients (months 6-33)

Enrollment of the first patient occurred 02/23/2022 and an additional 17 patients have been screened. 10 participants have been enrolled, and enrollment is ongoing. Admissions to the Burn Unit are screened daily, and those deemed potential candidates are recorded on a screening log.

Major Task 3: Data Collection/Analysis (data collection, cleaning, dissemination, and reporting) (months 6-36
Data collection began concurrently with the enrollment of our first patient on 02/23/2022 and is ongoing.

Type/Site	Subjects Approved	Subjects Screened	Subjects Enrolled	Subjects Completed	Subjects Lost
Core, UCD	100	17	10	9	0

Key Findings or Accomplishments:

No key findings have been established yet as the study is still currently in data collection and no analysis has occurred. However, a key accomplishment is that the study site has enrolled 10 patients, a big milestone for both the PI and study coordinator.

c. What opportunities for training and professional development has the project provided?

While this project was not intended to provide specific training or professional development, the PI of the study does many outreach lectures and courses for medical facilities around Colorado to increase burn care knowledge. Since the results of the study have not been analyzed yet, the study has not provided specific training to any of these medical centers but has the opportunity to do so in the future once the study is concluded.

d. How were the results disseminated to communities of interest?

Nothing to report as the study is still in data collection.

e. What do you plan to do during the next reporting period to accomplish the goals?

We continue to screen the Burn Unit admissions daily to identify potential candidates for the research. Once potential candidates are identified, the study team will continue to reach out to patients to obtain consent and enrollment. Data collection will be ongoing.

We plan to add two new investigators to the study, both of which are newly hired attending burn surgeons, who will be able to help the PI with screening and enrollment of participants during nights and weekends.

We also plan to add an additional medical student who will assist with laboratory blood processing to help the study coordinator with this task during nights and weekends.

4. IMPACT

a. What was the impact on the development of the principal discipline(s) of the project?

Nothing to Report.

b. What was the impact on other disciplines?

Nothing to Report.

c. What was the impact on technology transfer?

Nothing to Report.

d. What was the impact on society beyond science and technology?

Nothing to Report.

5. CHANGES/PROBLEMS

a. Changes in approach and reasons for change

An amendment was submitted 21 March 2022 something in order to increase the number of patient blood draws and timepoints of these blood draws. The PI and lab technician had a discussion in which they concluded that having a blood draw at the 48hr mark would be integral to the statistical analysis for the study. Amendment documents were submitted to HRPO and information regarding this amendment was included in Quarterly Report Y1Q3.

b. Actual or anticipated problems or delays and actions or plans to resolve them

As burn patients do not come in at standardized times, it is important to have adequate coverage for consenting, enrollment, and lab processing during nights and weekends. The hiring process for these positions was initially difficult due to finding qualified individuals, however we have recently overcome that obstacle. Two new attending burn surgeons have been hiring and will be put on the study as co-investigators in the coming months, as well as a qualified medical student added as personnel to assist with lab processing.

Another problem the study ran into was finding the correct blood tubes to use for specimen collection due to ongoing backorders from vendors. This is still an ongoing problem. The study coordinator has created contacts with hospital and different laboratory staff to order blood tubes and will continue to find alternatives to ordering directly from the vendor.

c. Changes that had a significant impact on expenditures

Nothing to Report.

d. Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to Report.

6. PRODUCTS

a. Journal publications

Nothing to Report.

b. Books or other non-periodical, one-time publications

Nothing to Report.

c. Other publications, conference papers, and presentations

Nothing to Report.

d. Website(s) or other Internet site(s)

Nothing to Report.

e. Technologies or techniques

Nothing to Report.

f. Inventions, patent applications, and/or licenses

Nothing to Report.

g. Other Products

Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

a. What individuals have worked on the project?

Name:	Arek Wiktor, MD FACS
Project Role:	Principal Investigator
Researcher Identifier:	
Nearest person month worked:	12
Contribution to Project:	Principal Investigator, initiator of the protocol.

Name:	Adit Ginde MD, MPH
Project Role:	Co-Investigator
Researcher Identifier:	
Nearest person month worked:	3
Contribution to Project:	Assist in implementation of the trial and gives support where needed.

Name:	Jerome McKay, PhD
Project Role:	Co-Investigator
Researcher Identifier:	
Nearest person month worked:	9
Contribution to Project:	Assist in laboratory
es assays.	

Name:	Erik Schmidt, MD
Project Role:	Co-Investigator
Researcher Identifier:	
Nearest person month worked:	12
Contribution to Project:	Responsible for performance of assays, ensuring delegated staff are trained on proper blood collection and processing.

Name:	Kathryn Colborn, PhD, MSPH
Project Role:	Co-Investigator/Biostatician
Researcher Identifier:	
Nearest person month worked:	4
Contribution to Project:	Biostatician for protocol. Constructing and testing the REDCap databse to ensure it is complete for our purposes.

Name:	Jaimielyn Burke, CCRC
Project Role:	Regulatory Manager
Researcher Identifier:	0000-0003-3546-7375
Nearest person month worked:	12
Contribution to Project:	Manages submissions to the sIRB (COMIRB), performs regulatory management throughout startup activity and lifetime of protocol.

Name:	Tracey MacDermott, CCRC
Project Role:	Research Manager, Department of Surgery
Researcher Identifier:	
Nearest person month worked:	12
Contribution to Project:	Provides clinical research expertise during startup activity and lifetime of protocol, ensures proper resources are available through the Department of Surgery to carry out protocol activities.

Name:	Maggie McGing
Project Role:	Medical Student/Research Coordinator
Researcher Identifier:	
Nearest person month worked:	12
Contribution to Project:	Medical student who fulfilled the role of research coordinator to aid in startup organization prior to enrollment initiation and identification of Primary Research Coordinator. Helped create REDCap database and continues to provide backup to Primary RC for on call coverage of patient enrollment.

Name:	Patrick Hosokawa
Project Role:	Biostatician
Researcher Identifier:	
Nearest person month worked:	4
Contribution to Project:	Part of Dr. Colborn's team, assisted in creation and validation of REDCap database.

Name:	Blaire Balstad
Project Role:	Primary Research Coordinator
Researcher Identifier:	
Nearest person month worked:	12
Contribution to Project:	Primary research coordinator hired to manage data collection and support enrollment.

Name:	Emilee Bergl
Project Role:	Medical Student/Research Coordinator
Researcher Identifier:	
Nearest person month worked:	12
Contribution to Project:	Provides backup to Primary RC for on call coverage of patient enrollment.

b. Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report.

c. What other organizations were involved as partners?

Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS
QUAD CHART

9. APPENDICES

APPENDIX I – QUAD CHART

Randomized Trial of Fresh Frozen Plasma versus Albumin in Acute Burn Resuscitation

MB200032, No Task Title, W81XWH-21-1-0843

PI: Arek Wiktor, MD **Org:** University of Colorado School of Medicine; CU Center for COMBAT Research **Award Amount:** $ 1,500,000

Study/Product Aim(s)

Our **overall objective** is to determine which colloid (FFP or albumin) is best at decreasing the amounts of fluids given in burn resuscitation, while also examining the effects on the endothelium.

Aim 1: Evaluate the total fluids administered in FFP (intervention) and albumin (control) groups.
Aim 2: Determine overall complication rates (pulmonary compilations, ARDS, ACS, over-resuscitation) in the FFP and albumin administration groups.
Aim 3: Characterize the effects of FFP and albumin administration on endothelial dysfunction, measuring glycocalyx degradation products (e.g. syndecan-1, glycosaminoglycans) in the serum.

Approach

A single-center, randomized controlled trial of FFP versus albumin in adult patients with extensive burns (≥ 20% TBSA) admitted to the UCH Burn Center.

Optimizing resuscitation using fluids by stabilizing the endothelial glycocalyx (lower electron micrograph picture).

Accomplishment: HRPO approval received 02/08/2022, study locally open to accrual 02/14/2022, enrollment of first patient occurred 02/23/2022. Ten patients enrolled.

Timeline and Cost

Activities CY	21	22	23	24
Regulatory approvals				
Begin enrollment of patients				
Ongoing enrollment of patients				
Final enrollment, analysis, dissemination				
Estimated Budget ($K)				

Updated: August 2022

Goals/Milestones

CY21 Goal: Preparatory Work
☒ Finalize Protocol
☒ Central IRB Approval
☒ Develop Data Collection Infrastructure
CY22 Goal: Implementation
☒ Develop Standard Operating Procedures (SOPs)
☒ Site Training
☒ HRPO Approval – ***received 02/08/2022***
☒ Begin enrollment of patients with randomization – ***started Y1Q2, ongoing***
☒ Processing and storage of samples with data collection – ***started Y1Q2, ongoing***
CY23 Goal: Continued Enrollment and Monitoring
☐ Ongoing monitoring and education/training of staff
☐ Ongoing enrollment with data collection and periodic evaluations
CY24 Goal: Data Collection/Data Analysis
☐ Finalize Enrollment
☐ Finalize Data Collection and Perform Analysis
☐ Dissemination of Results and Report Findings

Comments/Challenges/Issues/Concerns
- Finding on-call coverage has proven difficult. The supply for blood tubes is delayed

Budget Expenditure to Date
Projected Expenditure: $494,340
Actual Expenditure: $352,338