F011 EFFECT OF IVABRADINE ON MYOCARDIAL SYSTOLIC FUNCTION FOLLOWING POST-INFARCTION IN CONSCIOUS RABBITS

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Purpose – Heart rate reduction by the selective If current inhibitor ivabradine improves systolic cardiac function in experimental congestive heart failure. Here, we investigated whether its administration would be also beneficial in early post-infarction remodelling following ischemia-reperfusion and particularly at the level of the contractile function of the viable reperfused area.

Methods – Rabbits were submitted to 20 min of coronary artery occlusion (CAO). Throughout the subsequent 3 weeks of reperfusion, they received continuous infusion of either ivabradine (10 mg/kg/day, n=8) or vehicle (control, n=9) using implanted osmotic pumps. Global and regional systolic functions were assessed by echocardiography and tissue tracking imaging (TTI) (Vingmed System 7), respectively, at baseline (1 week before CAO) and throughout the 3 weeks of reperfusion. TTI was performed in the left ventricular (LV) free wall within the territory subjected to ischemia-reperfusion.

Results – Throughout the 3 weeks of reperfusion, ivabradine significantly and constantly reduced heart rate (~20%) (Table). Ejection fraction and regional systolic displacement assessed by TTI were significantly improved in ivabradine vs vehicle groups (29±2 and 29±3 % of LV, respectively). This area consisted into a thin infarcted scar (7±1 and 9±2 % of LV, respectively) surrounded by salvaged myocardium and fibrosis.

Conclusion — Heart rate reduction induced by ivabradine improves global systolic function in the post-infarction period and moreover improves the regional contractility of the remodeled myocardium salvaged by reperfusion. These benefits suggest the potential interest of ivabradine in the management of post-infarction myocardial dysfunction.

F012 INFARCTION AGGRAVATION INDUCED BY INTERMITTENT HYPOXIA IS ABOLISHED BY THE ANTIOXIDANT DRUG TEMPOL IN THE RAT HEART

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Coronary heart disease is frequently associated with obstructive sleep apnea syndrome and treating obstructive sleep apnea appears to significantly improve the outcome in coronary heart disease. We have previously shown in the rat that chronic intermittent hypoxia increases heart sensitivity to infarction. In this study, deleterious mechanisms potentially involved in this IH-induced infarction aggravation were explored using the anti-ischemic drug trimetazidine (TMZ), and a free radical scavenger Tempol, investigating the role of oxidative stress, and myocardial vascularization.

Wistar male rats were divided in two experimental groups subjected to chronic IH (IH group) or normoxia (N group). IH consisted of repetitive cycles of 1 min (40 s with inspired O2 fraction 5 % followed by 20 s normoxia) and was applied for 8 h during daytime, for 14 or 35 days. Normoxic cycles were applied in the same conditions, inspired O2 fraction remaining constant at 21 %. After the 14-day exposure, mean arterial blood pressure (MABP) was measured. Isolated hearts were then submitted to an ischemia-reperfusion protocol at the end of which infarct size were measured.

MABP was significantly increased in IH group compared to N group. Infarct sizes (expressed in percent of ventricle’s area) were significantly higher in IH group (34.0 ± 2.8 %) compared with N group (21.8 ± 3.1 %). Tempol (1 mM administered in water during the 14-day exposure) prevented this deleterious effect since infarction was comparable between IH (24.8 ± 2.8 %) and N (27.9 ± 4.0 %) groups. Moreover, Tempol also prevented the IH-induced increase in MABP after the 14-day exposure.

Trimetazidine (10 mg/day administered in food during the 14-day exposure) did not prevent the IH-induced infarction aggravation (40.1 ± 3.6 % in IH+TMZ group significantly higher than 29.1 ± 2.9 % in N+TMZ group) and has no effect on IH-induced increase in MABP. After a 35-day exposure, IH significantly increased ventricular vascular density and VEGF expression.