Circulation

FREE ACCESS | ABSTRACT

SURGERY AND ANESTHESIA
SESSION TITLE: SURGICAL TREATMENT OF HEART FAILURE AND TRANSPLANTATION POSTERS

Abstract 9706: A Novel High Energy Phosphate Source Resuscitates Poorly Functioning Donor Hearts

Salwa A Elgebaly, Robert Poston, Charles Van Buren, Robert Todd, Reem Arafa, Nashwa El-Khazragy, Mostafa Rabie, Ahmed Mohamed, Lamiaa Ahmed and Nesrine El Sayed

Originally published 30 Oct 2022 | Circulation. 2022;146:A9706

Abstract

Introduction: Over 60% of the time donor hearts cannot be *utilized* for transplant, mostly because of poor left ventricular ejection fraction (EF) of ≤40% due to stress cardiomyopathy (i.e., demand ischemia) with depletion of myocardial adenosine triphosphate (ATP). The bioenergetic cyclocreatine phosphate (CCrP) is an *FDA OrphanDesignatedDrugfor heart transplantation*. When CCrP is given prophylactically in an isoprenaline (ISO) rat model of demand ischemia, it restored ATP and maintained contractility.

Hypothesis: We hypothesized that administering CCrP therapeutically after ISO-induced myocardial dysfunction in rats (simulating rejected donor hearts), will prevent ischemic injury and sustain long-term restoration of EF.

Methods: Wistar male rats (180-220 g) were injected SC with ISO (85 and 170 mg/kg/day) for two consecutive days. CCrP (n=6, 0.8 gm/kg/day ip) and saline control (n=4) were administered *1 hour* after completing the course of ISO injections and then daily for 2 weeks. A negative control group was injected with saline (n=4). Serum CK-MB and ECG/ST were measured 24 hours after last ISO injection. Evidence of stress cardiomyopathy was assessed after 14 days by ECHO analysis for EF and levels of hs-Troponin I (TnI) and BNP. One-way ANOVA analysis was used.

Results: Table I shows two main benefits of therapeutically administered CCrP in this stress cardiomyopathy model: 1) poor heart function was quickly restored in the *acute phase* (24 hours), as indicated by normal ECG/ST and CK-MB levels; and 2) the restoration of function was sustained over the long term (14 days), as indicated by normal EF% and levels of hs-TnI and BNP.

Conclusions: The bioenergetic CCrP is a novel cardioprotective drug that appears to *salvagecardiac dysfunction* and restore *normal EF%* in a rat model of stress cardiomyopathy. If this benefit translates into clinical organ donors with poor heart function, CCrP could be used to increase heart utilization for transplantation.

Table 1: CCrP *therapeutically* administered post drug-induced stress cardiomyopathy (ISO x 2 days) in rats prevented myocardial injury, salvaged cardiac dysfunction, and sustained long-term restoration of EF%.

	24 hours		14 days			
	ST (mv)	CK-MB (U/L)	EF (%)	hs-TnI (pg/ml)	BNP (pg/ml)	Activity score
Control saline	0.053±0.004	75.67±2.52	65.70±1.07	4.71±0.74	32.45±2.32	4.0± 0.17
Stress + saline	0.144±0.016*	207.8±5.13*	35.58±1.53*	148.0±11.16*	185.0±10.39*	1.5± 0.28*
Stress + CCrP	0.056±0.004#	61.33±2.89#	56.68±1.42#	21.08±2.99#	57.71±4.11#	3.7± 0.20#

The results are presented as mean and standard error of mean, *: Statistically significant difference compared to the control saline group, #: Statistically significant difference compared to the stress saline group. Abbreviations: CCrP: Cyclocreatine phosphate, ST: Elevated ST segment, mv: millivolt, CK-MB: Creatine kinase-MB, EF: Ejection fraction, hs-TnI: High sensitive Troponin I, BNP: Brain natriuretic peptide.

Download figure

Footnotes

Author Disclosures: For author disclosure information, please visit the AHA Scientific Sessions 2022 Online Program Planner and search for the abstract title.

Back to top

Circ: Heart Failure
Circulation Research
Hypertension
Journal of the American Heart Association (JAHA)
Stroke
Stroke: Vascular and Interventional Neurology
AIM: Clinical Cases

Journal Information

About
Editorial Board
Reprints
Customer Service and Ordering Information
AHA Journals RSS Feeds
For International Users
Institutions/Librarians FAQ
For Subscribers
Subscriber Help
Wolters Kluwer Privacy Policy

Subjects

All Subjects
Arrhythmia and Electrophysiology
Basic, Translational, and Clinical Research
Critical Care and Resuscitation
Epidemiology, Lifestyle, and Prevention
Genetics
Heart Failure and Cardiac Disease
Hypertension
Imaging and Diagnostic Testing
Intervention, Surgery, Transplantation
Quality and Outcomes
Stroke
Vascular Disease

Features

Bridging Disciplines
Circulation at Major Meetings
Special Themed Issues
Global Impact of the 2017 ACC/AHA Hypertension Guidelines
Circulation Supplements

Cardiovascular Case Series
ECG Challenge
Hospitals of History
On My Mind
Podcast Archive
- Circulation on the Run
- Subscribe to Circulation on the Run
- #FITFAVES
Circulation Doodle

Resources & Education

AHA Guidelines and Statements
Circulation CME
Information for Advertisers

For Authors & Reviewers

Instructions for Authors
Submission Site
AHA Journals EDI Editorial Board
Author Reprints

American Heart Association®

National Center
7272 Greenville Ave.
Dallas, TX 75231

Customer Service
1-800-AHA-USA-1
1-800-242-8721
Local Info
Contact Us


PUTTING PATIENTS FIRST
National Health Council
Standards of Excellence
Certification Program®


BBB
ACCREDITED
CHARITY


COMODO
SECURE