Intravenous administration of IV-STATIN CARDIOSHIELD during myocardial infarction renders higher cardioprotection than oral atorvastatin given shortly after reperfusion: a translational CMR study

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Background: Statins are known to exert rapid cardioprotective effects irrespective of their lipid-lowering properties. Several trials have suggested that high-dose statin treatment may reduce cardiovascular complications in patients undergoing invasive management. However, the ideal timing and administration regime is not clear.

Purpose: We compared the cardioprotective effects derived from IV-STATIN CARDIOSHIELD® administered intravenously during myocardial infarction (MI) with those attained by oral atorvastatin administration shortly after reperfusion. This study was conducted in a preclinical pig model of MI by serial CMR imaging.

Methods: Diet-induced hypercholesterolemic pigs (N=21; cholesterol: 387±74mg/dL) were subjected to 90 minutes of complete coronary occlusion (closed-chest model of MI), then reperfusion was established and animals were kept for 42days. Within this experimental design animals were distributed in 3 groups (G) (7animals/arm): G1) animals received an intravenous bolus (0.3mg/kg) of IV-STATIN during MI; G2) animals received an intravenous bolus of the vehicle during MI (placebo-control); and G3) animals were administered atorvastatin p.o. initiated within the first 2h post-MI (Atorva-post-MI). G1 and G3 animals remained on atorvastatin p.o. for the following 42days whereas G2 controls received placebo-pills. We assessed cardiac damage and global and regional functional parameters by CMR at day3 and day42 post-MI. Myocardial samples were processed for molecular studies on cardiac remodeling-related parameters (collagen and AMPK).

Results: CMR analysis at day-3 revealed that G1 pigs showed a marked reduction in infarct size as compared to both G3 and G2 animals (19.1±2.8% LV vs. 29.0±1.8% and 29.3%±3.2%, respectively; p<0.05) with a resultant 50% increase in myocardial salvage (p<0.05 vs. both). At day-42 both G1 and G3 animals showed a significant decrease in the size of the scar vs. G2 animals; however, G1 animals showed a further 24% scar reduction as compared to G3 (14.4±1.1% vs. 18.8±1.0% LV; p<0.05). Functional analyses revealed higher LVESV in G1 animals as compared to G2 (p<0.05) and less wall motion abnormalities in the jeopardized myocardium (p<0.05) vs. both groups at day42 post-MI. Collagen expression and AMPK activation were found to be significantly enhanced in the scar of G1 (p<0.05 vs. both groups). No changes were detected in lipids levels or liver and renal parameters throughout the study in any pig group.

Conclusions: Intravenous IV-STATIN CARDIOSHIELD® treatment during MI limited cardiac damage and improved cardiac function and remodeling to a larger extent than when atorvastatin was administered orally shortly after reperfusion. Our results support this novel regime of intravenous administration of IV-STATIN CARDIOSHIELD® as a routine procedure during MI. Further investigation of the potential benefits of this new therapeutic approach in STEMI patients is warranted.