Ascorbic Acid (Vitamin C) Infusion in Human Sepsis

This study is currently recruiting participants.

Verified September 2011 by Virginia Commonwealth University

First Received on August 9, 2011. Last Updated on September 12, 2011 History of Changes

Sponsor:	Virginia Commonwealth University
Information provided by (Responsible Party):	Virginia Commonwealth University
ClinicalTrials.gov Identifier:	NCT01434121

Purpose

The major goal of this project is to determine whether intravenously infused **ascorbic acid** is safe for use as a viable therapeutic strategy in adult humans with sepsis.

Condition	Intervention	Phase
Sepsis Septic Shock Hypotension Acute Lung Injury	Drug: **Ascorbic Acid** vs. Placebo	Phase I Phase II

Study Type: Interventional

Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Single Group Assignment
Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: **Ascorbic Acid** (**Vitamin C**) Infusion in Human Sepsis

Resource links provided by NLM:

MedlinePlus related topics: Low Blood PressureSepsisShockVitamin C

Drug Information available for: Ascorbic acid
U.S. FDA Resources

Further study details as provided by Virginia Commonwealth University:

Primary Outcome Measures:

- Determine whether **Ascorbic Acid** Infusion causes arterial hypotension, vomiting, or tachycardia in septic patients [Time Frame: during time of infusion-96 hours from time of enrollment] [Designated as safety issue: Yes]

Secondary Outcome Measures:

- Intensive care unit length of stay [Time Frame: subject will be followed until discharged from the ICU, has deceased, or study duration has reached 28 days from time of enrollment, whichever is first] [Designated as safety issue: No]
- Duration of mechanical ventilation [Time Frame: subject will be followed until mechanical ventilation has been discontinued, the subject has deceased, or study duration has reached 28 days from time of enrollment, whichever is first] [Designated as safety issue: No]
- Ventilator-free days [Time Frame: subject will be followed until discharged from the hospital, has deceased, or study duration has reached 28 days from time of enrollment, whichever is first] [Designated as safety issue: No]
- Length of time on vasopressor medication [Time Frame: during time of infusion - 96 hours from time of enrollment] [Designated as safety issue: No]
- Multiple organ dysfunction score [Time Frame: during time of infusion - 96 hours from time of enrollment] [Designated as safety issue: No]
- Plasma cytokine/chemokine levels [Time Frame: during time of infusions - 96 hours from time of enrollment] [Designated as safety issue: No]

Estimated Enrollment:	30
Study Start Date:	May 2010
Estimated Study Completion Date:	April 2012
Estimated Primary Completion Date:	April 2012 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Active Comparator: High Dose **Ascorbic Acid** Subject receives a high dose of infused **Vitamin C**	Drug: **Ascorbic Acid** vs. Placebo The infusion of either a high dose of **ascorbic acid**, low dose **ascorbic acid**, or placebo Other Name: **Vitamin C**
Active Comparator: Low Dose **Ascorbic Acid** Subject receives a low dose of	Drug: **Ascorbic Acid** vs. Placebo The infusion of either a high dose of **ascorbic acid**, low dose **ascorbic acid**, or placebo

infused **Vitamin C**	Other Name: **Vitamin C**
Placebo Comparator: Placebo Subject receives an infusion of saline	Drug: **Ascorbic Acid** vs. Placebo The infusion of either a high dose of **ascorbic acid**, low dose **ascorbic acid**, or placebo Other Name: **Vitamin C**

Detailed Description:

Evolving data from experimental animals strongly suggests that ascorbic acid potently interrupts multiple biological processes which lead to organ injury following onset of sepsis. Data presented below suggests that ascorbic acid potently attenuates lung injury produced by septic insults. Sepsis and septic shock secondary to bacterial and fungal blood stream infections are a leading cause of death in critically ill patients. At present, 28 day mortality in septic patients averages 40% in the best of ICUs. In sepsis, disseminated intravascular coagulation produces widespread systemic microvascular thrombosis that leads to multiple organ injury (i.e., lung, liver, kidney, intestinal, cardiovascular). Despite aggressive intravascular volume resuscitation and vasopressor support, appropriate antibiotic administration, and expert critical care management, mortality remains high. Only a single agent has been approved to disrupt progressive sepsis-associated microvascular thrombosis (activated protein C, [Drodrecogin Alpha, brand name: Xigris, Lilly]). No other non-antibiotic pharmaceutical agent is currently approved for use in sepsis. Activated protein C (APC) continuous infusion protocol spans a 96 hour period. APC infusion produces significant anticoagulation, and therefore the major risk from its use is hemorrhage. Thus, recent surgery, especially neurosurgical procedures, is a major contraindication to APC use. Finally, cost stands as an important issue for APC use. A 96 hour APC infusion in a 70 kg patient at VCUHS costs the patient over $33,000 (source VCUHS Pharmacy Services). Use of APC in sepsis remains controversial and has failed to achieve widespread acceptance. The goal of the current study is to determine the safety of ascorbic acid infusion in septic humans.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

1. systemic inflammatory response: fever (38°C or greater) or hypothermia (36°C or lower), tachypnea (20 breaths/min) or need for mechanical ventilation for an acute process, tachycardia (rate 90/min or more), white blood cell count ≥ 12,000 cells/mm3 or ≤ 4,000 cells/mm3 or more than 10% band forms.
2. Presumed or Known Site of Infection: Purulent sputum, chest radiograph with new infiltrate, spillage of bowel contents, radiographic or physical examination evidence of an infected collection, white blood cells in a normally sterile body fluid, positive blood culture, evidence of infected mechanical hardware by physical, radiographic, or ultrasonographic evidence.
3. Evidence of Dysfunction of One or More End Organs: cardiovascular dysfunction: mean arterial pressure 60 mm Hg or less, the need for

vasopressors to maintain this pressure in the presence of adequate intravascular volume (central venous pressure 12 mmHg); respiratory failure: (arterial PO2-to-FiO2 ratio of less than 250 or less than 200 in the presence of pneumonia; renal dysfunction: Urine output ≤ 0.5 ml/kg/hr for 2 hours in the presence of adequate intravascular volume or doubling of the serum creatinine; hematologic dysfunction: thrombocytopenia ≤ 80,000 platelets/mm3 or 50% decrease from baseline during the acute illness; Unexplained metabolic acidosis: arterial pH ≤ 7.3 and a plasma lactate level higher than 2.5. Hepatic Dysfunction: Acute Serum transaminase elevation greater than five times normal.

4. Informed Consent: Ability to obtain informed consent within 48 hours.

Exclusion Criteria:

1. Demographic Characteristics: Children (age < 18 years), pregnant women, prisoners, and other wards of the state are excluded from participation in this study.
2. Informed Consent: Inability to obtain informed consent within 48 hours.
3. Cognitive Impairment: In the absence of family or next of kin, if the investigators feel the patient is cognitively impaired, and unable to provide informed consent, the patient will not be accessed to the study.
4. Non-English Speaking Patients: Patients who are non english speaking will not be accessed to this study.

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01434121

Contacts

Contact: Christine Dewilde, RN	804-628-5710	dewildect@vcu.edu
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Locations

United States, Virginia

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Sponsors and Collaborators

Virginia Commonwealth University
Investigators

Principal Investigator: Alpha Fowler, MD Virginia Commonwealth University

More Information

No publications provided

Responsible Party:	Virginia Commonwealth University
ClinicalTrials.gov Identifier:	NCT01434121 History of Changes
Other Study ID Numbers:	HM12903
Study First Received:	August 9, 2011
Last Updated:	September 12, 2011
Health Authority:	United States: Institutional Review Board

Additional relevant MeSH terms:

Ascorbic Acid	Pathologic Processes
Hypotension	Lung Diseases
Sepsis	Respiratory Tract Diseases
Toxemia	Respiration Disorders
Shock	Thoracic Injuries
Shock, Septic	Wounds and Injuries
Acute Lung Injury	Vitamins
Respiratory Distress Syndrome, Adult	Antioxidants
Lung Injury	Molecular Mechanisms of Pharmacological Action
Vascular Diseases	Pharmacologic Actions
Cardiovascular Diseases	Protective Agents
Infection	Physiological Effects of Drugs
Systemic Inflammatory Response Syndrome	Micronutrients
Inflammation	Growth Substances

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