Does glucagon improve survival in a porcine (Sus Scrofa) of adult asphyxial cardiac arrest in addition to standard epinephrine therapy?

Objective: There is no difference in the rate of return to spontaneous circulation between treatment with epinephrine versus glucagon or glucagon plus epinephrine.

Method: 24 female swine 30-50kg were sedated with IV anesthesia, and instrumented (continuous aortic diastolic pressure via Millar transducer and Swan-Ganz catheter placed in pulmonary artery). Endotracheal tube was clamped. Four minutes post loss of arterial pressure, CPR was initiated via LUCAS device.

Conclusion: We were able to create a reproducible model of asphyxia arrest. We were able to show that an active mechanical compression device (specifically LUCAS device) can provide adequate coronary perfusion pressure and there is no significant difference in CPP in relation to pig weight. We detected the ventricular fibrillation was the most common rhythm after asphyxial cardiac arrest. This rhythm then degraded to asystole or bradystole.

Cardiac arrest, asphyxial cardiac arrest, glucagon, LUCAS device
PROTOCOL NUMBER: A-2007-03

PROTOCOL TITLE: Does Glucagon Improve Survival in a Porcine (Sus scrofa) Model of Adult Asphyxial Cardiac Arrest in Addition to Standard Epinephrine Therapy?

PRINCIPAL INVESTIGATOR: Dr. Bebarta, BAMC

ASSOCIATE INVESTIGATOR(S): Dr. Williams, Mr. Jordan RN, Dr. Batchinsky

LOCATION OF STUDY: BAMC

OBJECTIVE/HYPOTHESIS: Null hypothesis: There is no difference in the rate of return to spontaneous circulation between treatment with epinephrine versus glucagon or glucagon plus epinephrine.

Alternative hypothesis 1: Glucagon will have a higher rate of return to spontaneous circulation than epinephrine alone.

Alternative hypothesis 2: Glucagon plus epinephrine will have a higher rate of return to spontaneous circulation than epinephrine alone.

PROTOCOL STATUS:

[ ] Active (animal experiments, data gathering ongoing)
[X] Closed (animal experiments complete; data analysis, biochemical/lab analyses may be ongoing)
[ ] Request Termination (study will be terminated prior to completion of animal research)

[ ] FIRST YEAR REVIEW
[ ] SECOND YEAR REVIEW
[ ] THIRD YEAR — Please select one of the following options:
  [ ] Research ongoing, replacement protocol to be submitted for re-approval NLT ________.
    (if this option is selected, stop here and return signed form)
  [X] FINAL STUDY REPORT — (if study is closed/terminated, this form must be completed and signed.)

SPECIES: Swine

PAIN CATEGORY: [ ] C [X] D [ ] E

ANIMAL USAGE:

<table>
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<th>List model development, experimental groups, replacements*, etc.</th>
<th>Total Animals Authorized:</th>
<th>Used in first year:</th>
<th>Used in second year:</th>
<th>Used in third year:</th>
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* Clarify where replacement animals were used and explain why they were necessary in the section below.
Protocol No: A-2007-03
Protocol Title: Does Glucagon Improve Survival in a Porcine (Sus scrofa) Model of Adult Asphyxial Cardiac Arrest in Addition to Standard Epinephrine Therapy?

REASON(S) FOR USE OF REPLACEMENT ANIMALS: Not used

ADVERSE EVENTS/UNEXPECTED PROBLEMS: (Describe any unanticipated adverse events, morbidity, or mortality, the causes(s), if known, and how these problems were resolved. If none, please indicate.)

SUMMARY OF PROGRESS/FINDINGS: We had difficulty sustaining the original model and had to revise the anesthesia protocol. We did not complete all animals because the original PI (Williams) left the military and the funds he obtained expired, but were able to create a reproducible model of asphyxia arrest. We were also able to show two results and presented these at national meetings.

First, we were able to show that an active mechanical compression device (specifically the LUCAS device) can provide adequate coronary perfusion pressure and there is no significant difference the CPP as related to pig weight. We found that the LUCAS device was a useful adjunct in a swine model of asphyxia cardiac arrest.

Second, we detected the ventricular fibrillation was the most common rhythm after asphyxial cardiac arrest (59%). This rhythm then degraded to asystole or bradystole. This incidence is higher than in pediatrics which implies that the low rate of VF in children may be attributed to other factors besides asphyxia. Treatments for adults asphyxial arrest may be different that for pediatrics.

The team is preparing both observations for publication.

FINAL REPORTS ONLY – We were not able to complete all of the animals to evaluate the original hypothesis because the original PI (Williams) left the military and the funds he obtained expired; however we were able to determine that active mechanical compression device (specifically the LUCAS device) can provide adequate coronary perfusion pressure and there is no significant difference the CPP as related to pig weight. We were also able to determine that ventricular fibrillation was the most common rhythm after asphyxial cardiac arrest (59%).

NUMBER AND TITLE OF APPROVED ADDENDA:

#1 “Amendment to anesthesia/analgesia protocol and epinephrine dose to facilitate experimental objectives”
Approved 21 Apr 09
#2 “Anesthesia/Analgesia Regimen, Automated CPR Device and Malignant Dyshythmia Treatment”
Approved 29 Apr 09
#3 “Decrease in Duration on Non-Intervention Period”
Approved 17 July 09
#4 “Change in Principle Investigator”
Approved 15 Oct 10

ALTERNATIVES TO ANIMAL USE: (Alternatives to the use of animals should be considered and used when possible. Since the last IACUC approval, have alternatives that are potentially less painful or distressful become available that could be used to achieve your specific project aims? If none, please indicate.)

None

CHANGE IN PERSONNEL: (Principal Investigator, Associate Investigators, Technicians)

<table>
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Protocol No: A-2007-03
Protocol Title: Does Glucagon Improve Survival in a Porcine (Sus scrofa) Model of Adult Asphyxial Cardiac Arrest in Addition to Standard Epinephrine Therapy?

ABSTRACTS/MANUSCRIPTS/PRESENTATIONS: (Include where published/presented.)

Society of Academic Emergency Medicine – poster
Government Services Chapter of the American College of Emergency Physicians – poster
"In Vivo measurement of coronary perfusion pressure (CPP) during CPR by an active mechanical compression-decompression device (LUCAS) in a porcine model of asphyxia cardiac arrest"

Society of Academic Emergency Medicine – oral
Government Services Chapter of the American College of Emergency Physicians – oral
"Ventricular fibrillation and other terminal cardiac rhythms in a porcine model of asphyxia cardiac arrest"

DUPICATION: The activities of this project remain in compliance with the requirement that there must be no unnecessary duplication.

None

PRINCIPAL INVESTIGATOR'S CERTIFICATION: I hereby certify that this study is being conducted IAW the approved protocol and that all required records are being maintained IAW current IACUC policy, Army Regulation and/or Public Law.

Principal Investigator

IACUC
[ ] Active: approved for continuation
[ ] Suspended: pending major revision
✓ Closed
[ ] Terminated/Canceled

Chair, IACUC