Cardioprotection during cardiac surgery: impact of temperature of cardioplegic solution on microRNA profile in a pig model of cardiopulmonary bypass

Authors:
A Kiss¹, D Santer¹, A Kramer¹, S Hallstrom², H Fallouh³, M Hackl⁴, S Skalicky⁴, D Chambers³, BK Podesser¹, ¹Medical University of Vienna, Center for Biomedical Research - Vienna - Austria, ²Medical University of Graz, Institute of Physiological Chemistry, Center for Physiological Medicine - Graz - Austria, ³St Thomas’ Hospital, Cardiac Surgical Research, The Rayne Institute (King’s College London), Guy’s and St Thomas’ NHS Fou - London - United Kingdom, ⁴TAmiRNA GmbH, Vienna - Vienna - Austria,

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Background: Data on the use of warm or cold cardioplegia solutions to achieve protection during cardiac surgery are controversial. There is substantial evidence that numbers of microRNAs (miRNAs) have either deleterious or protective effect in setting of myocardial ischemia/reperfusion (IR). The present study was aimed to clarify 1) the impact of warm blood or cold blood cardioplegia solutions on the expression of microRNAs in left ventricle tissue sample in a relevant model of human cardiopulmonary bypass (CPB) in pigs. Methods: Adult pigs were anesthetized (mean body weight 52±2 kg) and monitored for baseline hemodynamic function. Hearts were arrested by antegrade administration of St. Thomas’ blood cardioplegia (cold: 4°C, n=6 vs. warm: 37°C, n=6) for 60 min of ischemia followed by 60 min of on-pump reperfusion. Hemodynamic functions were monitored for further 90 min of reperfusion. Left ventricular (LV) tissue samples were taken for the assessment of microRNA expression profiling using next-generation sequencing technology and pathways enrichment analysis was performed using DIANA-miRPath. Results: The warm group showed improved systolic left ventricular pressure (p<0.05) and reduced wedge pressure during reperfusion (p<0.01). CK-MB levels were lower in the warm group (p<0.01). Overall 238 miRNAs were detected in all samples with a minimum read count of 1 Tags per million (TPM, expression level). Principal component analysis suggested that miRNAs expression was primarily influenced by the temperature of cardioplegia solution. The following microRNAs showed significant difference between groups; miR-451, miR-144, miR-146b, miR-9-1, miR-455 and miR-503. Interestingly, microRNAs having cardioprotective effects such as miR-144, miR-451 showed higher expression in the warm cardioplegia group in comparison to cold (miR-144: 570±153 vs 453±199 TPM; P<0.05, respectively). According to the hallmark of IR, the most relevant KEGG-pathways revealed by enrichment analysis were Hippo – and TGF-β signalling pathways, which were previously found to be differentially regulated in setting of myocardial IR-injury. Conclusion: Regulation of miRNA expression in myocardial tissue samples is primarily influenced by the temperature of cardioplegia solutions following IR. Of importance, improved hemodynamic function and reduction of IR-injury are associated with the elevation of cardioprotective miRNAs expression after warm cardioplegic arrest.