Interleukin-10 treatment attenuates sinus node dysfunction caused by streptozotocin-induced hyperglycemia

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Purpose: Mechanisms underlying hyperglycemia-induced sinus node dysfunction (SND) remain unclear. We aimed to test the hypotheses whether systemic interleukin-10 (IL-10) administration would attenuate SND observed in streptozotocin (STZ)-induced diabetic mice.

Methods: Six-week old CL57/B6 (WT) mice were divided into control group, STZ injection group (WT-STZ mice) and STZ injection with systemic administration of IL-10 group. IL-10 knockout (IL-10KO) mice were similarly treated.

Results: We observed followings. 1) STZ-induced hyperglycemia for eight weeks depressed serum levels of IL-10 in WT mice ($p<0.01$). 2) STZ-induced hyperglycemia significantly reduced resting heart rate (HR) in WT and IL-10KO mice ($p<0.05$ and $p<0.001$, respectively). In isolated perfused heart experiments, corrected-sinus node recovery time (CSNRT) was prolonged in WT-STZ mice and IL-10KO mice treated with STZ injection (IL-10KO-STZ mice) compared to corresponding control mice ($p<0.01$ and $p<0.001$, respectively). 3) IL-10 administration significantly attenuated the prolongation of CSNRT in WT-STZ and IL-10KO-STZ mice. 4) The fibrosis of sinus node in WT-STZ and IL-10KO-STZ mice was greater than that in corresponding control mice ($p<0.05$ and $p<0.01$, respectively). 5) Immunohistochemical staining demonstrated that hyperpolarization activated cyclic nucleotide-gated potassium channel 4 expression in sino-atrial node was depressed in WT-STZ and IL-10KO-STZ mice compared to corresponding control mice.

Conclusions: Our results suggest that the decrease or deletion of IL-10 plays an important role in the development of hyperglycemia-induced SND in STZ-induced diabetic mice. The results also suggest IL-10 administration could be a novel therapeutic strategy to prevent those electrophysiological pathology caused by hyperglycemia.