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TITLE: Crozer-Chester Medical Center Burn Research Project

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14. ABSTRACT

he purpose of the research is to conduct burn research that will benefit combat casualties in the current conflict. The Nathan Speare Regional Burn Treatment Center is under contract with the U.S. Army Institute for Surgical Research and the Army Burn Center to carry out two studies according to protocols established by Army researchers. The purpose of Study 1, Automated Fluid Resuscitation of Burn Patients, is to collect data which will be used to create an effective resuscitation algorithm for the development of a closed loop resuscitation system. Approximately 20 patients will be enrolled in the Crozer Burn Treatment Center. Study 2, Evaluation of Aquacel Ag, will compare the performance of Aquacel Ag to the normal standard of care (Xeroform). Approximately 20 patients will be enrolled. A third study, A Comparison of Clinical and Microbiological Efficacy of Three Separate Antibiotic Regimens Against Acinetobacter baumannii, has been designed by the Principal Investigator and will be carried out at Crozer only. During the past year, Crozer began enrolling patients in Study 2 (see above).

15. SUBJECT TERMS
Automated fluid resuscitation devices, Closed-Loop algorithms, Kramer resuscitation; Aquacel Ag Dressing, Donor site care; Acinetobacter baumannii

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Crozer-Chester Medical Center Nathan Speare Regional Burn Treatment Center

ANNUAL REPORT TO THE U.S. ARMY INSTITUTE OF SURGICAL RESEARCH FOR THE PERIOD 6/19/2008 to 6/18/2009

Title: "Crozer-Chester Medical Center Burn Research Projects"

Contract Number: W81XWH-07-1-0311, as amended

INTRODUCTION:

The purpose of the proposed project is to conduct burn research that will benefit combat casualties in the current conflict. The Army Burn Center, which is part of the Brooke Army Medical Center in Fort Sam Houston, Texas, has demonstrated the applicability of burn research in civilian populations to combat populations. The Nathan Speare Regional Burn Treatment Center is under contract with the U. S. Army Institute for Surgical Research to carry out two projects according to protocols that have been already established by Army researchers. A third project has been defined by Crozer's Principal Investigator. These projects are:

Study 1: "Automated Fluid Resuscitation of Burn Patients"
The purpose of Study 1 is to collect data which will be used to create an effective resuscitation algorithm for the development of a closed loop resuscitation system. The actual use of the closed loop resuscitation system will occur in a future study. Approximately 20 patients will be enrolled. The projects are expected to improve resuscitation of burn patients by creating a feedback loop of actual patient response to resuscitation volumes, and titrating the fluid therapy to changes in urinary output. Data from urometers, cardiac monitors and IV pumps will be measured at 10-minute intervals and fed to a DAQ, which is a computer system designed to collect data from this equipment at the bedside.

Study 2: "Evaluation of Xxx Dressing for Autogenous Skin Donor Sites"
This study will compare the performance of an agreed upon dressing to the normal standard of care (Xeroform). Patients who are scheduled for excision of burns or other injuries will have one of two donor sites covered with the Xxx dressing, and the other treated according to standard care. Approximately 30 patients will be enrolled. The hypothesis is that mean healing time for wounds treated with Xxx dressing will be less than the mean healing time for wounds treated with Xeroform dressing. Specific aims are: 1) that pain as perceived by the patient will be equal to or less than with the Xxx dressing as compared with the standard dressing, and 2) the cosmetic effect of healing at post surgery day 30-45 will be equal or less with the Xxx dressing as compared with the standard of care dressing.

Study 3: A Comparison of Clinical and Microbiological Efficacy of Three Separate Antibiotic Regimens Against *Acinetobacter baumanni*.
A. baumannii has been steadily emerging as a poly-resistant organism in burn treatment centers. In addition to the problem of widespread colonization of patient care areas, there has been the progressive development of multiple resistance genes. The goal of this project is to evaluate the microbiological and clinical efficacy of three potential antimicrobial agents over 24-months in

three groups of 20 adult patients with documented *A. baumannii* infections to determine if there are any subtle or frank differences in outcome with the use of these antimicrobials. Using standard manufacturer-recommended doses, we intend to compare two agents that have not been routinely used, colistin and tigacycline, to imipenem-cilistatin to guide best practices in *A. baumannii* treatment. Using standard statistical testing methods the duration of treatment, time to onset of infection, and other parameters will be investigated. Standard assessment of infection response will be used to evaluate and compare these three agents. Pilot data on Crozer burn patients with *A. baumannii* pneumonia will also be analyzed.

BODY:

The approved Statement of Work is as follows:

Study 1, Protocol Title: "Automated Fluid Resuscitation of Burn Patients – Phase 1"

Task 1: To collect data from 20 study subjects which will be used to create an effective resuscitation algorithm for the development of a closed loop resuscitation system.

a. Complete project start-up activities (hiring and training of research staff, purchasing equipment) (Year 1, Quarter 1)
b. Enroll 15 study subjects and collect data (Year 1, Quarters 2-4)
c. Enroll 5 study subjects and collect data (Year 2, Quarter 1)

Study 2, Protocol Title: "Evaluation of Xxx for Autogenous Skin Donor Sites"

Task 1: Enroll up to 30 patients in this multi-center trial to evaluate the performance of the identified dressing versus standard of care dressing (Xeroform) for skin donor sites in terms of day of healing, comfort, cosmetics and ease of use.

a. Complete project start-up activities (hiring and training of research staff) (Year 1, Quarter 1)
b. Enroll 75% of study subjects, harvest subject's donor sites, randomize dressing to donor sites, and conduct clinical assessments (Year 1, Quarter 2-4)
c. Enroll 25% of study subjects, harvest subject's donor sites, randomize dressing to donor sites, and conduct clinical assessments (Year 2, Quarter 1)
d. Summarize results (Year 2, Quarter 1)

Study 3, Protocol Title: "A Comparison of Clinical and Microbiological Efficacy of Three Antibiotic Regimens Against *Acinetobacter baumannii*"

Task 1: To collect data from three groups of 40 patients and to compare the responses to antibiotic therapy with specific focus on: 1) differences in duration of therapy; 2) differences in time to eradication of infection (laboratory findings changes, vital signs, culture results); 3) differences in adverse reaction profiles of the patients; and 4) impact on the susceptibility of *A. baumannii* to these agents over a two year period.

a. Complete project start-up activities (hiring and training research staff) (year 1, quarter 1)
b. Enroll 45 subjects and collect data (year 1, quarters 2-4)
c. Enroll 15 subjects and collect data (year 2, quarters 1)
d. Enroll 60 additional subjects (year 2, quarters 2-4, Year 3, quarter 1)
e. Compose report, submit abstract for national meeting presentation, write manuscript for publication (year 4, quarter 2)

(Note: 'd' and 'e' will extend beyond the grant period. See Proposal Narrative)

Discussion

The approval letter needed to begin Study 2 was received in the first week of December, 2008. Project staff from Crozer-Chester Medical Center conducted a site visit to the Army Burn Center in January, 2009 to see the USAISR, participate in the weekly research meeting, tour the facility, meet the staff we are collaborating with on studies, see the DAQ machine and how it interfaces with actual Burn Center critical care bedsides (unfortunately, there were no active patients in the resuscitation study to observe). We also reported on the status of each study and discussed possible future studies between the two sites.

On April 23, 2009, Crozer enrolled its first patient in the donor study (Study 2). The second patient was enrolled on May 5, 2009. Two patients have completed the study according to the study protocol. One other donor had a wound that was determined to be too small and was not enrolled; one patient declined to participate. Two other patients met wound criteria, but due to other exclusion factors related to their medical conditions, were not enrolled. The Research Nurse makes daily rounds on the burn unit to identify possible candidates for the study.

The Resuscitation Study (Study 1) has not begun due to the need to finalize the CRADA. As a result, none of the clinical equipment required for the study has been purchased due to the unsigned CRADA and Statement of Work. The CRADA will be signed by Crozer once the Statement of work is approved by the USAISR. We are awaiting this approval. (Note: under this CRADA, services a of part-time clinical engineer will be provided by the Army to assist Crozer in installing the DAQ and in troubleshooting problems that may arise. Funds for these services were deducted from the grant award between USAISR and Crozer and should therefore be available to the USAISR for this purpose – see Contract W81XWH-07-1-0311, amendment 1). The purchase orders to purchase the DAQ and other equipment are ready to go once the CRADA is fully executed.

Study 3 has not begun because Crozer has not had any patients that met the criteria for inclusion since April, 2008.

The narrative below summarizes the project activities for each month of the project year, as documented in the project's quarterly reports:

July, 2008 – August 2008: All studies have been approved through the IRB at CCMC and the Army. The Burn Research Nurses have been hired (2-FTE). We are awaiting the go ahead letter from the Army that the studies are approved and permission is granted to enroll the first patient

in to the Resusitation Protocol and the Donor Site Protocol. The Research Nurses will begin after the permission letter has been received. At that time the trip to San Antonio will be arranged to learn the data collection process of the Resusitation Project. The plant has been modified to accommodate a Research Office that includes space for the Research Coordinator, the Research Nurses, the Army Technician and locked files to secure confidential data. The Burn Center is ready to begin both studies.

September – October, 2008: The CCMC IRB required a renewal of the consent form for Study #1 Resuscitation Study. This approval was received the second week in October, 2008. ALL required documents are in the hands of the Army as of the second week of October. The annual report and quarterly reports are all current. The Crozer Burn Center has completed the renovation of the Research Office; computers are ready to turn on; equipment purchase orders are ready to go. Crozer is awaiting the letter from the Army to enroll the first patient into the Resuscitation Project and also the ability to begin drawing down the grant funds designated to completion of the study project. Once this letter is received the next step is to purchase the DAQ machine (3 day turn around time from order to delivery) and related equipment for the Resuscitation Study, the Research Nurses will be transferred to the Study Cost Center and the project will commence. There will be education required in San Antonio, TX for the Research Team. This will be arranged as soon as the letter to enroll is received. We are eager and excited to begin our research. We await the green light.

November – December 2008: November was spent waiting for the letter from the Army. The letter was received the first week of December. All of these documents then went to CCMC IRB for verification and finalization to begin actual enrollment of patients. This was completed the last week in December. At this point, we contacted the Army, to make arrangements for a date for a site visit in San Antonio to participate in their weekly Research Meeting and discuss the DAQ machine and meet the engineers that would be our site consultant.

January 2009: Arrangements for the San Antonio visit confirmed for the third week in January. Site visit completed and are now in the purchase process for the equipment to begin the Resuscitation Study.

February 2009: In servicing of the Burn Center Staff is in process. Anticipate first patients to be enrolled in the Wound Study. Equipment purchasing process is on going. Final quotes for all equipment have been received with the exception of the DAQ machine. Protocols have been distributed to the Research Nurses and preliminary charts for documentation for all studies have been prepared. Final purchase and arrangements for copier/scanner and laptops will be completed.

March 2009: Education of Burn Center Staff continued and completed for the Donor Site Study. CCMC Grant Representative in contact with USAISR Contract writer in reference to the CRADA and SoW for the Fluid Resuscitation Project – first draft pending from the USAISR. Equipment purchases placed on hold until CRADA is signed.

April 2009: Received first Draft of the CRADA/SoW related to the Fluid Resusitation Study. CCMC Grant Department working closely with BTC Study Administrator and CKHS Legal

Department to prepare Rebuttal document for the CRADA/SoW. Patient #1 entered into the Donor Site Study on April 1, 2009. Month ending 4-30-09 with a total of 2 patients completely through the Donor Site Study.

May 2009: Rebuttal CRADA/SoW returned to USAISR; awaiting response. Hope to have a signed CRADA/SoW by the beginning of next month. Plan to purchase equipment during the signing period to be ready for the Fluid Resusitation Study to begin. Patient #3 identified for Donor Site Study – however was thrown out during surgical procedure due to donor site not meeting minimal size requirement for study inclusion**.** Anticipate purchase of all equipment and begin enrolling patients into the Fluid Resusitation Study in June, 2009.

June 2009: Study #2 - Donor Site Study continues. To date 2 patients have completed the study; pt #3 was removed from the study due to the donor site not meeting the minimal size requirement; pt #4 and #5 were identified as possible candidates however, their medical history prevented inclusion into the study. The Burn Research Nurse completes daily rounds to identify patients for the donor site study, however to date we do not have any candidates. **Study #1** – Resuscitation Study Status: CRADA/SoW Rebuttal has been passed back and forth between the parties. It currently sits with the USAISR for final approval. Signatures will be obtained at CCMC and the PO's for clinical equipment will be executed when the CRADA/SoW is properly signed by both parties.

KEY RESEARCH ACCOMPLISHMENTS:

Study 2 has begun enrolling patients. Once the CRADA is finalized, Crozer will begin enrolling patients in the Resuscitation Study (Study 1). It is hoped that this will occur no later than September, 2009.

REPORTABLE OUTCOMES:

There are no outcomes to report. However, one of the studies has begun enrolling patients.

CONCLUSION:

Conclusions will be drawn at the completion of the research projects.

REFERENCES:

No publications have been completed.

APPENDICES:

Not applicable.