

epinephrine (NE) and relaxed dose-dependently to sodium nitroprusside (SNP), a nitric oxide donor. Pre-incubation of HSV with SB203580 (50 μ M), an inhibitor of p38 MAP Kinase, which is upstream of MAPKAP kinase II (the kinase that directly phosphorylates HSP27), increased SNP (1 μ M) relaxation of HSV from 20% \pm 8% to 62% \pm 12% ($p < 0.05$, $n=5$, \pm SEM). SB203580 pretreatment also reduced the magnitude of NE induced contraction by (50% \pm 9%). SB treatment decreased the basal phosphorylation of HSP27 (Ser 82 and Ser 15) by 68% and increases SNP stimulated phosphorylation of HSP20 (Ser 16) by 20%. These results suggest that SB203580 treatment can reduce the magnitude of agonist induced contraction. This was associated with a decrease in the basal level of HSP27 phosphorylation. In addition, decreases in HSP27 phosphorylation were associated with increased SNP induced phosphorylation of HSP20 and relaxation. These results suggest that the two small heat shock proteins, HSP20 and HSP27 may have opposing effects in mediating vascular tone and that inhibiting the phosphorylation of HSP27 may be a therapeutic approach for preventing vasospasm.

13. RIBOSE TREATMENT HELPS PRESERVE FUNCTION OF THE REMOTE MYOCARDIUM AFTER MYOCARDIAL INFARCTION. N. Befera, A. Rivard, D. Gatlin, S. Black, J. Zhang, J. E. Foker; University of Minnesota, Minneapolis, MN

Introduction: The myocardium, stressed from a variety of causes including pressure or volume overload, may develop increasing dysfunction and go on to apoptosis and remodeling. This progression produces the increasingly common problem of chronic cardiac failure (CCF). The progression has been well characterized, but what controls it is unknown. We hypothesized that the progression begins by increased cardiac load producing an unfavorable myocardial energy supply/demand ratio which leads to depressed myocardial energy levels. We have begun to study this progression in a myocardial infarction (MI) model. Following an MI, the uninvolved, remote myocardium (RM) must assume the entire workload of the ventricle, and this additional strain on the RM has been shown to lead to apoptosis and remodeling. The hypothesis that a fall in RM energy levels leads to decreased function was tested by infusing ribose in a rat MI model. We have shown in a global ischemia and reperfusion model that ribose infusion will greatly enhance return of myocardial ATP levels and function. Because ribose is the rate-limiting precursor to adenine nucleotide synthesis and is not itself a fuel source, increased AMP synthesis must be the reason for the enhanced recovery. **Methods:** Male Lewis rats received continuous venous infusion of 0.9% NaCl solution with or without 2.5% D-ribose ($N=6$ for each group) via implanted osmotic mini-pump (Durect, Inc.) for 14 days. Animals underwent ligation of the left anterior descending coronary artery to produce an anterior wall MI, 1-2 days after pump placement. Echocardiographic analysis was performed preoperatively and at 2 and 4 weeks post-MI to assess changes in function by ejection indices, chamber dimensions, and wall thickness. **Results:** By all three indices, the function of the RM was better maintained with ribose treatment following an anterior MI. Contractility (EF, SF) and wall thickness were increased, and less ventricular dilation occurred. These data show that ribose infusion reduces the impairment of RM function that follows an MI. **Conclusion:** These data show (1) the RM shows a significant decrease in function four weeks following an MI, and (2) ribose infusion prevents, to a significant degree, the dysfunction. The benefit of ribose suggests the increased workload on the RM produces an unfavorable energy supply/demand ratio which results in lower myocardial energy levels. Studies are underway to determine the changes in energy metabolism and apoptotic pathways which occur. These data show that raising myocardial energy levels clearly improves function and we propose it may also delay chronic changes, including apoptosis, in a variety of surgically treatable CCF conditions.

Echo Indices	Treatment	Pre-MI	4 wks after MI
LV diastolic diameter (cm)	Ribose	0.64 \pm 0.04	0.76 \pm 0.07*
	Control	0.68 \pm 0.03	0.94 \pm 0.07
LV systolic diameter (cm)	Ribose	0.39 \pm 0.06	0.64 \pm 0.09*
	Control	0.40 \pm 0.03	0.95 \pm 0.07
Septal diastolic thickness (cm)	Ribose	0.13 \pm 0.02	0.12 \pm 0.02
	Control	0.12 \pm 0.01	0.10 \pm 0.01
Posterior wall diastolic thickness (cm)	Ribose	0.13 \pm 0.02	0.13 \pm 0.03*
	Control	0.13 \pm 0.03	0.10 \pm 0.01
Ejection fraction (EF) %	Ribose	76.4 \pm 5.9	49.1 \pm 9.4*
	Control	76.3 \pm 2.3	31.2 \pm 4.8
Shortening fraction (SF) %	Ribose	38.6 \pm 5.3	19.9 \pm 6.1*
	Control	38.9 \pm 2.1	10.7 \pm 1.1

* $P < 0.05$ vs. control.

14. IMPROVEMENT IN CARDIAC FUNCTION BY MESENTERIC LYMPHATIC DIVERSION (LD) IN THE SETTING OF INTESTINAL ISCHEMIA/REPERFUSION (IR) IS NOT MEDIATED BY NFKB OR TNF-ALPHA DEPENDENT PATHWAYS. R. S. Radhakrishnan, H. Xue, K. Felix, S. D. Moore-Olufemi, F. A. Moore, S. J. Allen, C. S. Cox, JR.; University of Texas Health Sciences Center, Houston, TX

Introduction: We have previously shown that mesenteric LD in the setting of intestinal IR can improve cardiac function, reduce myocardial tissue water, and reduce cardiac PMN infiltration. This led us to believe that LD decreased the proinflammatory response in the heart. The purpose of this study was to determine if LD decreased the proinflammatory response via NfKB and TNF-alpha dependent pathways. **Methods:** Dogs were randomized to 2 groups: IR (one hour of celiac and superior mesenteric artery occlusion with 3 hours of reperfusion) and IR+LD (IR with mesenteric lymphatic cannulation and external diversion). Micromanometer and sonomicrometry crystals were placed in the heart to determine cardiac function parameters. The slope of end-systolic pressure-volume relationship (E_{max}), preload recruitable stroke work (PRSW), and cardiac output (CO) were measured to determine systolic function. Isovolemic relaxation time (τ), $-dp/dt$ max, and the end-diastolic pressure-volume relationship (EDPVR), and were calculated to determine diastolic function. Cardiac parameters were measured after 1 hour of ischemia and 3 hours of reperfusion. In addition, intestine and cardiac biopsies were taken for determination of tissue water, NfKB binding activity, and TNF alpha activity. In a separate study, lymph collected from the IR+LD group was reinfused into a third group of dogs (IR lymph reinfusion) to evaluate the effect of IR mesenteric lymph on cardiac function. **Results:** Lymphatic diversion caused a significant increase in cardiac systolic function while decreasing cardiac and intestinal edema. There was no significant effect on diastolic function, cardiac TNF alpha and NfKB, or intestinal TNF alpha and NfKB levels. IR lymph reinfusion decreased E_{max} , PRSW, and CO similar to IR alone. There were no differences in $-dp/dt$ max, τ , or EDPVR. **Conclusion:** In the setting of intestinal IR, lymphatic diversion causes a significant improvement in cardiac systolic function. In addition, lymphatic diversion does not seem to affect cardiac diastolic function. Finally, these cardiac functional changes are not associated with changes in cardiac or intestinal NfKB or TNF-alpha.