International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2025: 7.089

Assessment of Renal and Electrolyte Safety of Sacubitril / Valsartan in Patients with Heart Failure with Reduced Ejection Fraction in the Medicine Department of SMS Hospital, Jaipur

Arun Kumar[1], Surendar Kumar[2], Jyotsana Bhargava[3], Kavita Bajiya[4]

[1]Senior Resident, Department of Pharmacology, PNKS Medical College Dausa, India
Email: *arunkumar10bm0016[at]gmail.com*

[2]Senior Resident, Department of Pharmacology, SMSMC, Jaipur, India

[3]Professor, Department of Pharmacology, SMSMC, Jaipur, India

[4]Senior Resident, Department of Opthalmology, PNKS Medical College Dausa, India

Abstract: ***Background**: Heart failure with reduced ejection fraction is associated with high morbidity and mortality. Sacubitril/Valsartan is an important treatment option, but renal dysfunction and hyperkalemia remain important safety concerns requiring regular monitoring. **Methods**: This prospective observational study included 65 HFrEF patients receiving Sacubitril/Valsartan. Serum creatinine and serum potassium were assessed at baseline, 1 month, and 3 months and Statistical analysis was performed using SPSS, and associations were evaluated using the Chi-square test. **Results**: Among 65 patients, mean serum creatinine increased slightly from 0.87 to 0.89 mg/dL, and mean serum potassium increased from 4.19 to 4.69 mmol/L over 3 months. These changes were not statistically significant. **Conclusion**: Sacubitril/Valsartan showed acceptable short-term renal and electrolyte safety in HFrEF patients, with no significant change in serum creatinine or serum potassium over 3 months.*

Keywords: Sacubitril/Valsartan; HFrEF; Renal safety; Electrolyte safety; Hyperkalemia

1. Introduction

Heart failure is a major cardiovascular syndrome associated with high morbidity, repeated hospitalization, reduced quality of life and mortality. Cardiovascular diseases remain the leading cause of death globally, and heart failure represents one of the important chronic consequences of cardiac disease.[1] The burden of heart failure is increasing due to ageing population, improved survival after myocardial infarction, hypertension, diabetes, obesity and ischemic heart disease.[2]

In India, heart failure is also becoming an important clinical and public health problem. The burden is mainly related to ischemic heart disease, hypertension, diabetes, rheumatic heart disease and cardiomyopathies. Earlier Indian estimates suggested approximately 1.3 to 4.6 million prevalent cases and 0.5 to 1.8 million new cases of heart failure annually.[3] Indian patients with heart failure often present at a younger age and with multiple comorbidities, which makes long-term drug safety monitoring important.[4]

Heart failure with reduced ejection fraction is characterized by impaired systolic function and activation of neurohormonal pathways. Sacubitril/Valsartan, an angiotensin receptor–neprilysin inhibitor, combines neprilysin inhibition with angiotensin receptor blockade and acts on two important mechanisms involved in heart failure progression.[5] The PARADIGM-HF trial showed that Sacubitril/Valsartan was superior to enalapril in reducing cardiovascular death and hospitalization for heart failure.[6]

However, despite its proven benefit, Sacubitril/Valsartan requires safety monitoring in routine clinical practice. Worsening renal function and hyperkalemia are important concerns, especially in patients receiving other heart failure medications such as diuretics, beta-blockers, ACE inhibitors or ARBs.[7] Serum creatinine reflects renal safety, while serum potassium helps identify electrolyte imbalance during therapy.[8]

2. Methodology

This was a descriptive prospective observational study conducted in the Medicine Department of SMS Medical College and Hospital, Jaipur among patients with heart failure with reduced ejection fraction receiving Sacubitril/Valsartan. The study was carried out from approval of the study to completion of data collection. Patients aged 18–80 years, of either gender, having ejection fraction <45%, with or without comorbidities, and willing to participate were included. Patients who were non-cooperative, difficult to follow-up, having pre-existing renal dysfunction, history of hypotension, hypersensitivity, angioedema or hyperkalemia, pregnant or lactating women, and those already enrolled in another study were excluded.

The sample size was calculated at 95% confidence level, considering 21.3% incidence of hyperkalemia among patients receiving Sacubitril/Valsartan as reported in the seed article, with an absolute allowable error of 10%. Based on this, the minimum required sample size was 65 patients, and these patients were included for final analysis. Relevant

demographic and clinical details were recorded, and renal and electrolyte safety was assessed by measuring serum creatinine and serum potassium at baseline, 1 month, and 3 months. Data were entered in Excel and analyzed statistically, with results expressed mainly as mean values over the follow-up period.

3. Result

A total of 65 patients with HFrEF receiving Sacubitril/Valsartan were analyzed for renal and electrolyte safety. The mean serum creatinine showed only a minimal rise from 0.87 mg/dL at baseline to 0.88 mg/dL at 1 month and 0.89 mg/dL at 3 months. On statistical analysis, this change was not significant, indicating no meaningful deterioration in renal function during the follow-up period. Similarly, the mean serum potassium increased gradually from 4.19 mmol/L at baseline to 4.37 mmol/L at 1 month and 4.69 mmol/L at 3 months. Although a mild upward trend was observed, the change was also statistically non-significant.

Table 1: Distribution of Study Participants According to Age Group (65)

Age group	Frequency (n)	Percentage (%)
<50 years	18	27.69
≥50 years	47	72.31
Total	65	100

It is evident from the above table that the majority of study participants belonged to the ≥50 years age group, comprising 47 patients (72.31%), while 18 patients (27.69%) were below 50 years of age.

Table 2: Distribution of Study Participants According to Sex (n=65)

Sex	Frequency (n)	Percentage (%)
Male	45	69.23
Female	20	30.77
Total	65	100

It is evident from the above table that the majority of study participants were male, comprising 45 patients (69.23%), while 20 patients (30.77%) were female.

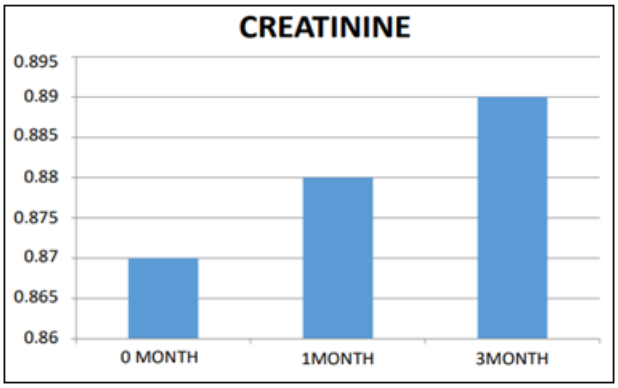

Figure 1: Bar Diagram Showing Mean Serum Creatinine Levels at Baseline, 1 Month and 3 Months (n=65)

The figure shows a slight increasing trend in mean serum creatinine from 0.87 mg/dL at baseline to 0.88 mg/dL at 1 month and 0.89 mg/dL at 3 months. However, the rise was minimal and statistically non-significant, suggesting no significant renal function deterioration during Sacubitril/ Valsartan therapy.

Table 2: Mean Serum Potassium Levels at Baseline, 1 Month and 3 Months (n=65)

Time interval	Mean serum potassium level (mmol/L)
Baseline	4.19
1 month	4.37
3 months	4.69

It is evident from the above table that the mean serum potassium level increased from 4.19 mmol/L at baseline to 4.37 mmol/L at 1 month and 4.69 mmol/L at 3 months. Although a mild increasing trend was observed, the change was statistically non-significant, indicating no significant electrolyte derangement during the follow-up period.

Table 3: Statistical Comparison of Renal and Electrolyte Parameters over 3 Months (n=65)

Parameter	Baseline (Mean)	1 Month (Mean)	3 Months (Mean)	p-value
Serum creatinine (mg/dL)	0.87	0.88	0.89	>0.05
Serum potassium (mmol/L)	4.19	4.37	4.69	>0.05

It is evident from the above table that both serum creatinine and serum potassium showed only minimal changes over the 3-month follow-up period, and these changes were not statistically significant ($p > 0.05$), indicating no significant renal or electrolyte derangement.

4. Discussion

The present prospective observational study evaluated the renal and electrolyte safety of Sacubitril/Valsartan in 65 patients with HFrEF over 3 months. Most patients were ≥50 years (72.31%), with a male predominance (69.23%). The mean serum creatinine increased minimally from 0.87 to 0.89 mg/dL (absolute rise 0.02 mg/dL), while serum potassium increased from 4.19 to 4.69 mmol/L (rise 0.50 mmol/L). However, both changes were not statistically significant ($p>0.05$), indicating no clinically significant renal or electrolyte derangement.

The renal safety findings are comparable with McMurray et al. (2014) in the PARADIGM-HF trial involving >8000 patients, where elevated creatinine was reported in 3.3% with Sacubitril/Valsartan vs 4.5% with enalapril. Similarly, Desai et al. (2015) reported no significant increase in renal adverse outcomes. The minimal rise observed in our study (0.87 to 0.89 mg/dL) is consistent with these findings, supporting the renal safety of the drug.

With regard to electrolyte safety, the present study showed a modest increase in potassium (4.19 to 4.69 mmol/L) without statistical significance. Vardeny et al. (2014) reported that hyperkalemia risk was not significantly increased, and in PARADIGM-HF, hyperkalemia (>5.5 mmol/L) occurred in 16.1% vs 17.3% in comparator groups. Similarly, Velazquez et al. (2019) found no significant difference in potassium-related adverse events, aligning with our findings.

Mechanistically, Hubers et al. (2016) explained that ARNI therapy provides balanced neurohormonal modulation without major renal compromise. Berg et al. (2021) also reported good tolerability even in high-risk patients. In the Indian context, as highlighted by Huffman et al. (2010) and Harikrishnan et al. (2020), where patients are younger and have multiple comorbidities, the present study demonstrates that Sacubitril/Valsartan has a favorable renal and electrolyte safety profile with minimal and non-significant changes.

5. Conclusion

Sacubitril/Valsartan showed a favorable short-term safety profile in patients with HFrEF. Mean serum creatinine increased slightly from 0.87 to 0.89 mg/dL, and serum potassium from 4.19 to 4.69 mmol/L over 3 months. These changes were not statistically significant ($p>0.05$). No clinically significant renal dysfunction or electrolyte imbalance was observed. The drug appears safe and well tolerated, though regular monitoring is recommended.

References

[1] World Health Organization. Cardiovascular diseases (CVDs). WHO; 2025.
[2] Shahim B, Kapelios CJ, Savarese G, Lund LH. Global public health burden of heart failure: an updated review. *Card Fail Rev*. 2023.
[3] Huffman MD, Prabhakaran D. Heart failure: epidemiology and prevention in India. *Natl Med J India*. 2010;23(5):283-288.
[4] Harikrishnan S, Sanjay G, Anees T, Viswanathan S, Vijayaraghavan G, Bahuleyan CG, et al. National Heart Failure Registry, India: design and methods. *Indian Heart J*. 2020.
[5] Hubers SA, Brown NJ. Combined angiotensin receptor antagonism and neprilysin inhibition. *Circulation*. 2016;133(11):1115-1124.
[6] McMurray JJV, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, et al. Angiotensin–neprilysin inhibition versus enalapril in heart failure. *N Engl J Med*. 2014;371(11):993-1004.
[7] Desai AS, McMurray JJV, Packer M, Swedberg K, Rouleau JL, Chen F, et al. Effect of LCZ696 compared with enalapril on mode of death in heart failure patients. *Eur Heart J*. 2015;36(30):1990-1997.
[8] Vardeny O, Miller R, Solomon SD. Combined neprilysin and renin-angiotensin system inhibition for heart failure. *JACC Heart Fail*. 2014;2(6):663-670.
[9] Velazquez EJ, Morrow DA, DeVore AD, Duffy CI, Ambrosy AP, McCague K, et al. Angiotensin–neprilysin inhibition in acute decompensated heart failure. *N Engl J Med*. 2019; 380: 539-548.
[10] Berg DD, Samsky MD, Velazquez EJ, et al. Efficacy and safety of Sacubitril/Valsartan in high-risk patients in the PIONEER-HF trial. *Circ Heart Fail*. 2021;14: e007034.