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**EFFECTS OF COMBINED SACUBITRIL AND EMPAGLIFLOZIN THERAPY ON
HEMODYNAMIC AND HEMORHEOLOGICAL PARAMETERS IN PATIENTS WITH
CHRONIC HEART FAILURE**

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Abstract: Chronic heart failure (CHF) is characterized by progressive hemodynamic deterioration, neurohormonal activation, and hemorheological imbalance. Optimization of arterial pressure, heart rate, and coagulation status is essential for improving prognosis. To evaluate the effects of combined sacubitril and empagliflozin therapy on hemodynamic and hemorheological parameters in patients with CHF. A total of 43 patients with CHF were assessed before and after treatment. Systolic and diastolic blood pressure (SBP/DBP), heart rate (HR), and blood coagulation parameters (Sukharev method) were analyzed. Significant reductions in SBP (-9.87 mmHg, $p=0.0227$) and DBP (-5.97 mmHg, $p=0.0059$) were observed. HR decreased by 7.72 beats/min ($p=0.010$). Coagulation initiation time increased significantly ($p=0.003$), indicating reduced hypercoagulability. Combined sacubitril and empagliflozin therapy significantly improves hemodynamic stability and reduces thrombotic risk in CHF patients.

Keywords: Chronic heart failure; sacubitril; empagliflozin; combination therapy; arterial blood pressure; heart rate; hemodynamics;

Introduction: Chronic heart failure (CHF) is a complex clinical syndrome associated with progressive impairment of cardiac pump function, neurohormonal activation, and systemic circulatory dysfunction. Hemodynamic parameters such as arterial blood pressure (ABP) and heart rate (HR) reflect cardiac workload, peripheral vascular resistance, and myocardial oxygen demand.

Elevated sympathetic activity and renin–angiotensin–aldosterone system (RAAS) activation contribute to persistent tachycardia, increased afterload, and adverse cardiac remodeling. In addition, CHF is frequently associated with hemorheological disturbances, including a prothrombotic state, endothelial dysfunction, and altered blood coagulation dynamics.

Modern therapeutic strategies, including angiotensin receptor-neprilysin inhibition (ARNI) and sodium-glucose cotransporter-2 (SGLT2) inhibitors, provide not only symptomatic relief but also neurohormonal and vascular protection. Sacubitril and empagliflozin represent a promising combination targeting multiple pathophysiological pathways in CHF.

Aim of the Study: To evaluate the impact of combined sacubitril and empagliflozin therapy on: Arterial blood pressure, heart rate, blood coagulation parameters in patients with chronic heart failure.

Materials and Methods: This study was designed as a prospective, observational clinical analysis aimed at evaluating the effects of combined sacubitril and empagliflozin therapy on hemodynamic and hemorheological parameters in patients with chronic heart failure (CHF). The investigation focused on before-and-after treatment comparisons within the same patient cohort.

A total of 43 patients diagnosed with chronic heart failure were included in the study. The diagnosis was established based on standard clinical, instrumental, and laboratory criteria. All patients received combination therapy with sacubitril and empagliflozin as part of their treatment regimen.

Hemodynamic and hemorheological parameters were evaluated at two time points: prior to initiation of therapy and after completion of the treatment course.

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All collected data were processed using standard statistical methods. Results are presented as mean $\pm$ standard error of the mean ($M \pm m$). Comparative analysis between pre-treatment and post-treatment values was performed using paired statistical tests. A p-value of less than 0.05 was considered statistically significant.

Results: In this study, a total of 43 patients with chronic heart failure were evaluated before and after combined therapy with sacubitril and empagliflozin. Overall, the results demonstrated moderate but statistically significant improvements in key hemodynamic and hemorheological parameters.

At baseline, patients showed elevated arterial blood pressure values, with a mean systolic blood pressure (SBP) of 136.05 ± 3.74 mmHg and a mean diastolic blood pressure (DBP) of 88.60 ± 1.72 mmHg.

After treatment, both systolic and diastolic blood pressure values decreased in a consistent manner. The mean SBP decreased to 126.18 ± 2.02 mmHg, showing an average reduction of 9.87 mmHg ($p = 0.0227$). The mean DBP also decreased to 82.63 ± 1.23 mmHg, with a reduction of 5.97 mmHg ($p = 0.0059$). These changes indicate a moderate reduction in vascular resistance and cardiac afterload.

At the beginning of the study, the mean resting heart rate was 92.40 ± 2.02 beats per minute, reflecting increased sympathetic activity typical of chronic heart failure.

Following therapy, a moderate but statistically significant decrease in heart rate was observed, with values declining to 84.68 ± 2.02 beats per minute. This corresponds to an average reduction of 7.72 beats per minute ($p = 0.010$). The observed decrease suggests partial suppression of sympathetic overactivity and improved neurohormonal balance.

Assessment of blood coagulation using the Sukharev method revealed moderate changes in hemostatic activity.

Before treatment, coagulation initiation occurred at 0.90 ± 0.08 minutes, while coagulation completion was recorded at 2.02 ± 0.78 minutes. After therapy, coagulation initiation time increased to 1.30 ± 0.10 minutes ($p = 0.003$), indicating a statistically significant but moderate reduction in hypercoagulability. Coagulation completion time also increased to 4.07 ± 0.70 minutes, although this change showed borderline statistical significance ($p = 0.059$).

Overall, combined therapy with sacubitril and empagliflozin resulted in moderate improvements in cardiovascular and hemorheological parameters. The observed reductions in blood pressure and heart rate, along with the partial normalization of coagulation dynamics, suggest improved hemodynamic stability and a trend toward reduced thrombotic risk in patients with chronic heart failure.

Discussion: The observed reduction in arterial blood pressure suggests decreased cardiac afterload and improved vascular compliance. SBP reduction of approximately 10 mmHg reflects reduced left ventricular workload and improved myocardial efficiency.

DBP reduction indicates decreased peripheral vascular resistance and improved coronary perfusion during diastole, which is particularly important in CHF patients with concomitant ischemic heart disease.

The significant decrease in heart rate reflects attenuation of sympathetic nervous system overactivation and improved neurohormonal balance. This contributes to prolonged diastolic filling time, reduced myocardial oxygen consumption, and improved cardiac efficiency.

Hemorheological improvements, demonstrated by prolonged coagulation time, suggest a reduction in hypercoagulable state. This may decrease the risk of thromboembolic complications, improve microcirculation, and enhance overall hemodynamic stability.

The combined effects of sacubitril (vasodilation and anti-remodeling effects) and empagliflozin (osmotic diuresis, natriuresis, and vascular stiffness reduction) likely explain the observed multi-system benefits.

Conclusion: Combined therapy with sacubitril and empagliflozin in patients with chronic heart failure results in:

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Significant reduction in systolic and diastolic blood pressure

Decrease in heart rate with improved neurohormonal balance

Improvement in coagulation profile with reduced hypercoagulability

These findings demonstrate that the therapy provides not only hemodynamic stabilization but also beneficial hemorheological effects, supporting its pathogenetically grounded use in CHF management.