Effect of sodium-glucose co-transporter inhibitors on arterial stiffness in patients with type 2 diabetes mellitus

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Introduction: Selective sodium-glucose co-transporter 2 inhibitors (SGLT2i) reduce cardiovascular morbidity and mortality in patients with type 2 diabetes mellitus (T2DM). In addition to glucose homeostasis the impaired arterial stiffness may participate in this morbidity and mortality.

Purpose: The aim of this study was to investigate the effect of administration of SGLT2i therapy on arterial stiffness parameters, including aortic pulse wave velocity (PWV) and central systolic blood pressure (SBPao), which have significant prognostic value for predicting cardiovascular events.

Methods: Our prospective, observational study included 40 patients with T2DM (mean age: 60.3±9.9 years, 24 males). Biochemical and arterial stiffness parameters were analysed before starting SGLT2i therapy (14 patients on dapagliflozin, 25 patients on empagliflozin, 1 patient on ertugliflozin), at 3, 6 months and an average of 3.3±1.3 years follow-up period. Arterial stiffness parameters were determined using an invasively validated oscillometric based Arteriograph (AG) method. Changes in the variables and their interrelation was analysed by repeated data ANOVA and multivariate linear regression.

Results: Significant decrease in PWV and HgbA1c were observed 3 months after the initiation of SGLT2i therapy (PWV: 10.68±1.35 m/s vs. 10.05±1.40 m/s and HgbA1c: 7.86±0.55 vs. 6.83±0.66 %, p<0.05) and this long-term effect continued during the 3.3-years follow-up period (PWV: 9.96±1.25 m/s and HgbA1c: 7.19±0.81 %, p<0.005, Figure 1). Pearson's correlation analysis and multivariate linear regression analysis showed no association between decreased PWV and BMI, brachial diastolic blood pressure (DBPb) while significant, but weak correlation was observed with HgbA1c and brachial systolic blood pressure (SBPb) (r=0.22-0.26, p<0.05, Figure 2). SBPao results showed non-significant decrease and a subsequent non-significant long-term increase comparing to baseline during the 3.3 years follow-up.

Conclusion: Short and long-term SGLT2i therapy in T2DM significantly improved PWV values and this effect is independent of changes in SBPao. All these findings emphasize the clinical relevance of arterial stiffness as a biomarker in the SGLT2i induced beneficial effect on the vasculature, however further clarification, long-term evaluation needed to define the role of PWV in the prediction of cardiovascular events.
Figure 2: Relation between PWV and HgbA1c in T2DM patients.

\[ r = 0.26 \]
\[ p = 0.01 \]