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TITLE: Crozer-Chester Medical Center Burn Research Projects

PRINCIPAL INVESTIGATOR: Linwood R. Haith, Jr., M.D.FCCM

CONTRACTING ORGANIZATION:
Crozer-Chester Medical Center
Upland, PA 19013

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Linwood R. Haith, Jr., MD, FACS, FCCM

Email: linwoodhaith@crozer.org

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Crozer-Chester Medical Center
One Medical Center Boulevard
Upland, Pennsylvania 19013-3995

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14. ABSTRACT
The 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.

The research protocols are pending final IRB approvals; upon approval from the Army, Crozer will begin enrolling patients.

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 4/18/2007 to 7/18/2008

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 Aquacel Ag 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 Aquacel Ag dressing, and the other treated according to standard care. Approximately 20 patients will be enrolled. The hypothesis is that mean healing time for wounds treated with Aquacel Ag 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 Aquacel Ag 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 Aquacel Ag 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 Aquacel Ag 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

A Clinical Research Coordinator was identified at the inception of the research period. Bruce Ackerman, Pharm.D. (Pharmacy), is the Burn Treatment Centers' dedicated clinical pharmacist since 1999 and Pharmacy Residency Program Director in Crozer's Department of Pharmacy. His responsibilities were redefined to support the 0.5 FTE Clinical Research Coordinator position.

As noted in the quarterly reports that have been submitted to date, most of this period has been spent engaging in communication and submission of documents required to obtain IRB approval from both the Crozer IRB and the Army IRB. These approvals have now been obtained. The Research Coordinator, Bruce Ackerman, Pharm. D., and the Project Administrator, Cynthia Reigart, BSN, RN (Burn Nurse Manager) have had primary responsibility for communications with the two IRBs and have worked with the Principal Investigator, Linwood R. Haith, Jr. MD, to meet these IRB requirements. Crozer is now awaiting a letter from the USAISR authorizing the research team to begin enrolling patients in the studies.

At the end of the period, Crozer had successfully completed start-up activities in anticipation of obtaining the required approval to begin the research. The research office was completely renovated and furnished to allow for space for staff to carry out the research. The Burn Research Nurse positions were posted, interviews were conducted, and nurses were identified to fill the positions. These nurses will be formally hired when both studies have been given written approval from the USAIR to enter patients. Purchase orders to purchase the equipment for Study 1 are complete and will be submitted once the required approval is obtained from the Army.

A time extension was approved (Mod P00002) during the period which extends the grant for 24 months to 7/18/2010.

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

July, 2007 to September, 2007: All work has been dedicated to getting the IRB approval on all three studies; multiple re-writes on individual studies; Project Management in regards to the physical space; purchasing equipment, quotes, vendor meetings etc; job description development and implementation;

October, 2007: Study #2: coordinated more changes for Army IRB; Study #1 and Study #2: for final review at CCMC IRB; Pending approval of both studies after minimal changes to the

consents; Researching products necessary for purchase; obtaining quotes and communications between vendors and Army for DAQ machine. Multiple meetings with research team including the foundation office; finance dept. and clinical engineering.

November, 2007: Study #2: more written changes for the Army IRB; Study #1 approved by CCMC IRB except for the consent form; multiple changes to the consent form; continued development of equipment quotes and final determination of product purchasing will be completed in December; Staff for actual study completion will be posted by mid-December.

December, 2007: Multiple communications between the Army and the Crozer Research Team to accomplish IRB approval of Study #2. Problems arise with each change to the document, as each change must again be reviewed at the monthly IRB meetings. Each change taking 1 month to approve.

January, 2008: Continued communication with both IRB committees in regards to the Study on Donor Sites. The Study #1 on Burn Resuscitation remains at the Crozer IRB with multiple word changes to the required consent form. Monthly presentation to committee continues with each study.

February, 2008: Continued communication with both IRB committees in regards to the Study on Donor Sites. The Study #1 on Burn Resuscitation remains at the Crozer IRB with multiple word changes to the required consent form. Monthly presentation to committee continues with each study.

March, 2008: Approval of Study #2 by the Army IRB. Complete package must again return to the Crozer IRB for final review and the next meeting in April. Study #1 is approved at the Crozer IRB and now sits with the Army IRB for first review.

April, 2008: Approval of Army IRB for Study #2 is pending. Review of Study #1 with the Army IRB is pending.

May, 2008: Burn Research Position has been posted at Crozer at the end of the month. Interviews will begin in June. Army IRB approved the Study #2 with an expedient review through the Crozer IRB. We now await the letter from the Army to enter the first patient. Study #1 still pending from the Army IRB.

June, 2008: Burn Research Interviews are completed. Two Full time Research Nurses will be hired when both studies have been given written approval to enter patients. At that time, the trip to San Antonio, TX to learn the Resuscitation Project process will be completed. Equipment will be ordered after written confirmation is received for the Resuscitation Project. Study #1 – Resuscitation, continues to be pending from the Army IRB at this point. Study #2 still awaits the letter from the Army to enroll the first patient.

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

into the Resuscitation 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 Resuscitation 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.

KEY RESEARCH ACCOMPLISHMENTS:

The research has not begun. Once approval from the USAISR is received, Crozer will make arrangements for the research team to visit the Army Burn Center for orientation and training on the studies. Crozer is in the process of arranging for CRADAs (subcontracts) that will govern the Army's contributions to the research, as described in the original proposal. This includes engineering support for Study 1, biostatistical support, and travel.

REPORTABLE OUTCOMES:

Outcomes will be reported in the next Annual Report.

CONCLUSION:

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

REFERENCES:

No publications have been completed since the research has not begun.

APPENDICES:

Not applicable.