EMPAGLIFLOZIN REDUCES OF INORGANIC PHOSPHATE EXCRETION IN RATS WITH CHRONIC HEART FAILURE?

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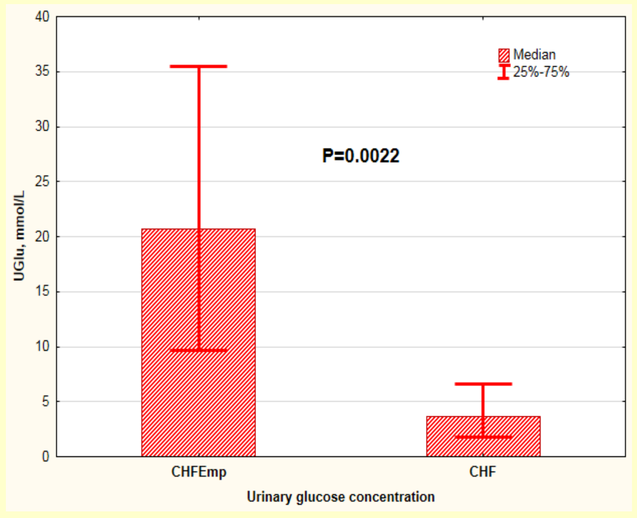
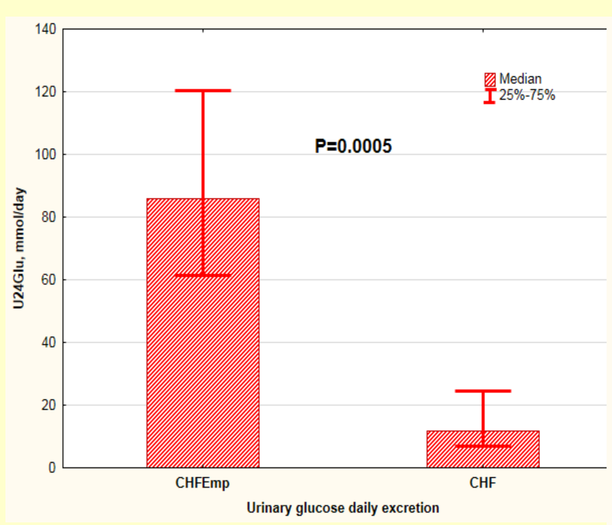
Objectives:

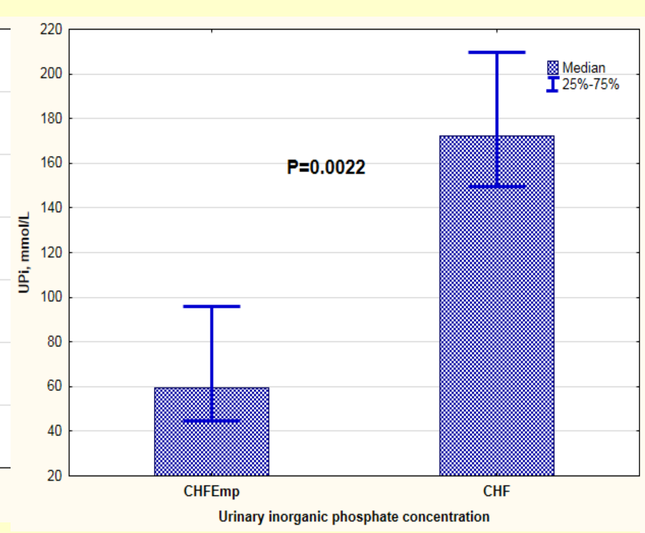
Sodium-glucose co-transporter 2 (SGLT-2) inhibitor (iSGLT-2) empagliflozin (Emp) reduces death from cardiovascular (CV) causes, hospitalisation for heart failure and progression to end stage renal disease (ERSD) in patients with type 2 diabetes mellitus (DM) and established CV disease. However, not all cardiovascular and renal effects of iSGLT-2 well established. In addition the majority of studies that have confirmed nephro- and cardioprotective actions of iSGLT-2, performed on patients with DM or experimental models of this disease. In this situation, nephro- and cardioprotective effects of these drugs could be a consequences of their antihyperglycemic action. So the direct influence of iSGLT-2 on the cardiovascular system and kidneys may be masked. In this regard, we investigated renal and CV effects of Emp treatment in normoglycemic Wistar rats with experimental chronic heart failure (CHF). This study is devoted mainly to the results of Emp impact on the renal electrolyte excretion.

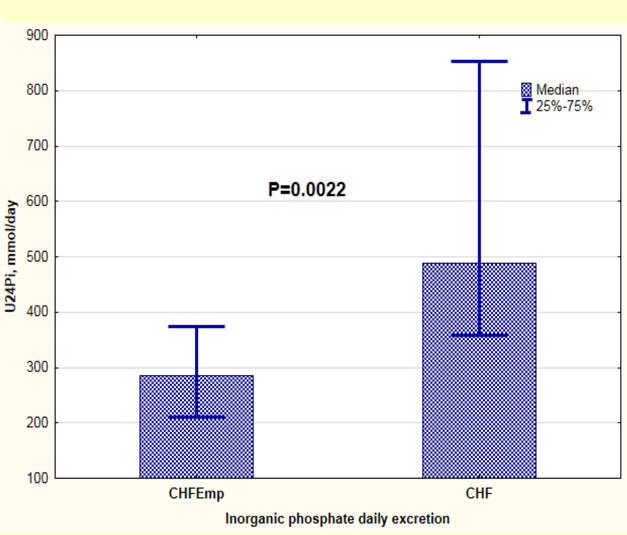
Methods:

CHF was induced by ligation the left coronary artery. In one month after the operation 11 animals with CHF (CHFEmp group) received 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. Urinary concentrations (U, mmol/l) and daily urinary excretion (U24, μmol/day) of glucose (Glu), creatinine (Cr), urea (Ur) and essential ions were measured. All data are presented as median [interquartile range]. Mann-Whitney test for statistical analysis was used.









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], P=0.0022; 85.9[61.3-120.5] *vs* 11.6[6.7-24.4], P=0.0005, respectively). There were no significant difference between CHFEmp and CHF groups in UNa (32.7[10.0-51.0] *vs* 10.0[10.0-48.9]; UK 109.4[91.6-111.5] *vs* 107.7[104.7-110.1]; UCa 2.76[1.24-4.74] *vs* 2.58[2.34-3.20]; UMg 12.76[7.16-14.12] *vs* 13.1[12.12-13.44]; UCr 17.65[12.6-23.85] *vs* 21.9[15.5-26.7]; UUr 1337.5[877.0-1674.5] *vs* 1516.0[1426.5-1898.0]; P=NS in all cases. Values of daily urinary excretion of the same substances were also comparable in CHFEmp and CHF groups: U24Na 137.3[102.0-208.3] *vs* 64.1[28.1-190.0]; U24K 451.7[329.6-547.0] *vs* 346.2[308.3-526.6]; U24Ca 10.4[6.6-17.1] *vs* 10.6[6.4-14.1]; U24Mg 48.8[31.6-67.2] *vs* 41.3[34.9-66.1]; U24Cr 71.0[52.5-89.8] *vs* 81.9[56.7-95.4]; U24Ur 5752[4550-6199] *vs* 5988[3994-7116]; P=NS in all cases. On the contrary urinary inorganic phosphate concentration and urinary inorganic phosphate daily excretion in CHFEmp group were significantly less than in CHF group (UPi 59.5[44.5-96.0] *vs* 172.3[149.5-209.5], P=0.0022; U24Pi 285.6[211.2-374.4] *vs* 487.5[358.0-853.1], P=0.02, respectively).

Conclusions:

SGLT-2 is sodium/glucose co-transporter. Its suppression by Emp should lead to an increase in both glucose and sodium excretion. However in our study sodium excretion after Emp did not change. Possible, reduction of Na reabsorption by SGLT-2 causes reciprocal rise of the sodium absorption by sodium/phosphate co-transporter NAPI-IIa. In this situation sodium excretion would be restored by increasing phosphate reabsorption.

References:

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