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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 cardioprotection 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 cardioprotection of Methylcobalamin therapy in isolated DM mice hearts is related to the recovery of the expression and activation of TRPV1 and SPR.