Empagliflozin, a sodium glucose co-transporter-2 inhibitor, alleviates atrial remodeling and improves mitochondrial function in high-fat diet diabetic rats

Tong Liu
Qingmiao Shao
Lei Meng
Sharen Lee
Gary Tse
Mengqi Gong
Zhiwei Zhang
Jichao Zhao
Yungang Zhao
Guangping Li

Introduction: Sodium-glucose co-transporter-2 (SGLT-2) inhibitors were recently reported to have cardioprotective effects in diabetes mellitus (DM) patients. However, the role of SGLT-2 inhibition in atrial remodeling, especially of the arrhythmogenic substrate, remains unclear. To gain insights on the effects of SGLT-2 inhibition on atrial fibrillation (AF), we investigated the effects of empagliflozin (EMPA), a commercially available and highly selective SGLT-2 inhibitor, on atrial remodeling in high-fat diet diabetic rats.

Methods: A total of 96 rats were randomized into 4 groups as follows: control group; DM group; low dose of empagliflozin (10 mg/kg/d); and high dose of empagliflozin (30 mg/kg/d). Biochemical examination, echocardiography, hemodynamic examination, histology, electrophysiology, western blot, mitochondrial respiratory function and membrane potential were assessed amongst the groups.

Result: Diabetic rats exhibited left ventricular hypertrophy and left atrial dilation with obvious hemodynamic abnormalities. All changes in the diabetic rates were attenuated by empagliflozin. Compared with the control group, higher atrial fibrillation inducibility was observed in the DM group, and was markedly reduced under empagliflozin treatment. Moreover, empagliflozin improved mitochondrial biogenesis by peroxisome proliferator–activated receptor-c coactivator 1α (PGC-1α) / nuclear respiratory factor-1(NRF-1) / mitochondrial transcription factor A (Tfam) signaling.

Conclusion: Empagliflozin can alleviate atrial remodeling by reversing electrophysiological abnormalities, improving mitochondrial function and mitochondrial biogenesis under DM, hence may be potentially used in the prevention of DM-induced atrial fibrillation.