Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 5s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

The Assessment of Effect of Sacubitril/Valsartan Combination in Patients with Heart Failure and Reduced Ejection Fraction: A Single Center Study

Zainab Abbass Hassan[*1], Nagham Yahya Ghafil[2]

[1*]Pharmacist, Al-Hussein Teaching Hospital, Thi-Qar Health Directorate.

Email ID: zainaba.alzirjawi@student.uokufa.edu.iq

Orcid: https://orcid.org/0009-0007-8326-0105

[2]Assistant Professor, Faculty of Pharmacy, Kufa University.

Email ID: nagamy.kimiaowi@uokufa.edu.iq

Orcid: https://orcid.org/0000-0001-5346-0287

***Corresponding Author:**

Email ID: zainaba.alzirjawi@student.uokufa.edu.iq

Cite this paper as: Zainab Abbass Hassan, Nagham Yahya Ghafil, (2025 The assessment of effect of sacubitril/valsartan combination in patients with heart failure and reduced ejection fraction: a single center study. *Journal of Neonatal Surgery*, 14 (5s), 901-908

ABSTRACT

Background: sacubitril/valsartan approved in 2015 to use in heart failure patients with reduced ejection fraction and dramatic results gained, the effects of it in heart failure patients is assessed by many clinical parameters.

Aims: Assessment the role of sacubitril/valsartan combination as Angiotensin Receptor Neprilysin Inhibitor in heart failure patients in AL Nasiriyaha Heart Centre-Iraq by explain the dramatic effect of sacubitril/valsartan in improve the clinical state of patients.

Patients and Methods: This is interventional study that included 73 patients with heart failure patients and reduced ejection fraction who visited the cardiac outpatient clinic in AL Nasiriyaha Heart Centre Thi-Qar Iraq who received Sacubitril/Valsartan as Angiotensin Receptor Neprilysin Inhibitor, study period was two months.

Results: This study explained the role of sacubitril/valsartan combination in improve clinical states of patients by follow-up the sample from heart failure and reduced ejection fraction patients.

Conclusions: Sacubitril and Valsartan demonstrated clinical efficacy in treatments of heart failure patients with reduced ejection fraction in the Nasiriyah Heart Center, Thi-Qar province, by improving vital signs related to disease.

Keywords: *sacubitril/valsartan, ARNi, Heart failure with reduced ejection fraction, Clinical pharmacist.*

1. INTRODUCTION

Abbreviations

NP: Natriuretic Peptides

S/V: Sacubitril and Valsartan

ARNI: Angiotensin Receptor Neprilysin Inhibitor

RAS: Renin-Angiotensin System

NEPi: Isolated NEP Inhibition

AgII: Inhibits Angiotensin II

2. INTRODUCTION

The combination of sacubitril and valsartan (S/V), is an angiotensin receptor neprilysin inhibitor (ARNI, formerly known as LCZ696), has gotten a lot of attention as a way to treat heart failure because it works on both the renin-angiotensin system (RAS) and the natriuretic peptide system [1]. Sacubitril and Valsartan combination is a drug with dual-acting, this is

due to its combination of two components; first ingredient, Sacubitril is a prodrug that, after activation converts to sacubitrilat by esterase. Sacubitril prevents breakdown of endogenous natriuretic peptides (NP). The NP system can be improved by blocking neprilysin or neutral endopeptidase (NEP), the major enzyme responsible for NP degradation. Sacubitril inhibits the metabolism of endogenous enkephalins, which causes a rise in their levels. Isolated NEP inhibition (NEPi) activates the reflex RAS (renin-angiotensin system) and inhibits angiotensin II (AgII) breakdown, preventing endogenous (NP) deterioration while counteracting any potentially positive effects. Sacubitril alone does not have an evident superiority; thus it must be paired with a RAAS blocker, represented by the second portion of the medicine, valsartan [2]. The RAS is activated in heart failure, boosting sympathetic nerve activity and causing cardiac remodeling, which exacerbates the course of HF. Renin and angiotensin-converting enzyme generate angiotensin II from angiotensinogen. Valsartan suppresses (Ang II) effects by specifically inhibiting the type-1 angiotensin receptor (AT1 receptor). As a result, this unique mechanism prolongs the beneficial benefits of NPs while also preventing the detrimental consequences of renin-angiotensin aldosterone system (RAAS). Collectively, the net results following systemic vasodilation, a decrease in peripheral vascular resistance, an increase in both diuresis and natriuresis with the resultant decrease in plasma volume, and inhibition of the release of Ang II-dependent aldosterone, inhibiting deleterious effects mediated by Ang II, such as vasoconstriction, hypertrophy, and fibrosis, as well as improvement of cardiac remodeling and dysfunction in HF patients. The synergistic actions of neprilysin inhibition and angiotensin receptor blocking boost effectiveness and provide a novel mechanism of action [3].

Primary barriers to implementation of S/V

Although (S/V) combination was accepted in clinical practice as Class I recommendation in HF guidelines, use of this combination has been lower than prognosticated [4].The highest barrier to clinical application is hypothesized that the price of this novel agent despite there are several cost-effective analyses that can predict the collective advantages when an ARNI (S/V) is used suitably. Despite data proving the advantages of ARNI treatment above standard of care, only a percentage of eligible patients receive the (S/V) combination, and barriers preventing practitioners from prescribing it in those eligible patients may address practitioners' unfamiliarity with (S/V) combination; some cardiologists may lack confidence in identifying the appropriate patient population in clinical practice for compelling indication of (S/V) combination, safety concerns, and fear of causing worsening symptoms in the optimal utilization of the (S/V) combination in clinical practice has the potential to minimize the total burden of heart failure [5]. According to HF recommendations of US, European Union, and Canadian, as well as developing evidence, implementing (S/V) combination in recommended patients can lead to additional mortality reductions. The proper and timely application of this powerful drug has the possibility to greatly enhance global and public health. Medication intolerance and adherence difficulties remain a barrier to medication optimization [6].

Aims of the study

Explain the real role of S/V in AL Nasiriyah Heart Centre Thi-Qar by making interventions and assessing the impact of these interventions to optimize the benefit (S/V) combination as one of the fundamental therapeutics in HF.

3. METHODOLOGY

Study design

This current study had quasi-experimental design was conducted at the Al–Nasiriyah Cardiac Center–Thi-Qar governorate-Iraq, during seven months (from November 2023 to May 2024) during2 months. The study included 73patients who previously diagnosed with HF. The collection of patient’s data during their visiting’s to the cardiac outpatient clinic in the center.

Inclusion Criteria

- Men and women above 18 years of age.
- Patients with chronic symptomatic HFrEF according to (2022 AHA/ACC/HFSA guidelines for the management of HF).
- NYHA functional class II- IV [7]
- At least three readings of systolic BP more than or equal to 100 mmHg over the previous 6 to 12 hours, accompanied by no indications of peripheral hypo perfusion or poor cardiac output syndrome.
- Euvolemic status.
- Appropriately managed with medication and device treatment for HFrEF in accordance with clinical guidelines [8].

Exclusion Criteria

- Unstable hemodynamic circumstances, such as systolic blood pressure below 100 mm Hg and correlated symptoms of hypotension.
- Present hyperkalemia (serum potassium level more than 5.5 mEq / liter)

- Known history of angioedema related to previous ACEi or ARB therapy and multiorgan dysfunction
- Severe liver dysfunction, cholestasis and biliary cirrhosis
- Pregnancy's second and third trimesters
- Significant hypovolemia
- Renal artery stenosis [9]

The data collection for every patient included the following

Patients socio-demographic characteristics, such as age, gender, education level, and smoking status, were also considered, and by measurement of height and weight, which were obtained utilizing a standard electrical scale, body mass index (BMI) was calculated for each patient after removing excessive things (e.g., shoes, bags, coats, and jackets). Disease characteristics of the patients as EF% that was calculated by the cardiologist in the echocardiogram report in each visit. A pulse oximeter was used for rapid measurement of oxygen saturation, and systolic BP and diastolic BP were measured with a mercury sphygmomanometer on the left arm or an electronic blood pressure monitor while seated. The modality of cardiac imaging to calculate LVEF was transthoracic echocardiography performance by cardiologists. The clinical and biochemical data below were gathered at the beginning (baseline) of the experiment and two months later: NT-proBNP, total cholesterol, triglycerides (fasting), Hb, WBC count, CRP, serum electrolytes such as potassium and sodium, renal function tests like serum creatinine and BUN. Dyspnea assessment for intervention group patients by use of a dyspnea scale, which classified dyspnea related to activity to grades depending on the patient's description.

Grade	Dyspnea related to activity
0	Breathlessness only on strenuous exercise
1	Breathless when hurrying on the level or walking up a slight hill
2	Walks slower than other people of same age on the level due to shortness of breath or need to stop for breath when walking at own pace
3	Short of breath after walking few minutes on the level or about 100 yards (90 m)
4	Too Breathless to leave the house, or Breathless when dressing or undressing

Examination of blood sampling

The venous blood sample was about five milliliters (5ml) received from each patient with HFrEF and it had been divided into two parts:

Part (1) as four milliliters put it in sterile plastic tube for measurement of serum levels of NTproBNP, total cholesterol, triglycerides (fasting), C-reactive protein, electrolytes as potassium and sodium, renal functions tests like creatinine and blood urea nitrogen (BUN), then these tubes placed in the centrifuge at speed 4000 rpm for about 6 minutes to isolate the serum and put it in Eppendorf tubes and labeled, then kept their at deep freeze in degree (-25 Cº) until examined by ELIZA kits; on the other hand.

Part (2) was one milliliter placed it in sterile EDTA tubes to prevent coagulation of blood and then sent to the blood analysis laboratory for assessment of hemoglobin and White blood cells.

Statistical analyses

The data that obtained were analyzed by use Statistical Package for the Social Sciences (SPSS) software version 25. Descriptive statistics were conducted for all study items. Continuous variables were expressed as means ± standard deviation (SD), whereas categorical variables were expressed as frequencies and percentages. The statistically significance was regarded when P-value was less than 0.05.

4. RESULTS

The distribution of socio-demographic characteristics in (HFrEF) patients on (S/V) combination. Data as age, BMI, gender distribution and smoking number explained in table (2)

Table 1: The distribution of socio-demographic characteristics for (S/V) combination received group

Characteristics	Number	Mean ± SD	Range	P-value
Age	73	63.89±10.65	36-80	0.469
BMI(Kg/m^2)	73	29.57±4.48	20.7-42	0.056
		Male	Female	
Gender Number (%)	73	48 (65.8 %)	25 (34.2 %)	0.307
		No	Yes	
Smoking Number (%)	73	37 (50.7 %)	36 (49.3 %)	0.74

*: significant difference (P- value < 0.05)

Assessment of the levels of cardiac function parameters

There were significant differences (increase) in the levels of ejection fraction and oxygen saturation, while there were significant differences (decrease) in the level of N-terminal pro Brain Natriuretic peptide (NT-proBNP); also there were no significant differences in the values of blood pressure (BP) ; systolic BP and diastolic BP for intervention group after two months from received combination (S/V), as shown in table (2).

Table 2: Differences in the levels of cardiac function parameters between pre and post switching to (S/V) combination in the intervention group

Intervention group	Cardiac Parameters	Number	Mean ± SD	P-value
Pre switching to S/V	Systolic BP	73	148.23±20.37	0.0001**
Post switching to S/V	Systolic BP	73	125.76±23.56	
Pre switching to S/V	Diastolic BP	73	89.85±17.35	0.0001**
Post switching to S/V	Diastolic BP	73	76.60±13.19	
Pre switching to S/V	Ejection Fraction	73	36.96±4.75	0.0001**
Post switching to S/V	Ejection Fraction(EF)	73	43.59±6.97	
Pre switching to S/V	Oxygen saturation	73	89.52±4.39	0.0001**
Post switching to S\V	Oxygen saturation	73	95.26±3.70	
Pre switching to S/V	NT-proBNP	73	3957.79±5195.91	0.037*
Post switching to S/V	NT-proBNP	73	3003.36±4963.81	

*: significant difference (P-value <0.05)

**: higher significant difference (P-value <0.05)

Evaluation of renal function parameters for pre and post switching to (S/V) combination in the intervention group

There was a significant increase in the level of serum creatinine, but there was not a significant difference in the levels of blood urea nitrogen (BUN) within the intervention group for post switching as compared with pre switching to the (S/V) combination, as shown in (table 3)

Table 3: Differences in the levels of renal function parameters between pre and post switching to the S/V combination in the intervention group

Intervention group renal parameters		Number	Mean ± SD	P-value
Pre switching to S/V	BUN	73	40.25±10.37	
Post switching to S/V	BUN	73	40.69±17.97	0.827
Pre switching to S/V	Serum creatinine	73	1.22±0.38	0.031*
Post switching to S/V	Serum creatinine	73	1.45±0.86	

*: significant difference (P-value <0.05)

**: higher significant difference (P-value <0.05)

Evaluation of blood parameters and electrolytes for pre and post switching to (S/ V) combination in the intervention group

There were higher significant decreases in the levels of c-reactive protein (CRP) and serum sodium, also there was higher significant increase in potassium level; in addition, there were a significant decrease in white blood cells(WBC) count and hemoglobin(Hb) level, but there was a not significant difference in the levels of total cholesterol and fasting triglyceride

within the intervention group for post switching as compared with pre switching to (S/V) combination, as noticed in table (4).

Table 4: Differences in the levels of blood parameters and electrolytes between pre and post switching to (S/ V) combination in the intervention group

Intervention group	Blood Parameters	Number	Mean ± SD	P-value
Pre switching to S/V	Total cholesterol (mg/dl)	73	166.05±40.67	0.183
Post switching to S/V	Total cholesterol (mg/dl)	73	158.32±42.89	
Pre switching to S/V	Triglyceride (mg/dl)	73	150.16±61.33	0.119
Post switching to S/V	Triglyceride (mg/dl)	73	138.83±53.29	
Pre switching to S/V	Hb (g/dl)	73	12.87±1.36	0.001*
Post switching to S/V	Hb (g/dl)	73	12.27±1.70	
Pre switching to S/V	WBC count (10^3/mm^3)	73	8.68±3.32	0.001*
Post switching to S/V	WBC count (10^3/mm^3)	73	7.19±2.94	
Pre switching to S/V	CRP (mg/dl)	73	10.66±24.77	0.0001**
Post switching to S/V	CRP (mg/dl)	73	5.46±6.19	
Pre switching to S/V	Serum potassium (mEq/L)	73	4.10±0.61	0.001*
Post switching to S/V	Serum potassium (mEq/L)	73	4.58±0.99	
Pre switching to S/V	Serum sodium (mEq/L)	73	144.53±7.56	0.0001**
Post switching to S/V	Serum sodium (mEq/L)	73	132.68±11.37	

*: significant difference (P-value <0.05)

**: higher significant difference (P-value <0.05)

Evaluation grade of exertional dyspnea for pre and post switching to S/V combination in the intervention group

The modified Medical Research Council *(mMRC) defined the* dyspnea scale as a self-assessment tool used to measure the level of impairment caused by breathlessness during daily activities. mMRC was used to assess the grade of exertional dyspnea in HF patients, as shown in table. As noted in table 5, the grade of exertional dyspnea reduced significantly in post switching as compared with pre switching to the S/V combination for two months.

Table 5: Distribution grade of exertional dyspnea for pre and post switching to (S/V) combination in the intervention group

Grade of exertional dyspnea	Pre switching to (S/V) combination		Post switching to (S/V) combination	
	Number	%	Number	%
0			1	1.4
1	1	1.4	15	20.5
2	3	4.1	25	34.2
3	48	65.8	24	32.9
4	21	28.8	8	11.0
Total	73	100	73	100

Grade of exertional dyspnea according to mMRC:

Grade 1: Breathless when hurrying on the level or walking up a slight hill.

Grade 2: Walks slower than others of the same age or needs to stop for breath when walking at own pace.

Grade 3: Short of breath after walking for a few minutes on the level or about 90 meters.

Grade 4: Too breathless to leave house or breathless when dressing or undressing.

Table 7: Evaluation of the exertional dyspnea grade for the intervention group pre and post switching to (S/V) combination

Measurement time	Number	Mean± SD	P-value
Grade of exertional dyspnea-pre switching to S/V	73	3.22±0.583	0.0001**
Grade of exertional dyspnea-post switching to S/V	73	2.32±0.970	

**: higher significant difference (P-value <0.05)

5. DISCUSSION

Socio-demographic Characteristics of Patients

The current study stated that the age ranges of patients were 36-80, of note that this result inconsistent with another study performed on Chinese HF patients included age range 51-72 [10]. This difference might be explained by longer survival and better treatment results for HF patients in China compared to Iraq. The younger ages of Iraqi patients with HF may be reflected by the delay in treatment of HF etiologies and no or little adherence to CVD medications. There is a lack of understanding of the variables that contribute to medication nonadherence in CVD patients, with insufficient research on knowledge, attitudes, beliefs, and associated behaviors. Most Iraqi hospitals were trying to recover after years of violence, health facility and personnel shortages, insufficiently qualified healthcare workers, and limited healthcare financing. Iraq's healthcare system, particularly heart disease management, is still in the early stages of development, which might explain the poor rates of adherence to cardiac drugs. Iraqi individuals with CVD may have had difficulty receiving effective health treatments because to a lack of or restricted resources, such as shortage of drugs in public hospitals [11]. The number of male patients in the current study was 48 patients 65.8% and it included 25 female patients 34.2%, the male-to-female ratios were 1.92:1. This means that HF has greater incidence in male Iraqi patients than in female patients. This result came in line with that obtained by [12], the post-hoc study to evaluate the renal effects of S/V in patients with HFrEF, which showed that most patients were males 79.4% and the ratio of male to female was 3.6:1. This congruent with the facts related to the pathophysiology of HF in both male and female. A prospective study of HF patients who had been admitted to the Coronary Care Unit (CCU) of Teaching Hospital- Kurdistan, Iraq; females accounted for the majority of HFmrEF followed by HFpEF and HFrE. (HFrEF) has a greater prevalence in men [13]. Regarding BMI, there was similarity to some extent between this study finding in where 29.57±4.48 was the Mean ± SD of BMI and that presented by study performed by [14]. The present study showed that 49.3% of the patients were active smokers during the study period. The role of smoking in developing of CVD is clear. Smoking has been associated with nonadherence to medications, this could lead to less well controlled hypertension over time, and poorer adherence to HF drugs, causing more HF hospitalizations. Smoking is potentially associated with an increase in the left ventricular mass index, left ventricular concentric remodeling. A plethora of cytokines have been shown to induce, maintain and amplify the inflammatory. Also hypertrophy which is a risk factor for the onset of HF. In the community- based cohort study published in the journal of the AHA; on Black adults, current smoking was associated with both incident HFrEF and HFpEF hospitalizations [15].

Evaluation of the effect of S/V on the levels of cardiac function parameters

the mean ± SD of systolic BP was 125.76±23.56 for intervention group after 2 months from receiving (S/V).This result, to some extent, is conformed with that of PARADIGM-HF, where systolic BP; mean ± SD was 122.0±15.0, or that obtained from another real world prospective study that made in cardiology specialty clinic in Pakistan whereby the mean ± SD of systolic BP was 109.5 ± 16.94 [16], while its higher than that noted in a retrospective cohort study of HFrEF patients in the university hospital of Wales-UK; it showed that mean of systolic BP± SD was 112 mmHg to those treated with S/V [17]. That can be interpreted as the duration of patient's follow-up in this study was only 2-months; that's considered a short period for the effect of (S/V) to be pronounced on BP if compared with those in the other studies when the follow-up periods continue at least to 3 months or even to years. In meta-analysis study compared the vasodilating and antihypertensive properties of S/V with that of ARBs; S/V had a markedly superior antihypertensive impact compared to ARBs, for both seated and ambulatory blood pressure. As related to the impact of EF on HF patients, HF hospitalizations, cardiovascular death, and all-cause mortality decreased markedly with increasing LVEF after use of S/V in HFrEF patients. S/V played a significant role in the elevation of EF to values above 40%, as noticed in table (3), with the administration of S/V therapy, EF significantly improved from 36.96±4.75 to 43.59±6.97% S/V. These findings somewhat closed these obtained by [18] that involved several significant improvements in LVEF following treatment with S/V from 32.6 ± 5 to 36 ± 6 and from 25.33 %baseline to 30.14%, respectively, with P-values (less than 0.0001). Another study stated that there was no significant difference in EF changes between the S/V group and the enalapril group from baseline to 12weeks P-value 0.24 [2]. If EF was evaluated according to the received doses of S/V, the mean increase was somewhat more pronounced in the medium or high dosage phase compared to the low dose [19]. Worth noting that the reduction in NT-proBNP level occurs in 4 weeks of S/V therapy and at the same time as a relatively rapid improvement in hemodynamic parameters [20]. As related to the renal function, the fundamental issue to explain is most HF patients have more than one disease that causes renal impairment and

may progress to CKD or even renal failure if insufficiently controlled as HT and DM. In terms of renal safety, the assessment of renal functions in the current study was performed depending upon the measurement of BUN and serum creatinine only without the calculation of eGFR or specific markers of glomerular and tubular injury like albuminuria due to absence of accuracy in such procedures, making these results not enough to reflect the renal effect of drug combination (Palazzuoli *et al.*, 2024). Most studies focused on serum creatinine level to estimate renal changes after S/V switching. On the basis of the above, it was found that the creatinine elevated after 2 months for the S/V received group; the mean ± SD was 1.45±0.86, compared with the baseline of 1.22±0.38, (P-value 0.031), table (3); but as compared with the control group, creatinine was significantly lower (P-value 0.005). In contradistinction, the PARADIGM-HF study showed that S/V was aided with a reduction in the incidence of renal impairment or elevation in serum creatinine as done with enalapril. Significant decrease in the levels of Hb for post switching as compared with pre switching to the S/V combination. Firstly, its known that anemia due to iron deficiency is one of the most common comorbidities that could be found in HF patients with worse prognosis. Inhibition of the RAS could have a role in the development of anaemia by several mechanisms; also, the use of ACEi, or ARBs was observed to be related to a diminishing Hb level. In the PARADIGM-study, it was observed, that 5% of HFrEF patients had more than a 20% decrease in their levels of Hb/HCT. Also, a retrospective cohort study stated that in more than one-third of HF patients who were on S/V, Hb levels decreased during 12 months, while another study was performed on patients with HFrEF; the mean Hb mostly elevated by 0.7 g/dl after 3 month from the start of S/V. As related to the inflammatory status, this study focused on the measurement of WBC count and CRP as systemic inflammatory markers reflecting clinical adverse prognosis and outcomes in HF patients. The myocardial injury in HFrEF is considered the origin of the inflammation in HFrEF [21]. Previous research has indicated that HF, raised CRP, and reduced serum albumin are related. More recently, research has revealed that elevated CRP and low serum albumin levels are linked to adverse cardiovascular events and can be utilized as indicators of systemic inflammation [22]. In a cohort study performed on Korean patients by Kim et al, CRP and WBC count were decreased significantly for the patient group on S/V if compared with the group on ARB (valsartan); these findings are compatible with results in this study [21]. Table (5) showed that there was a higher significant increase in potassium level within the intervention group after the switch over as compared with pre switching, (P-value less than 0.05). Hyperkalemia as a risky adverse effect of ARNI use, also as cough and diminished renal function, has been demonstrated to be lower than if compared with using ACEI [23]. Also, another outpatient study on 80 patients with HFrEF started S/V revealed that during the three months of therapy, sodium and potassium electrolytes remain constant (P value was 0.13). Solomon *et al* explained that S/V was related with lower incidence of hyperkalemia in HFpEF patients compared with those on ARB (valsartan) (Solomon *et al.*, 2019). Sodium levels highly significantly decreased in the intervention group after switching compared with pre switching, (P value 0.0001), as shown in table (5). The five-item modified Medical Research Council (MMRC) dyspnea scale was used in this study to assess dyspnea levels in HF patients. This test was easier to administer to most patients than the (6MWT) because it relied on asking them specific questions about their daily activities, such as walking up quickly or comparing their walking speed to that of others their ages or walking short distances, which is usually easy, or even dressing or undressing. Most cardiologists at Al-Nasiriyah Heart Center oversaw this type of questioning. It was found that the number of patients with grade 4 dyspnea (the most severe) fell from 21 to 8 after switching. Similarly, the number of patients in grade 3 declined. In grades 0 and 1 (which are considered better than 3 and 4), the number of patients increased after switching. This mirrored the patients' positive prognosis and demonstrated to some extent the effect of S/V in relieving their exertional dyspnea; see table 6. The results also demonstrated that there was a substantial improvement in dyspnea grade after S/V as compared to before S/V (P-value 0.0001), table (7). These results can be attributed to the decrease in volume overload due to the role of the sacubitril component in natriuresis and improvement in cardiac functions.

Limitations

There are some limitation in this study, first the small size sample for both patients and cardiologists. Second the absence of facilities in cardiac center. Third, the short duration of the study.

Recommendation

More studies should be performed on this combination to confirm its effects in heart failure patients.

REFERENCES

[1] Zhang R, Sun X, Li Y, He W, Zhu H, Liu B, Zhang A. The Efficacy and Safety of Sacubitril/Valsartan in Heart Failure Patients: A Review. J Cardiovasc Pharmacol Ther. 2022 Jan-Dec: 27: 10742484211058681. doi: 10.1177/10742484211058681.

[2] 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 Sep 11; 371(11): 993-1004. doi: 10.1056/NEJMoa1409077.

[3] Judge PK. Randomized multicentre pilot study of sacubitril/valsartan versus irbesartan in patients with chronic kidney disease: United Kingdom Heart and Renal Protection (HARP)- III - Rationale, trial design and baseline data. Nephrology Dialysis Transplantation. 2017; 32(12): 2043–2051. doi: 10.1093/ndt/gfw321.

[4] Tan NY, Sangaralingham LR, Sangaralingham SJ, Yao X, Shah ND, Dunlay SM. Comparative Effectiveness of Sacubitril-Valsartan Versus ACE/ARB Therapy in Heart Failure With Reduced Ejection Fraction. JACC Heart Fail. 2020 Jan; 8(1): 43-54. doi: 10.1016/j.jchf.2019.08.003.

[5] Veltri KT. Novel Agent, Sacubitril-Valsartan: Prescribing Patterns and Perceived Barriers to Hospital Formulary Inclusion. Clinical Studies & Medical Case Reports. 2019; 6(1): 1-7. https://doi.org/10.24966/csmc-8801/100062

[6] Patil T. Impact of Pharmacist-Led Heart Failure Clinic on Optimization of Guideline-Directed Medical Therapy (PHARM-HF). Journal of Cardiovascular Translational Research. 2022; 15(6): 1424–1435. https://doi.org/10.1007/s12265-022-10262-9.

[7] Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ,. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022; 45(18). https://doi.org/10.1161/CIR.0000000000001063.

[8] Ntalianis A. Angiotensin receptor-neprilysin inhibition in patients with acute decompensated heart failure: an expert consensus position paper. Heart Failure Reviews. 2022; 27(1): 1-13. https://doi.org/10.1007/s10741-021-10115-8.

[9] Buda V. An Up-to Date Article Regarding Particularities Drug Treatment in Patients with Chronic Heart Failure. Journal of Clinical Medicine. 2022; 11(7). https://doi.org/10.3390/jcm11072020

[10] Hu T, Liu Y. Lou Y. Sacubitril–valsartan versus enalapril for the treatment of acute decompensated heart failure in Chinese settings: A cost-effectiveness analysis. Frontiers in Pharmacology. 2023; 14. https://doi.org/10.3389/fphar.2023.925375

[11] Al-Ganmi AHA, Al-Fayyadh, S, Ali A, Alotaibi AM, Gholizadeh L, Perry L. Medication adherence and predictive factors in patients with cardiovascular disease: A comparison study between Australia and Iraq. Nurs Health Sci. 2020 Jun; 22(2): 454-463. doi: 10.1111/nhs.12681.

[12] Damman K, Gori M, Claggett B, Jhund PS, Senni M, Lefkowitz MP, et al. Renal Effects and Associated Outcomes during Angiotensin-Neprilysin Inhibition in Heart Failure. JACC Heart Fail. 2018 Jun; 6(6): 489-498. doi: 10.1016/j.jchf.2018.02.004.

[13] Regitz-Zagrosek V. Sex and Gender Differences in Heart Failure. International Journal of Heart Failure. 2020; 2(3): 157-181. https://doi.org/10.36628/ijhf.2020.0004.

[14] El-Battrawy I. The impact of sacubitril/valsartan on outcome in patients suffering from heart failure with a concomitant diabetes mellitus. ESC Heart Failure. 2023; 10(2): 943-954. https://doi.org/10.1002/ehf2.14239.

[15] Egan TD, Orgain N. Cigarette Smoking Cessation. Essence of Anesthesia Practice E-Book. 2010; 86. https://doi.org/10.1016/B978-1-4377-1720-4.00076-5.

[16] Hafizullah M, Aman W, Afridi H. Evaluation of Angiotensin Receptor and Neprlysin Inhibition (Arni) in Patients of Heart Failure With Reduced Ejection Fraction (Hfref) - a Real-World Study. Pakistan Heart Journal. 2023; 56(1): 22–27. https://doi.org/10.47144/phj.v56i1.2454.

[17] Ganesananthan S. Real-world treatment switching to sacubitril/valsartan in patients with heart failure with reduced ejection fraction: A cohort study. Open Heart. 2020; 7(2). https://doi.org/10.1136/openhrt-2020-001305.

[18] Bayard G, Da Costa A, Pierrard R, Roméyer-Bouchard C, Guichard JB, Isaaz K. Impact of sacubitril/valsartan on echo parameters in heart failure patients with reduced ejection fraction a prospective evaluation. Int J Cardiol Heart Vasc. 2019 Sep 3:25: 100418. doi: 10.1016/j.ijcha.2019.100418.

[19] Almufleh A. Ejection fraction improvement and reverse remodeling achieved with Sacubitril/Valsartan in heart failure with reduced ejection fraction patients. American journal of cardiovascular disease. 2017; 7(6): 108–113.

[20] Vardeny O. Reduced loop diuretic use in patients taking sacubitril/valsartan compared with enalapril: the PARADIGM-HF trial. European Journal of Heart Failure. 2019; 21(3): 337–341. https://doi.org/10.1002/ejhf.1402.

[21] Kim HJ. Cardiac and kidney outcomes after sacubitril-valsartan therapy: recovery of cardiac function relative to kidney function decline. Kidney Research and Clinical Practice. 2024; 43(5): 614-625. https://doi.org/10.23876/j.krcp.24.021.

[22] Arslan A. The Relationship between CRP to Albumin Ratio and Non Ischemic Cardiomyopathy in Atrial Fibrillation Patients. Research square. 2024; 1-18. https://doi.org/10.21203/rs.3.rs-5456454/v1.

[23] Usuda D. Angiotensin receptor blocker neprilysin inhibitors. World Journal of Cardiology. Baishideng Publishing Group Inc. 2021; 325–339. https://doi.org/10.4330/wjc.v13.i8.325..