CARDIOPROTECTIVE EFFICACY OF METHYLCOBALAMIN TREATMENT AGAINST ISCHEMIA/REPERFUSION INJURY IN ISOLATED HEART OF DIABETIC PERIPHERAL NEUROPATHY MOUSE

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Aims We performed this study to investigate the cardio-protection of Methylcobalamin therapy against ischemia/reperfusion (I/R) in isolated heart of diabetic peripheral neuropathy mouse, and the involvement of TRPV1 in this procedure.

Methods Streptozotocin (STZ)-induced diabetes mellitus was carried out in ICR mice. Four weeks treatment of Methylcobalamin (1 mg/kg/day intramuscularly) was carried out. Isolated mouse heart was perfused in Langendorff apparatus. Hemodynamic parameters and release of lactate dehydrogenase (LDH), calcitonin gene-related peptide (CGRP) and substance P (SP) in coronary effluent during reperfusion were measured. Expression of TRPV1, calcitonin receptor-like receptor (CRLR) and SP receptor (SPR) in myocardium was detected by Western Blot.

Results Compared with normal mice, the DM mice had slower SNCV (p<0.01) and longer hot plate latency (p<0.01), indicating the impairment of sensory nerve function in experimental DPN. After four week methylcobalamin treatment, treated DM mice had faster SNCV (p<0.01) and shorter hot plate latency (p<0.05) than untreated ones. Untreated DM hearts got far more severe ischemic/reperfusion injuries than treated ones, an observation validated by raised left ventricular end-diastolic pressure (LVEDP) (p<0.05), decreased left ventricular developed pressure (LVDP) (p<0.01), reduced coronary flow (CF) (p<0.01), and increased LDH release (p<0.05). The ischemic injuries manifested in normal hearts were not as severe as in DM hearts. Unlike the untreated DM hearts, treated ones had higher concentration of SP in coronary effluent (p<0.01) and higher expression of TRPV1 (p<0.01) and SPR (p<0.01) in myocardium. Normal hearts had more intensive release of CGRP and SP as well as higher expression of myocardium TRPV1, CRLR and SPR than DM ones (p<0.01). Conclusions: Thus, these data provide important evidence that the cardio-protection of Methylcobalamin therapy in isolated DM mice hearts is related to the recovery of the expression and activation of TRPV1 and SPR.