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 #: FDG20190020A **DATE:** 6/11/20

PROTOCOL TITLE: Comparison of peritoneal dialysis using a bag containing potassium-binding beads to conventional peritoneal dialysis in an anephric swine model of hyperkalemia (*Sus scrofa*).

PRINCIPAL INVESTIGATOR (PI) / TRAINING COORDINATOR (TC): Lt. Col Ian Stewart

DEPARTMENT: SGSE **PHONE #:** (858) 232-9081

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

FUNDING SOURCE: Air Force Surgeon General's Office

1. RECORD OF ANIMAL USAGE:

Animal Species:	Total # Approved	# Used this FY	Total # Used to Date
Sus scrofa domesticus	11	0	11

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 ( ) ___ 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
NONE		

6. FUNDING STATUS: Funding allocated: $ 11,288 Funds remaining: $ 11,288

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.

No problems or adverse events were encountered throughout the model development and experimental phases of this protocol.

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 alternatives to animal use have become available. For this experiment, we required an animal subject that could appropriately model the physiological response to hyperkalemia. Further, we required an animal model of similar body weight and peritoneal cavity size to that of humans to model the peritoneal dialysis procedure accurately to test the experimental device.

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?

Similar to the previous statement in replacement, there are no lower phylogenetic models that could both model the response to hyperkalemia while also accommodating the volumes of peritoneal dialysate fluid to appropriately test the device.

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

This study employed as few animals as necessary to properly develop the model and achieve sufficient power to compare the control and experimental groups.

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

We have yet to produce a publication from the data obtained from this study.

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

The objectives of the protocol were met. We were able to demonstrate an alternative method to Peritoneal Dialysis which utilized experimental potassium-binding beads to control hyperkalemia in an anephric animal model of hyperkalemia.

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.)

Background: Hyperkalemia results as a complication of combat injury and is a significant comorbidity in civilian patients suffering from severe trauma. While the standard of care is renal replacement therapy (RRT), it is not conducive to prolonged evacuation settings or field care facilities. Furthermore, novel hemorrhage control devices are associated with hyperkalemia. Taken together, there is a need to develop methods of controlling hyperkalemia that are less demanding of personnel and equipment as RRT. We have evaluated an adapted method of peritoneal dialysis, designed to recycle fluid that would otherwise be discarded, reducing the amount of dialysate fluid required.

Methods: This technique was evaluated in an anephric model of hyperkalemia in *Sus scrofa domesticus*. Six animals were placed under general anesthesia and were instrumented to monitor vital signs and hemodynamics. Animals underwent bilateral nephrectomy and peritoneal dialysis catheters were placed bilaterally. Subjects were administered a weight-dependent dose of potassium to induce hyperkalemia and were subsequently assigned to conventional peritoneal dialysis or our experimental method. For conventional peritoneal dialysis, 2 liters of dialysate fluid was administered into the abdominal cavity and allowed to dwell for 60 minutes. Fluid was drained over 20 minutes and discarded. This was then repeated for a total of 6 exchanges. For the experimental group, 2 liters of fresh dialysate was administered into the abdominal cavity, allowed 60 minutes to dwell, and was retrieved and regenerated in the experimental device over a 20-minute period. This fluid was readministered into the peritoneal cavity and this process was repeated for a total of 6 exchanges. If <75% of potassium in the dialysate was removed after incubation with the experimental device, the fluid was instead discarded and two liters of fresh dialysate were added. Serum biochemistry panels were conducted at baseline and hourly. Complete blood cell counts were obtained at baseline, start, and end of the experiment.

Results: Average dialysate fluid utilized in the experimental method was 3.33 L over the 6-hour period, while the conventional treatment used 12 L. There was no statistically significant difference in serum potassium between groups over time ($p = 0.766$)(Fig. 1). There were statistically significant differences between groups in serum calcium ($p = 0.0008$) but not ionized calcium ($p = 0.5956$) and lactate ($p = 0.0004$).

Conclusion: In this model, the experimental device used significantly less fluid and was able to control serum potassium levels with similar efficacy to that of conventional peritoneal dialysis.

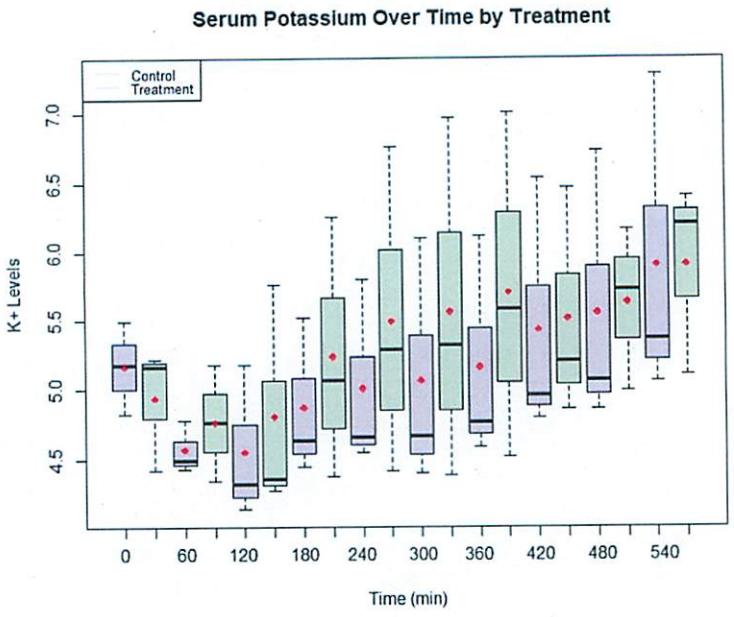

Fig. 1: Serum potassium levels between control (purple) and experimental treatment (green) groups over time. Red diamonds indicate the mean serum potassium level among subjects in the respective group and time point.

Lt Col Ian J. Stewart

17 Jun 20
(Date)

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

FD92019002011
~~FDGXXX~~

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.

Objectives:

The objective of this study was to compare an experimental method of peritoneal dialysis to a conventional method in an anephric model of hyperkalemia. The purpose of the experimental device was to achieve similar removal of serum potassium over a 6-hour critical care period using less peritoneal dialysate fluid.

Methods:

Six animals underwent bilateral nephrectomy and hyperkalemia was induced exogenously. Peritoneal dialysis catheters were placed. Subjects were randomized to conventional peritoneal dialysis (n=3) or the experimental treatment method (n=3) over a 6 hour time period. Samples were obtained from the peripheral bloodstream, the ingoing peritoneal dialysate (PD) fluid, and the outgoing PD fluid. Serum potassium, calcium, ionized calcium, lactate, were compared between groups over time.

Results:

Average dialysate fluid utilized in the experimental method was 3.33 L over the 6-hour period, while the conventional treatment used 12 L. There was no statistically significant difference in serum potassium between groups over time (p = 0.766)(Fig. 1). There were statistically significant differences between groups in serum calcium (p = 0.0008) but not ionized calcium (p = 0.5956) and lactate (p = 0.0004).

Conclusion:

In this model, the experimental device used significantly less fluid and was able to control serum potassium levels with similar efficacy to that of conventional peritoneal dialysis.

Grant Number:_____
From:_____
****If you utilized an external grant, please provide Grant # and where the grant came from. Thank you.**