Amino Acids as Cardioprotective Substrates in the Anoxic Heart

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***Short Abstract* — Dual-camera imaging and analysis of regional microdialysis effluents from the interstitial fluid of isolated perfused hearts using ion mobility-mass spectroscopy (IM-MS) will enable tests of the hypothesis that amino acid supplementation can reduce the electrical instabilities associated with anoxia, thereby reducing the incidence of cardiac arrhythmias, fibrillation and death.**

***Keywords* — Cardiac, Cardioprotection, Metabolism, Amino Acids, Ischemia.**

I. Purpose

The heart is a resilient organ, capable of maintaining contractile function even under ischemic and anoxic conditions. It has long been known that the key to maintaining cardiac function is maintenance of electrical activity using a variety of substrates.[1-3] Anoxia-induced shortening of APD, a source of electrical instability, has been shown to be enhanced after metabolic inhibition.[1,,3]

While amino acids normally only account for about 5% of the heart's metabolic energy, under ischemic conditions the amino acid pool becomes one of the heart's primary fuel sources.[4,5] It may be possible to prolong cellular function during anoxia and improve post-anoxia recovery by supplementing cells with select amino acids. The effect of amino acids on APD and cardiac electrical stability during anoxia is unknown, but may have potentially significant clinical utility.

Optical measurement of the cardiac action potential using our dual-camera imaging[6] allows us to image both the transmembrane potential and intracellular calcium levels. We anticipate continuous measurement of the concentrations of amino acids, glucose, fatty acids, lactate, calcium, and potassium directly from the interstitium of isolated perfused rabbit hearts using microdialysis and a combination of in-line and off-line analyses. Together, these techniques will provide a coherent record of the time course of metabolic changes during and after ischemia to allow deeper probing of the underlying physiology of the ischemic heart.

II. Results

Our optical approaches provide a quantitative assessment of the reduction in APD during ischemia and instabilities in cardiac electrical activity induced by rapid pacing.

Microdialysis probes can be inserted into the heart to dialyze the interstitium, allowing active monitoring even in the absence of coronary flow so that metabolites immediately around the cells are captured before these molecules enter the circulatory system, thereby eliminating the problems of time delay and dilution inherent in the sampling of whole heart effluent. We use IM-MS to identify proteins and small molecules of interest in the cardiac effluent in order to quantify the heart's response to anoxia. IM-MS is ideal for this as it is capable of separating signals from lipids, proteins and other molecules, thereby increasing the sensitivity of the measurements and allowing each class of molecules to be analyzed separately.[7]

III. Conclusion

We are combining several powerful techniques in a single experimental design that allows us to probe the ischemic myocardium more completely than has been done previously. These results will help researchers more clearly understand the complex interplay between cardiac metabolism, electrical function and ischemia.

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