The effect of sglt-2 inhibitor dapagliflozin on adropin serum levels in patients with chronic heart failure and concomitant type 2 diabetes mellitus

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Background: adropin plays a protective role in cardiac remodeling through supporting energy metabolism and water homeostasis and suppressing inflammation. Low circulating levels of adropin were positively associated with the risk of cardiovascular diseases and type 2 diabetes mellitus (T2DM). We hypothesized that sodium–glucose linked transporter 2 (SGLT2) inhibitor dapagliflozin might represent cardiac protective effects in T2DM patients with known chronic heart failure (HF) through the modulation of adropin levels.

Methods: The study was an open-label, multicenter non-randomized cohort investigation. Patients of both sexes were included from October 2020 to July 2022 who were aged ≥18 years and had established T2DM with HbAc1 <6.9%, hemodynamically stable HF (I-III NYHA functional classes), and written consent to participate in the study. According to these criteria, we prospectively enrolled 417 patients with T2DM and HF. The eligible patients were treated with the recommended guided HF therapy according to their HF phenotypes, including the consumption of SGLT2 inhibitor dapagliflozin at a dose of 10 mg OD orally, along with standard therapy of HF. Anthropometry, clinical data, echocardiography / Doppler examinations, and measurements of biomarkers were performed at the baseline and over a 6-month interval of SGLT2 inhibitor administration.

Results: Over a 6-month period after the initial prescription of SGLT2 inhibitor dapagliflozin, the levels of adropin in the entire group demonstrated a significant increase of up to 26.6% (from 2.37 [25–75% IQR = 1.91–2.75] ng/mL to 3.00 [25–75% IQR = 2.68–3.36] ng/mL, p = 0.042). In the female subgroup, the increase in the circulating levels of adropin was sufficiently higher (Δ% = 35.6%, from 2.69 [25–75% IQR = 2.31–2.99] ng/mL to 3.65 [25–75% IQR = 3.40–3.89] ng/mL, p = 0.010) when compared with those of the male subgroup (Δ% = 22.7%, from 2.11 [25–75% IQR = 1.90–2.37] ng/mL to 2.60 [25–75% IQR = 2.07–3.21] ng/mL, p = 0.161). A multivariate linear regression analysis of the entire group showed that the relative changes (Δ) in the left ventricular (LV) ejection fraction (LVEF), left atrial volume index (LAVI), and E/e` were significantly associated with increased adropin levels. In the female subgroup, but not in the male subgroup, ΔLVEF (p = 0.046), ΔLAVI (p = 0.001), and ΔE/e` (p = 0.001) were independent predictive values for adropin changes.

Conclusion: the levels of adropin seem to be a predictor for the favorable modification of hemodynamic performances during SGLT2 inhibition, independent of N-terminal brain natriuretic pro-peptide levels.