The Role and Mechanism of Macrophage Colony-stimulating Factor (M-CSF) in Ventricular Electrical Remodeling after Myocardial Infarction in Mice by Regulating Cardiac Macrophages

Introduction: To investigate the effect and mechanism of macrophage colony-stimulating factor (M-CSF) on ventricular arrhythmias (VAs) after MI in mice by regulating cardiac macrophages.

Methods: Firstly, C57BL/6J wild type mice were randomly divided into 3 Groups to investigate the relationship between M-CSF, macrophages and VAs after MI. Then C57BL/6J wild mice were randomly divided into Sham group, MC group and MM group. The Sham group mice were given ligation line through LAD without ligation, the MC group and MM group were ligated with LAD to prepare MI model, the M-CSF (500 ug/kg/d) was administered intraperitoneally for 5 days in MM group. Three groups of mice were fed for 1 week. At the end of the experiment, the relevant indexes of ventricular structural remodeling, serum and tissue inflammatory factors, M1 and M2 macrophage levels and ERP, APD90, threshold of action potential electrical alternating and the VAs inducibility, the concentrations of Cx43 and TH in myocardial tissues were measured.

Result: The levels of M-CSF significantly increased in MI/3d and MI/7d group than the Sham group, and the level of M-CSF in MI/3d group was higher than the MI/7d group. The M2 macrophage increased continuously after MI, while the M1 macrophage increased in the acute phase after MI, then decreased timely. The level of M2 macrophage in the MM group was significantly higher while the level of M1 macrophage was significantly lower than in the MC group. The ventricular function were significantly increased and also the ventricular ejection fraction, the infarction size significantly decreased. The levels of pro-inflammatory cytokines in serum and tissues all decreased while the levels of anti-inflammatory cytokines significantly increased (all P<0.05). The cell apoptosis, hypertrophy and fibrosis were all significantly improved. And the ERP of the MM group was significantly longer than in the MC group while the APD90 significantly shortened, the threshold of action potential electrical alternating significantly increased, the VAs inducibility in the MM group was markedly lower than in the MC group. The TH level of the infarction area of the MM group was significantly lower than in the MC group while the Cx43 level significantly increased.

Conclusion: M-CSF could significantly improve the ventricular electrical remodeling after MI in mice by regulating the levels of macrophages of different polarization types in heart tissue (increasing the level of M2 type macrophages and inhibiting the increase of M1 type macrophages), and then could inhibit the inducibility of VAs, which may have important relationship with M-CSF could significantly improve ventricular structural remodeling and function, inhibit sympathetic hyperdistribution in the peripheral area of infarction, and increase the expression level of Cx43.