

Animal Studies on Chronic Heart Failure and Oxidative Stress

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It has been well established through years of research and clinical practice that the causes of heart failure are multi-factorial. Treating this clinical syndrome requires several medications that address as many physiological pathways as possible to improve patient survival and reduce morbidity. Guidelines put forth by the American College of Cardiology/American Heart Association Task Force recommend a pharmaceutical assortment of beta-blockers, angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARB), diuretics, and vasodilators that are collectively referred to as the “standard of care.” As more research is being done to unveil the underlying causes of heart failure, there is a plethora of data that suggests that oxidative stress may be yet another culprit in the pathogenesis of this disease.

Oxidative stress results from the generation of reactive oxygen species (ROS) that occurs naturally in our bodies as a byproduct of metabolism. Our bodies also produce endogenous antioxidants that appear to counterbalance the generation of ROS as a defense mechanism. A study conducted by Dr. M. Keith and colleagues conducted a study of 58 heart failure patients that demonstrated an increase in cellular damage caused by ROS, and a decline in antioxidant reserves when compared to patients without heart failure. Their data also illustrated a significant correlation between the amount of oxidative stress and a patient’s New York Heart Association functional classification.

When studying drugs to treat heart failure in animals, it is important to have a model that resembles the steady progression of cardiac dysfunction under chronic pressure or volume overload. The aortovenous fistula (AVF) rat

model of heart failure simulates the progressive eccentric cardiac hypertrophy that results from chronic volume overload to the heart. In the AVF rat arterial blood from the abdominal aorta flows directly into the caudal vena cava, thereby increasing blood volume to the heart. In a 90-day study conducted by Shimamura and colleagues, they noted that the AVF rats exhibited a steady increase in diastolic blood pressure, dilation of left ventricular diameter, and a compensatory change in cardiac function according to Frank-Starling’s law. When the AVF rats progressed to end-stage congestive heart failure, there was depressed cardiac function with eccentric hypertrophy. This is similar to what is observed clinically in congestive heart failure patients.

Using the AVF rat model to explore the role of ROS in volume-overloaded heart failure may provide a better perspective on disease progression under a chronically stressed state. Animal studies using carvedilol, losartan and captopril have already demonstrated that these drugs maintain antioxidant reserve and decrease oxidative stress in heart failure models. Given the strong correlation between oxidative stress and heart failure progression, the AVF rat model can be used by researchers to evaluate novel compounds that exhibit antioxidant properties. In this way we may be able to develop additional drug therapies to further improve morbidity and mortality amongst heart failure patients.

References

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The Association of Black Cardiologists, Inc. is committed to rigor in science, including basic and clinical research. We also feel that it is extremely important that we nurture and develop younger professionals to become the future leaders in the health sciences.

This special article is submitted by the request of the ABC's Chief Science Officer from Ms. Darra M. Waller, MA.

Ms. Darra Walker is currently pursuing her Doctor of Pharmacy degree in conjunction with a Doctor of Philosophy in Pharmaceutical Sciences at Mercer University College of Pharmacy and Health Sciences in Atlanta, GA. Women than men die from cardiovascular diseases each year. While the overall cardiovascular disease rate for men has been steadily declining over the last two decades, the rate for women has risen slightly, especially among minority women. Nearly half of African American women (45 percent) have some form of cardiovascular disease, compared to 32 percent of white women.