Acute Coronary Syndromes

GLUCAGON-LIKE PEPTIDE-1 RECEPTOR ACTIVATION WITH LIRA GLUTIDE DURING MYOCARDIAL ISCHEMIA DECREASES INFARCT SIZE AND IMPROVES SYSTOLIC LEFT VENTRICULAR FUNCTION

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Background: Glucagon-like Peptide-1 (GLP-1) is essential for normal glucose tolerance and evidence suggests that it has anti-apoptotic and cytoprotective actions. Liraglutide is a GLP-1 receptor (GLP-1r) agonist used for the treatment of Type 2 diabetes, and may also confer clinical benefits through cardiac GLP-1r activation. The objective of our study was to investigate the cardioprotective effects of GLP-1r activation with Liraglutide in the setting of acute myocardial ischemia (MI) and reperfusion.

Methods: Acute MI was induced in Yorkshire pigs by balloon occlusion of the proximal LAD for 60 minutes, followed by reperfusion. Animals were randomly assigned to receive either Liraglutide (1.2 mg i.v.; n=4) 10 minutes prior to reperfusion and then twice daily for the next 3 days, or saline for controls (n=4). The extent of the MI and myocardial function were assessed by contrast-enhanced cardiac MRI, one week and one month post-MI induction.

Results: One week after MI induction, Liraglutide reduced infarct size by 17% compared with controls (33.9 ± 1.5% vs. 40.9 ± 0.7% of LV, p < 0.05), as measured by delayed gadolinium enhancement. Of note, there was no difference in the area at risk between the two groups as measured by T2 weighted imaging (42.2 ± 0.6% vs. 40.1 ± 1.4% of LV, p = 0.26). The myocardial salvage was five times higher in pigs treated with Liraglutide compared with controls (15.5 ± 2.2% vs. 3.1 ± 0.3%, p < 0.05). Importantly, Liraglutide treatment improved LV ejection fraction one week post MI compared with controls (41.0 ± 1.6% vs. 32.9 ± 0.7%, p < 0.05). The significant difference in systolic LV function between the groups persisted one month post MI (43.8 ± 2.3% vs. 31.2 ± 1.3%, p < 0.05).

Conclusions: Our results indicate that GLP-1r activation by Liraglutide initiated prior to reperfusion significantly reduces infarct size. In addition, Liraglutide significantly improved systolic left ventricular function at one week and one month post MI. These results strongly suggest a cardioprotective role for GLP-1 signaling. In conclusion, our observations underscore the therapeutic potential of the GLP-1 system in acute myocardial ischemia, and further studies in humans are warranted.