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THE GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST EXENATIDE IS SAFE AND MAY BE CARDIOPROTECTIVE IN ACUTE MYOCARDIAL INFARCTION: THE EXAMI PHASE I TRIAL

i2 Poster Contributions
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Background: The most effective therapy in acute myocardial infarction (MI) is early reperfusion by percutaneous coronary intervention (PCI). Reperfusion limits myocardial necrosis, however induces reperfusion injury leading to additional necrosis and apoptosis. Glucagon Like Peptide-1 (GLP-1), an incretin hormone, has anti-apoptotic properties and proved to be cardioprotective in experimental studies. This pilot study assessed the safety and feasibility of the GLP-1 receptor agonist exenatide in patients with acute MI undergoing primary PCI.

Methods: Seventy-one non-diabetic patients with acute MI undergoing primary PCI were randomized to placebo or exenatide 5µg bolus administered in 30 minutes prior to PCI, followed by continuous infusion of 20µg/ 24 hours for 72 hours. Blood samples were obtained including enzymatic infarct size and glucose levels. Magnetic resonance imaging and echocardiography were conducted 3-5 days and 4 months post MI for measurements including infarct size, cardiac function and myocardial salvage index (MSI), a predictor for mortality and major adverse cardiac events.

Results: Forty out of 71 randomized patients completed the full protocol. Exclusion was mainly due to angiographic criteria. Patient characteristics were well balanced between the groups. An equal amount of hypo- and hyperglycemic episodes (glucose < 4 mmol/L or > 10 mmol/L) were observed in both groups. No deaths, CABG or re-infarction occurred during the 4-month follow-up. Although more patients in the exenatide group experienced nausea (58% v 20%, p = 0.015), no decrease or cessation of exenatide was required. Infarct size, cardiac function and MSI at 4 months did not differ significantly. However, a trend towards a higher MSI was seen in patients with TIMI 0 and 1 flow receiving exenatide (0.65 ± 0.14 (n = 12) v 0.53 ± 0.17 (n = 11), p = 0.09).

Conclusions: We demonstrated that administering exenatide in patients with acute MI undergoing primary PCI is feasible and safe. Although not powered for this analysis, Exami phase I seems to show a trend towards a higher MSI in the exenatide group. A large randomized placebo controlled study is required to assess the efficacy of exenatide on myocardial salvage.