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Original Article

Role of Combination of Sacubitril and Valsartan for Management of Patients with Decompensated Heart Failure

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Abstract

Objective: To determine the outcome of sacubitril plus valsartan in patients with decompensated heart failure

Methods: This quasi experimental study was done at Department of Cardiology, Mayo Hospital, Lahore during March 2022 to March 2023. Total 200 patients with decompensated heart failure were enrolled through emergency and admitted in cardiology wards. All patients were given Sacubitril / valsartan (200 mg, twice daily) during hospital stay. Then all patients were followed-up until discharge from the hospital. If patient died during hospital stay, then mortality was noted. data was colelcted in proforma whiel analysed in SPSS version 25.

Results: In this trial, we enrolled total 200 individuals with decompensated heart failure with mean age of 55.02 ± 8.64 years. Out of 200 individuals, 111 (55.5%) were males and 89 (44.5%) were females. Out of 200 individuals, 34 (17.0%) individuals died during follow-up in the hospital after receiving sacubitril with valsartan combination drug. For ejection fraction, the mortality was significantly higher in individuals who had ejection fraction less than 22% (27.9%) as compared to individuals with ejection fraction was higher than 22% (3.4%, p-value < 0.05).

Conclusion: The outcome of sacubitril with valsartan combination drug is better and morality is less.

Key words: in-hospital mortality, sacubitril, valsartan, decompensated heart failure

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Introduction

Heart failure is a complicated pathophysiological and clinical disease that remains a major contributor to healthcare costs and patient suffering worldwide.[1] More than 23 million people throughout the globe are living with heart failure, making it a huge public health concern. Both the incidence and prevalence rates rise with age, with the former reaching, in the extremely old, prevalence rates that pose a challenge to the organisation of medical care systems. Most of the expenses associated with heart failure stem from the frequent and expensive need of hospitalisation for cases of acute heart failure.[2] Patients admitted to the hospital with decompensated heart failure who have blood urea nitrogen levels > 90 mg/dL, blood pressure 115 mmHg, and serum creatinine levels > 2.75 mg/dL have a high risk of death (21.9%) while those without these characteristics have a low risk of death (2.14%).[3] The left ventricular ejection fraction (LVEF) is still the gold standard for measuring cardiac function because of its correlation to patient outcomes throughout the whole spectrum of heart failure. Those at the lowest end of the ejection fraction spectrum were found to be at the highest risk for cardiovascular death, heart failure hospitalisation, and all-cause mortality in patients with heart failure and reduced ejection fraction.[4]

Even though pharmacological therapies have been identified and implemented to improve outcomes, such as those targeting the renin-angiotensin-aldosterone system, 5-year mortality and rates of hospitalisation for heart failure patients remain unacceptablely high despite the significant improvement in survival over the last few decades.[1,5] High mortality and hospitalisation rates remain a hallmark of heart failure despite the availability of many treatments backed by evidence.[6] Patients' baseline features are unique, and their risk of future cardiovascular events is greater than average.[7] In July 2015, the FDA gave their blessing to the combination of sacubitril and valsartan for the treatment of heart failure with decreased ejection fraction.[8] Patients consistently preferred sacubitril/valsartan over enalapril.[7,9]

One study found that the frequency of mortality was 21.5% with sacubitril plus valsartan for management of patients who were diagnosed to have decompensated heart failure.[10] Another study also reported that the frequency of mortality was 21.8% with sacubitril combined with valsartan for management of patients who were diagnosed to have decompensated heart failure.[11]
Literature showed that with sacubitril plus valsartan, the chances of mortality have been decreased. But still the frequency is high. But not much work has been done in this regard as well as local evince lacks. Therefore, the aim of this study was to find the role of sacubitril and valsartan combination in hospitalized heart failure patients. So that in future, we can rely on sacubitril with valsartan to decrease number of mortality in patients with heart failure. This can help us to plan management and preventive strategies for heart failure patients. Present syudy was undertaken to determine the outcome of sacubitril plus valsartan in patients with decompensated heart failure.

Methods

This Quasi experimental study was undertaken in Department of Cardiology, Mayo Hospital, Lahore in one year i.e. Mach 2022 to March 2023. A sample size (n) was 200 cases estimated by using 95% confidence level, 6% margin of error and percentage of mortality i.e. 21.5% with sacubitril with valsartan for decompensated heart failure.[10]

Inclusion and Exclusion Criteria: Patients aged from 40 to 70 years, both sexes, diagnosed with decompensated heart failure, which was defined as presence of chest congestion, pedal edema, fluid retention, difficult breathing while lying flat, episodes of waking up from sleep gasping for air, low urine output, weight loss, weakness, in peripheral parts along with EF<30% on echocardiography were enrolled through Non Probability, Consecutive sampling in the study. Patients with recurrent attack of heart failure (ongoing treatment), bronchial asthma, interstitial lung disease, smoker and other valvular heart diseases, patients already taking trial drug for >3years.

Data Collection Procedure: 200 patients fulfilled the selection criteria were enrolled from medical emergency. Informed consent was taken. Demographics like name, age, gender, duration of symptoms, h/o diabetes and h/o hypertension were also noted. Then patients were admitted in wards and were given combination drug i.e. Sacubitril / valsartan (200 mg, twice daily) during hospital stay. Then all patients were followed-up until discharge from the hospital. If patient died during hospital stay, then mortality was noted. All this information was recorded in proforma.

Data Analysis: Data was analyzed via SPSS version 25.0. Outcome variable i.e. mortality due to heart failure was presented as frequency and percentage. Data was stratified for effect modifiers. Post stratification, chi-square test was applied to compare mortality in stratified groups, keeping P-value ≤0.05 as significant.

Results

In this trial, we enrolled total 200 individuals with decompensated heart failure with mean age of 55.02 ± 8.64 years. Out of 200 individuals, 111(55.5%) were males and 89(44.5%) were females. The mean BMI of individuals was 23.12 ± 4.39 kg/m2. The mean duration of symptoms was 3.66±1.69 months. History of hypertension was positive in 72 (36%) individuals, diabetes mellitus in 115 (57.5%) individuals, anemia as positive in 118 (59%) individuals, and dyslipidemia was observed in 106 (53%) individuals. There were 102 (51%) individuals who had history of smoking while 14 (7%) individuals had positive family history of decompensated heart failure. On presentation, pedal edema was present in 167 (83.5%) cases, while mean ejection fraction was 21.89 ± 4.31%. The mean hospital stay after treatment was 8.69 ± 2.28 days. Table I
Out of 200 individuals, 34 (17.0%) individuals died during follow-up in the hospital after receiving sacubitril with valsartan combination drug. Fig 1

Table 1: *basic demographics and medical history of patients enrolled in the trial*

Characteristic	Mean ± SD, F (%)
N	200
Age (n years)	55.02 ± 8.64
Gender	
Males	111 (55.5%)
Females	89 (44.5%)
BMI (kg/m^2)	23.12 ± 4.39
Duration of symptoms (in months)	3.66 ± 1.69
History of	
Hypertension	72 (36%)
Diabetes	115 (57.5%)
Anemia	118 (59%)
Dyslipidemia	106 (53%)
Smoking	102 (51%)
Family history of heart failure	14 (7%)
Clinical presentation	
Presence of Pedal edema	167 (83.5%)
Ejection fraction at presentation (%)	21.89 ± 4.31
Hospital stay (in days)	8.69 ± 2.28

Data was stratified for effect modifiers and found no significant differences calculated in the frequency of in-hospital mortality in different groups (p-value > 0.05). But for ejection fraction, the in-hospital mortality was higher significantly in individuals who had ejection fraction less than 22% (27.9%) as compared to individuals with ejection fraction was higher than 22% (3.4%, p-value < 0.05). Table II

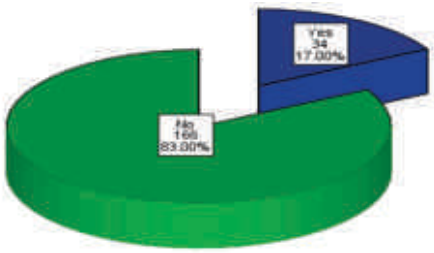

Fig 1: *Distribution of mortality*

Table 2: *Comparison of mortality in different effect modifiers groups*

		Mortality		p-value
		Yes	No	
	n	34	166	
Age group	40-55	19 (18.4%)	84 (816%)	0.575
	56-70	15 (15.5%)	82 (84.5%)	
Gender	Male	19 (17.1%)	92 (82.9%)	0.961
	Female	15 (16.9%)	74 (83.1%)	
BMI	Underweight	11 (26.8%)	30 (73.2%)	0.168
	Normal BMI	11 (13.9%)	68 (86.1%)	
	Overweight & obese	12 (15.0%)	68 (5.0%)	
Duration	1-3 months	14 (15.1%)	79 (84.9%)	0.495
	4-6 months	20 (18.7%)	87 (81.3%)	
Hyper-tension	Present	13 (18.1%)	59 (81.9%)	0.766
	Absent	21 (16.4%)	107 (83.6%)	
Diabetes mellitus	Present	17 (14.8%)	98 (85.2%)	0.156
	Absent	17 (20.0%)	68 (80.0%)	
Smoker	Yes	18 (17.6%)	84 (82.4%)	0.804
	No	16 (16.3%)	82 (83.7%)	
Anemia	Present	19 (16.1%)	99 (83.9%)	0.685
	Absent	15 (18.3%)	67 (81.7%)	
Dyslipi-demia	Present	19 (17.9%)	87 (82.1%)	0.712
	Absent	15 (16.0%)	79 (84.0%)	
Family history	Present	4 (28.6%)	10 (71.4%)	0.232
	Absent	30 (16.1%)	156 (83.9%)	
Pedal edema	Present	28 (16.8%)	139 (83.2%)	0.843
	Absent	6 (18.2%)	27 (81.8%)	
Ejection fraction	15-22 %	31 (27.9%)	80 (72.1%)	0.000
	23-30 %	3 (3.4%)	86 (96.6%)	
Hospital stay	5-8 days	17 (18.3%)	76 (81.7%)	0.653
	9-12 days	17 (15.9%)	90 (84.1%)	

Discussion

Prolonged life expectancy in the general population and an increase in the number of heart failure patients have contributed to heart failure's rise in frequency in recent decades, making it a serious public health concern worldwide, particularly in industrialised nations. Recent advances in the treatment of heart failure, especially the introduction of novel pharmacological and non-pharmacological therapies, have led to significant improvements in the clinical outcomes of heart failure patients, most notably in terms of longer life expectancy and enhanced quality of life.[12] An very high rate of death and morbidity (readmission to the hospital) is linked to this condition.[13] About 60% of all heart failure treatment costs are associated with hospitalisations for complications. About 10% of patients who are released die within 90 days, and about 25% are readmitted within the same time frame.[14] Heart failure prevalence, incidence, and survival rates vary greatly across nations and research designs. Even though treatment has improved, heart failure remains a leading cause of mortality among the elderly.[15] Sacubitril-valsartan is a combination angiotensin receptor-neprilysin inhibitor used to alleviate the symptoms of heart failure in individuals with a low ejection fraction. Patients who took sacubitril-valsartan in the PARADIGM-HF trial had a reduced risk of death from cardiovascular causes or hospitalisation for heart failure compared to patients who took enalapril.[16,17] According to our findings, 17% of patients who took Sacubitril with valsartan died while hospitalised. Patients were eligible for participation in the PARADIGM-HF trial if they had been taking either an angiotensin-converting-enzyme inhibitor or an angiotensin receptor blocker at a stable dosage equivalent to 10 milligrammes (mg) of enalapril per day for at least 4 weeks. Patients in the study were given high dosages of enalapril and sacubitril-valsartan in a sequential run-in phase before being randomly assigned to receive either treatment.[18]

Consistent with the PIONEER-HF study, the use of sacubitril/valsartan was associated with lower rates of heart failure-related readmission and death.[19] Patients with an eGFR below 30 mL/min/1.73 m^2 (12.8% of our research sample) or those already undergoing dialysis (8.8% of our research population) were not included in the PIONEER-HF study. About a third of our patients had moderate to severe mitral regurgitation, thirteen percent had acute myocardial infarction at the time of the initial hospitalisation, and fifteen and a half percent underwent PCI. Similar exclusion criteria were used to patients who did not qualify for the PIONEER-HF study.[20] Despite the fact that both ACEIs and ARBs are recommended for the treatment of HF by worldwide cardiology organisations, the prescription rate for ARBs

is much higher in Taiwan when compared to ACEIs.[21] The present study's finding of a greater prescription rate of ARBs than ACEIs (34.6% vs 27.5%) in patients with HFrEF is in line with data from the Taiwan Society of Cardiology's HFrEF registry.[22] The high incidence of ACEI-related cough in Chinese people may help explain these results.[23]

Conclusion

The outcome of sacubitril with valsartan combination drug is better and morality is less. Thus in future, we can rely on combination of sacubitril and valsartan for management of patients with decompensated heart failure. But further trials and randomized studies should be done to confirm the evidence and effect on other parameters should also be assessed, instead of only in-hospital mortality.

Conflict of Interest: None

Funding Source: None

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