THE INFLUENCE OF EMPAGLIFLOZIN ON microRNA-21 URINARY EXPPRESSION IN WISTAR RATS WITH LEFT CORONARY ARTERY LIGATION

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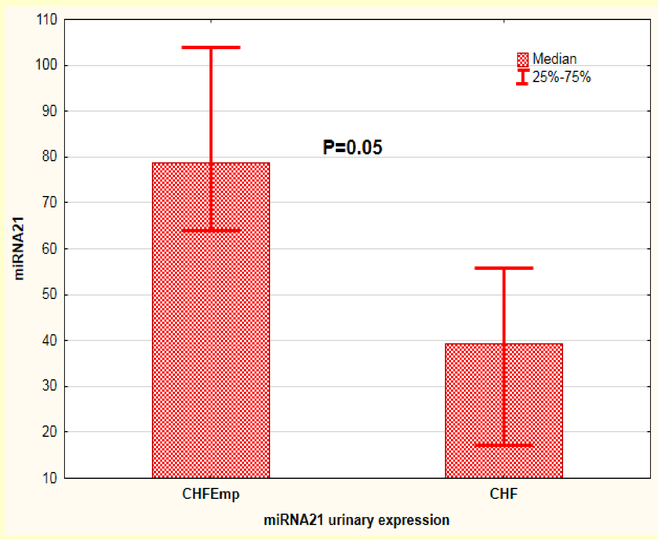
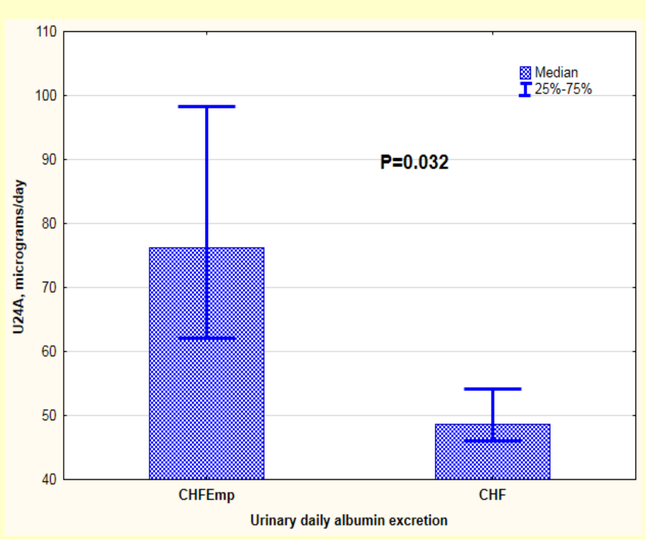
OBJECTIVES

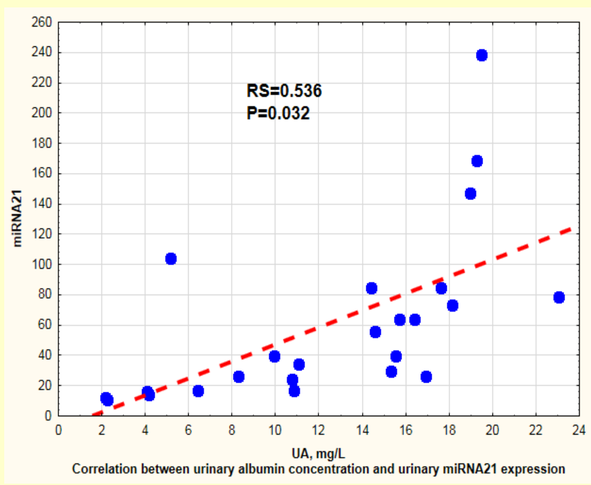
Results of some clinical and experimental investigations suggest that the sodium-glucose co-transporter 2 (SGLT-2) inhibitor (iSGLT-2) class of glucose lowering medications had cardio- and nephroprotective effects. iSGLT-2 empagliflozin (Emp) reduces death from cardiovascular (CV) causes, death from any cause and hospitalisation rate for heart failure in patients with diabetes mellitus type 2 (T2DM). On the other hand the iSGLT2, including Emp, could reduce systemic and intraglomerular pressure, glomerular hyperfiltration, and accordingly, the progression of chronic kidney disease. Administration of these medications associated with significant reductions of new onset or worsening of nephropathy and the composite renal endpoints of doubling of serum creatinine, initiation of renal replacement therapy or death from renal cause in patient with T2DM. Available information suggests that the nephroprotective effect of the study we examined the renal effects of Emp treatment in Wistar normoglycemic rats with iSGLT-2 is mainly due to their ability to counteract hyperglycemia. However it is little known about the possible direct actions of these drugs on the kidneys.

METHODS

In our study we examined the renal effects of Emp treatment in Wistar normoglycemic rats with experimental chronic heart failure (CHF). CHF was induced by ligation the left coronary artery. In one month after the operation 11 animals with CHF (CHFEmp group) started receive empagliflozin (Jardiance®, Boehringer Ingelheim) orally (1 mg/kg/day) for 1 mo. Second group of rats with CHF (CHF group; n = 10) did not receive Emp. The relative level of miRNA-21 in urine samples was determined (CHFEmp: n=9; CHF: n=7). miRNA-21 and reference RNA U6 cDNA was prepared based on StemLoop-technology. Expression was examined using semiquantitative RT-PCR protocol. Relative expression levels for miRNA were calculated (2–ΔCt method), using the mean Ct values of the miRNA control as respective internal reference. Urinary albumin (UA) and glucose (UGlu) concentration and values of daily excretions of these substances (U24A and U24Glu, respectively) were measured. All data are presented as median [interquartile range]. Mann-Whitney test and rank Spearmen correlation coefficient were used for statistical analysis.







RESULTS

In CHFEmp group UGlu and U24Glu were significantly higher than in CHF group (20.7[9.6-35.4] *vs* 3.69[1.77-6.57] mmol/l, P=0.0022; 85.9[61.3-120.5] *vs* 11.6[6.7-24.4] µmol/day, respectively, P=0.0005). UA in CHFEmp and CHF groups were comparable (18.14[11.1-23.0] *vs* 14.5[10.8-16.9] mg/l, respectively, P=0.275). However U24A in the first group was significantly more high than in the second group (76.2[62.1-98.2] *vs* 48.6[46.0-54.2] µg/day, respectively, P=0.032). In rats on Emp treatment urinary miRNA-21 expression was significantly higher than in animals without medication (78.8[64.0-104.0] *vs* 39.4[17.1-55.7], respectively, P=0.05). In the whole group of rats significant direct correlations between UGlu and UA (RS=0.679; P=0.0008), U24Glu and U24A (RS=0.461; P=0035), UA and miRNA-21 (RS=0.536; P=0.032) were observed.

CONCLUSIONS

One cannot exclude that the iSGLT-2 may have some negative direct effect on the kidneys. However, possible negative effects of these drugs on the kidneys in diabetes mellitus may overlap its counteraction to hyperglycemia and glomerular hyperfiltration.

References

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