Salwa Ahmed Elgebaly, J Clin Exp Cardiolog 2016, 7:9(Suppl)
http://dx.doi.org/10.4172/2155-9880.C1.050

Nourexal™: A Novel Anti-inflammatory / Antiapoptotic Therapy Against Reperfusion Injury

Salwa Ahmed Elgebaly
Nour Heart Institute, USA

Myocardial tissue has an extreme sensitivity to ischemia and hypoperfusion. The current available options to address this problem are all directed at restoring tissue perfusion in the myocardium. However, the main mechanism of myocardial ischemia that leads to reduction in cardiac function and irreversible injury is through the exhaustion of the high-energy adenosine triphosphate (ATP). Depletion of ATP during ischemia is one of the major factors that accelerate the apoptotic process of healthy myocardial tissue, leading to tissue progression to necrosis and heart failure.

Our research has demonstrated that reduction of ATP during ischemia also resulted in the rapid release (within 5 minutes) of the potent inflammatory mediator Nourin by ischemic myocardial tissue and coronary arteries. The release of Nourin was associated with early cardiac inflammation characterized by large influx of neutrophils. Our studies also indicated that Nourin purified from human ischemic hearts, is an 'early inflammatory signal' which stimulates leukocyte chemotaxis, adhesion and activation to release high levels of chemokines, cytokines, adhesion molecules and digestive enzymes. Specifically, Nourin stimulates human monocytes to release high levels of tumor necrosis factor-α (TNF-α), which is a major contributor of myocardial apoptosis.

For early reperfusion injury, the first few minutes of reperfusion after ischemic infarct constitute a critical phase that leads to impaired microcirculations and the 'no reflow' phenomenon. Inflammation is central to microcirculation obstruction (MVO) in early reperfusion and also in late reperfusion injury. Since both inflammation and ATP depletion play a key role in MVO and infarct size, we tested the cardioprotective benefits of our patented *Nourexal™ therapy* in a number of animal models (dogs, rats and rabbits) of ischemia/reperfusion, including: acute myocardial infarction (AMI), global warm cardiac arrest, cardiopulmonary bypass for coronary revascularization and heart transplantation models (prolonged heart preservation and nonheartbeating donor hearts).

We have demonstrated that administrating *Nourexal™* (Cyclocreatine Phosphate - CCrP) minutes before ischemia (a) preserved high levels of ATP in ischemic myocardium; (b) reduced myocardial cell injury, acidosis and edema; (c) reduced Nourin formation in the myocardium and its blood levels; (d) reduced post-ischemic cardiac inflammation and apoptosis; and (e) restored immediate strong cardiac contractibility during reperfusion without arrhythmia.

Clinical application is where myocardial ischemia is predictable and pretreatment of patients with *Nourexal™* would improve the patients' outcome and quality of life. These include patients undergoing cardiopulmonary bypass for coronary revascularization, heart transplantation and AMI patients undergoing angioplasty procedures / Percutaneous Coronary Intervention (PCI).

For AMI patients, administering *Nourexal™* during myocardial infarction and reperfusion will likely (a) protect cardiomyocytes from energy depletion and early inflammation; (b) protect the adequacy of microcirculations; (c) increase the amount of salvaged myocardium; and (d) reduce the progression of the ischemic myocardium to necrosis during the critical first 4 to 6 hours of reperfusion. Furthermore, targeting the early inflammatory mediator Nourin will likely produce the right balance between reducing the early harmful effect of inflammation without affecting its beneficial healing and scar formation.

In summary, we believe that this novel *Nourexal™ therapy* will provide heart protection against ischemic and reperfusion injury and it will be particularly critical for AMI patients with long transport times to the hospital and for patients who cannot get timely pharmacologic or mechanical revascularization. This early protection will likely reduce the incidence of chronic heart failure and improve the patients' outcome and quality of life.

Biography

Dr. Salwa Elgebaly graduated from the University of Alexandria Faculty of Pharmacy and holds a Master's Degree from the University of Wisconsin Faculty of Medicine in Madison, Wisconsin; and a PhD from the University of North Carolina, Faculty of Pharmacy at Chapel Hill, North Carolina. She is a former Associate Professor at the University of Connecticut School of Medicine and she is currently the Executive Director of Nour Heart Institute (subsidiary of Nour Heart, Inc.). Dr. Elgebaly is the Inventor of 9 Patents Issued by the U.S. Patent Office. Dr. Elgebaly identified and patented the potent inflammatory mediator, Nourin as a key 'initial signal' in early reperfusion injury. Her research targets the development of new therapy for patients with Ischemic Heart Diseases (IHD). She is currently developing a new combined therapy of the anti-inflammatory Nourexin™ (Nourin specific competitive antagonist) and the anti-apoptotic *Nourexal*™ (ATP preservation during ischemia) to protect AMI patients from reperfusion injury.

selgebaly@nourheart.com