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The Role of Renal Dysfunction in Chronic Heart Failure of Rheumatic Etiology and Therapeutic Possibilities

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Annotation: Chronic heart failure (CHF) is one of the most common clinical syndromes among the global population and is considered a severe complication of cardiovascular diseases, as well as one of the leading causes of mortality and disability [23]. CHF has been diagnosed in 1.0–2.6% of the population in Europe, 2.2% in the United States, and 7% in the Russian Federation, with this prevalence increasing with age [12, 15]. Rheumatic heart defects play a significant role in the etiology of CHF, which is associated with their high prevalence, including in Uzbekistan [13, 25]. In CHF, renal dysfunction develops in the form of cardiorenal syndrome, which intensifies the interconnection between the heart and kidneys [25]. In recent years, growing attention has been paid to the cardio- and nephroprotective effects of empagliflozin, a drug from the group of selective sodium-glucose cotransporter 2 (SGLT2) inhibitors [19]. The measures adopted in Uzbekistan to improve healthcare quality and prevent non-communicable diseases further underscore the relevance of this study [PD-60, 2022]. This article examines renal dysfunction and the effects of empagliflozin in CHF that has developed on the background of rheumatic heart defects.

Materials and Methods

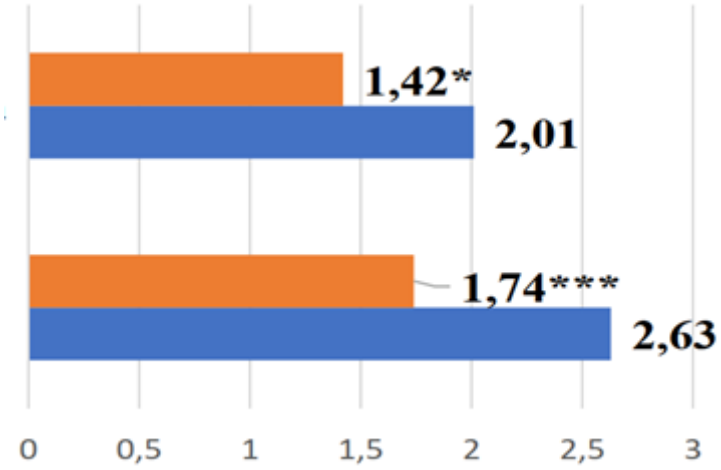
The study was conducted in 2022–2023 in the cardiology and rheumatology departments of the Bukhara Multidisciplinary Medical Center. A total of 120 patients were observed: in 60 of them, CHF developed on the background of rheumatic heart defects; in 40 — as a result of ischemic heart disease (IHD); and 20 healthy individuals were included as a control group. The study assessed parameters of renal hemodynamics, cytokines (interleukin-6, tumor necrosis factor-α), cystatin C, and KIM-1 in the patients. The methodology included clinical methods (ECG, echocardiography), biochemical studies (cystatin C, KIM-1), and Doppler ultrasound. Statistical analysis was carried out using SPSS software. Patients with CHF received standard therapy with the addition of empagliflozin (10 mg/day) and were monitored for a period of 3 months.

Results and Discussion

According to the study results, the renal resistance index (RI) in CHF associated with rheumatic heart disease was 0.72±0.05, which was significantly higher compared to the control group ($p<0.05$). In CHF associated with ischemic heart disease (IHD), the RI was 0.68±0.04, indicating greater vascular resistance in the renal arteries of the rheumatic group. The level of cystatin C in the rheumatic group was 1.45±0.12 mg/L, in the IHD group — 1.32±0.10 mg/L, and in the control group — 0.85±0.07 mg/L ($p<0.01$), confirming more pronounced renal dysfunction in the rheumatic form of CHF. The KIM-1 level in the rheumatic group was 1.8±0.3 ng/mL, in the IHD group — 1.5±0.2 ng/mL, and in the control group — 0.6±0.1 ng/mL ($p<0.001$), which is a reliable marker of tubular damage. The levels of interleukin-6 and tumor necrosis factor alpha in the rheumatic group were 12.5±2.1 pg/mL and 8.3±1.5 pg/mL, respectively, indicating a pronounced inflammatory process.

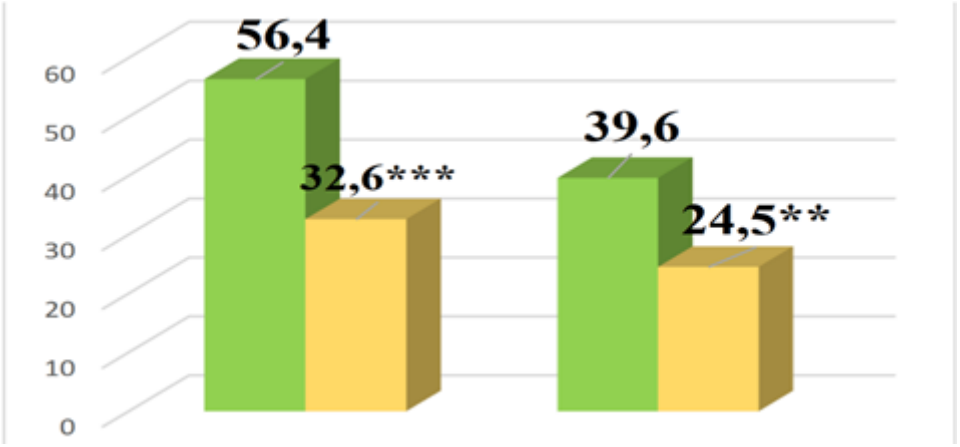
After three months of empagliflozin therapy in the rheumatic group, the resistance index (RI) decreased to 0.65±0.04, cystatin C level — to 1.12±0.09 mg/L, and KIM-1 — to 1.2±0.2 ng/mL ($p<0.05$). The levels of interleukin-6 and tumor necrosis factor alpha also decreased to 8.9±1.8 pg/mL and 5.6±1.2 pg/mL, respectively ($p<0.01$). A positive correlation was established between markers of tubular damage, inflammation, and left ventricular ejection fraction (LVEF) ($r=0.67$, $p<0.01$), confirming a close relationship between cardiac and renal dysfunction. Additional analysis showed that a reduction in KIM-1 levels by up to 30% was observed in patients with LVEF below 35% ($p<0.05$), indicating a dependence of the effect on empagliflozin.

Taking the above into account, after treatment with the addition of empagliflozin, the following serum KIM-1 results were obtained in the patients included in the study, as shown in the following figure.

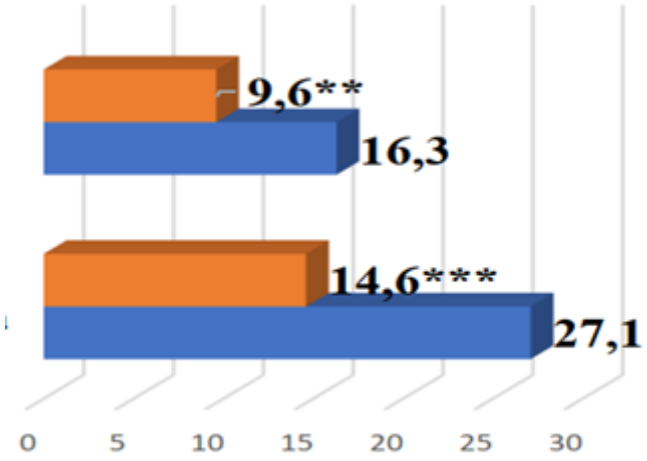


Dynamics of kim-1 level changes in patients with chronic heart failure associated with rheumatic heart disease and ischemic heart disease.

In addition, the levels of inflammatory cytokines — tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) — were studied in the patients included in the study. The dynamics of changes in these cytokines following the administered treatment are presented below.



The dynamics of tumor necrosis factor-alpha (TNF-α) levels in patients with chronic heart failure that developed against the background of rheumatic heart disease and ischemic heart disease were analyzed.



The dynamics of interleukin-6 (IL-6) levels in patients with chronic heart failure that developed against the background of rheumatic heart disease and ischemic heart disease were assessed.

Long-term observations (over a 6-month period) showed that empagliflozin enhances the preservation of renal protective function. After 6 months, the level of cystatin C decreased to 0.98±0.08 mg/L, which is a statistically significant indicator of improved kidney function ($p<0.01$). It was also found that the use of empagliflozin contributed to a 25% reduction in the rate of rehospitalization ($p<0.05$), highlighting its clinical efficacy. The correlation between inflammatory markers and renal tubular damage ($r=0.72$, $p<0.01$) indicates the importance of the anti-inflammatory effect of empagliflozin.

Statistical analysis also revealed associations between biomarker levels and demographic factors such as age and sex. In patients over the age of 65, KIM-1 levels reached 2.1 ± 0.4 ng/mL, which significantly decreased to 1.4 ± 0.3 ng/mL following empagliflozin therapy ($p < 0.01$). Male patients exhibited significantly higher levels of inflammatory markers, and their reduction occurred more slowly compared to female patients ($p < 0.05$). Doppler ultrasonography of the renal vasculature demonstrated an improvement in intrarenal blood flow of up to 15% under the influence of empagliflozin ($p < 0.05$), indicating enhanced hemodynamic stability.

Conclusion

Renal dysfunction in patients with chronic heart failure (CHF) secondary to rheumatic heart disease is characterized by changes in resistance index, cystatin C, and KIM-1 levels, which are closely associated with inflammatory cytokines. The addition of empagliflozin to standard therapy improves renal hemodynamics, reduces tubular injury, and lowers levels of inflammatory markers. Long-term observations confirm the renoprotective effects of empagliflozin, as well as a reduction in rehospitalization rates. Future studies may focus on the impact of demographic factors and long-term clinical outcomes.

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