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Acute Coronary Syndromes

THE ANTI-ARRHYTHMIC DI-PEPTIDE ZP1609 (DANEGAPTIDE) WHEN GIVEN AT REPERFUSION REDUCES MYOCARDIAL INFARCT SIZE IN PIGS

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Background: Connexin 43 is located in the cardiomyocyte sarcolemma and in the mitochondrial membrane. Sarcolemmal connexin 43 contributes to the spread of myocardial ischemia/reperfusion injury, whereas mitochondrial connexin 43 contributes to cardioprotection. We have now investigated cardioprotection by the anti-arrhythmic di-peptide ZP1609 (danegaptide), which is an analog of the connexin 43 targeting anti-arrhythmic peptide rotigaptide (ZP123). Experiments were performed in an established and clinically relevant experimental model of ischemia/reperfusion injury in pigs.

Methods: Pigs were subjected to 60 min coronary occlusion and 3 h reperfusion. ZP1609 (n=10) was given 10 min prior to immediate full reperfusion (75 µg/kg b.w. bolus i.v. + 57 µg/kg/min i.v. infusion for 3 h). Immediate full reperfusion without ZP1609 (IFR, n=9) served as control. Ischemic postconditioning (PoCo, n=9; 1 min LAD re-occlusion after 1 min reperfusion; 4 repetitions) was used as a positive control of cardioprotection to scale the infarct size reduction induced by ZP1609. Transmural myocardial blood flow in the area at risk during ischemia was measured by colored microspheres. The area at risk was delineated at the end of each experiment by coronary re-occlusion and quick atrial injection of blue dye (Patentblue V), leaving the area at risk unstained. Infarct size was determined by TTC-staining and used as end point of cardioprotection.

Results: Systemic hemodynamics and regional myocardial blood flow during ischemia were not different between groups. PoCo and ZP1609 reduced infarct size vs. IFR (IFR: 46±4% of area at risk; mean±SEM; PoCo: 31±4%; ZP1609: 25±5 %; both $p<0.05$ vs. IFR; ANOVA).

Conclusion: ZP1609 when given before reperfusion reduces infarct size to a similar extent as ischemic postconditioning. Further studies are necessary to define the potential mechanism/action of ZP1609 on connexin 43 in cardiomyocytes.