Anti-inflammatory effect of PDE5 inhibition in diabetic cardiomyopathy

Rita De Gaetano¹, Mary Anna Venneri², Giuseppe Panio², Andrea Isidori², Fabio Naro¹

¹Dipartimento di Scienze Istologiche, Anatomiche e dell'Apparato Locomotore, Università La Sapienza, Roma, Italy - ²Dipartimento di Medicina Sperimentale, Università La Sapienza, Roma, Italy

In patients with type 2 diabetes PDE5 inhibition (PDE5i) is associated with cardiac remodeling and reduced inflammatory cytokines¹. In this study it was investigated if PDE5 inhibition prevents the development of cardiomyocyte hypertrophy associated with diabetes by modulation of specific subsets of circulating monocytes and tissue macrophages.

Leptin receptor-deficient db/db mice develop diabetes mellitus and cardiac hypertrophy. The db/db mice were treated with the PDE5 inhibitor sildenafil (SILD) for 8 weeks. In the hearts of SILD treated mice cardiomyocyte showed a reduced cross-sectional area compared to the cardiomyocyte of untreated mice. Expression of the hypertrophic marker β-myosin was up-regulated in db/db mice hearts and this increase was prevented by SILD treatment. Circulating pro-inflammatory CD11b+Gr-1+ myeloid cells and the CD11b+Gr-1- monocyte cells, were monitored during SILD treatment. CD11b+Gr-1+ cells were reduced after SILD treatment in db/ db mice compared with untreated ones. No significant changes of CD11b+Gr-1- cells were detected in both control and SILD treated animals. After tissue dissociation, cardiac macrophages infiltration was characterized using specific markers such as F4/80 and TIE2. F4/80⁺ macrophages in diabetic mice were 2-fold increased compared to untreated mice and they were reduced by SILD treatment. Proangiogenic TIE2 expressing monocytes/macrophages (TEMs) percentage was highly increased in SILD treated db/db mice and correlated with an increase of vessel density, measured by the expression of the endothelial marker CD31.

These data suggest that PDE5 inhibition attenuates inflammation in diabetic cardiomyopathy reducing pro-inflammatory monocytes and in parallel increasing TEMs percentage and tissue vascularization.

References

 Giannetta E, Isidori A et al. Chronic Inhibition of cGMP Phosphodiesterase 5A Improves Diabetic Cardiomyopathy. Circulation. 2012; 125:2323-2333

Ke	/wo	rd	ς

Macrophages; cardiac hypertrophy; phosphodiesterase-5 inhibitor; diabetic mouse.