ACE Inhibitors vs. ARNIs: A Clash of Titans in the battle against Heart Failure with Reduced Ejection Fraction

Section A-Research paper

ACE Inhibitors vs. ARNIs: A Clash of Titans in the battle against Heart Failure with Reduced Ejection Fraction

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ABSTRACT

Background: Heart failure is a medical condition that occurs when the heart is unable to pump enough blood to meet the body's needs.[1] It is a chronic and progressive condition that can affect the heart's ability to supply oxygen-rich blood to the body's organs and tissues.[2] There are two main types of heart failure: systolic heart failure and diastolic heart failure. In systolic heart failure, the heart muscle becomes weakened and is unable to contract effectively, leading to reduced pumping ability. Diastolic heart failure occurs when the heart muscle becomes stiff and cannot relax properly, impairing its ability to fill with blood.

Aims and objectives: The present study was conducted to compare ACE inhibitors and ARNI (sacubitril/valsartan) in heart failure patients with reduced ejection fraction.

Materials & Methods: 80 patients of heart failure of both genders were divided into 2 groups of 40 each. Group I patients received ACE inhibitors and group II patients received ARNI. In both groups, SBP, DBP, urea, potassium and creatinine level was recorded. 2D echo findings at baseline and at 6 months follow-up was compared.

Results: Group I had 22 males and 18 females and group II had 21 males and 19 females. The mean SBP at baseline and at 6 months was 120.5 and 118.5 in group I and 126.8 and 122.9 in group II respectively. DBP was 81.9 and 76.4 in group I and 81.1 and 78.4, creatinine was 1.07 and 1.09 in group I and 1.09 and 1.08 in group II. The mean urea level was 32.1 and 36.2 in group I and 30.9 and 32.4 in group II. The mean potassium level was 4.51 and 4.41 and 4.36 and 4.20 in group I and II at baseline and 6 months respectively. The difference was non- significant (P> 0.05). At baseline and at 6 months, LVEF was 23.4 and 28.1 and 32.4 and 25.9 in group I and II respectively. LVIDD was 6.7 and 6.2 and 5.4 and 5.3. LVISD was 5.4 and 5.6 and 5.2   and 4.7 in group I and II respectively. LV systole mass (gram) was 216.7 and 210.5 and 208.4 and 20.1.4 in group I and II respectively. LV diastole mass (gram) was 238.4 and 230.1 and 231.3 and 219.5 in group I and II respectively. The difference was significant (P< 0.05).

Conclusion: LVEF, systolic function, LVIDD, six-minute walk, and functional NYHA class were all improved with ARNI compared to ACEI, demonstrating the considerable reverse remodelling capabilities of the drug.

Key words: systolic function, ARNI, ACEI

Introduction

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Heart failure is a medical condition that occurs when the heart is unable to pump enough blood to meet the body's needs.[1] It is a chronic and progressive condition that can affect the heart's ability to supply oxygen-rich blood to the body's organs and tissues.[2] There are two main types of heart failure: systolic heart failure and diastolic heart failure. In systolic heart failure, the heart muscle becomes weakened and is unable to contract effectively, leading to reduced pumping ability. Diastolic heart failure occurs when the heart muscle becomes stiff and cannot relax properly, impairing its ability to fill with blood.[3]

Heart failure cases are on the rise both internationally and in India. According to projections, there will be a 25% increase in heart failure (HF) patients by 2030. Heart failure affects the patient's quality of life and raises mortality and morbidity. Five years after receiving the initial HF diagnosis, the mortality rate is anticipated to be 50%.[4] A significant contributor to hospital admissions, HF accounts for 1-5% of all admissions. Approximately 2-17% of HF patients who are admitted will die. In India, the prevalence of HF is thought to range between 1.3 to 23 million. Heart failure instances with a lower ejection fraction (HFrEF) have been seen to occur more frequently.[5]

The available pharmacological therapy for HFrEF that follows guidelines includes angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin-receptor blockers (ARBs), mineralocorticoid receptor antagonists (MRAs), and beta blockers (BBs). It has been demonstrated that these treatments lower morbidity and death. The most recent HF guidelines have recently included the new pharmacological class, which includes angiotensin receptor neprilysin inhibitors (ARNI), which appears to further enhance symptoms and prognosis.[6]

Aims and objectives

The present study was conducted to compare ACE inhibitors and ARNI (sacubitril/valsartan) in heart failure patients with reduced ejection fraction.

Materials & Methods

The present study consisted of 80 patients of heart failure of both genders. All gave their written consent to participate in the study.

Data such as name, age, gender etc. was recorded. Clinical history, physical exam, vital signs, standard transthoracic echocardiography (TTE) parameters, and regular investigations was carried out. Patients were divided into 2 groups of 40 each. Group I patients received ACE inhibitors and group II patients received ARNI. In both groups, SBP, DBP, urea, potassium and creatinine level was recorded. 2D echo findings at baseline and at 6 months follow-up was compared. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I: Distribution of patients

Groups	Group I	Group II
Drug	ACE inhibitors	ARNI
M:F	22:18	21:19

Table I shows that group I had 22 males and 18 females and group II had 21 males and 19 females.

Table II: Assessment of parameters

Parameters	Group I		Group II		P Value
	Baseline	6months	Baseline	6months	
SBP	120.5	118.5	126.8	122.9	0.11

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DBP	81.9	76.4	81.1	78.4	0.17
Creatinine	1.07	1.09	1.09	1.08	1.0
Urea	32.1	36.2	30.9	32.4	0.05
Potassium	4.51	4.41	4.36	4.20	0.32

Table II, graph I shows that mean SBP at baseline and at 6 months was 120.5 and 118.5 in group I and 126.8 and 122.9 in group II respectively. DBP was 81.9 and 76.4 in group I and 81.1 and 78.4, creatinine was 1.07 and 1.09 in group I and 1.09 and 1.08 in group II. The mean urea level was 32.1 and 36.2 in group I and 30.9 and 32.4 in group II. The mean potassium level was 4.51 and 4.41 and 4.36 and 4.20 in group I and II at baseline and 6 months respectively. The difference was non- significant (P> 0.05).
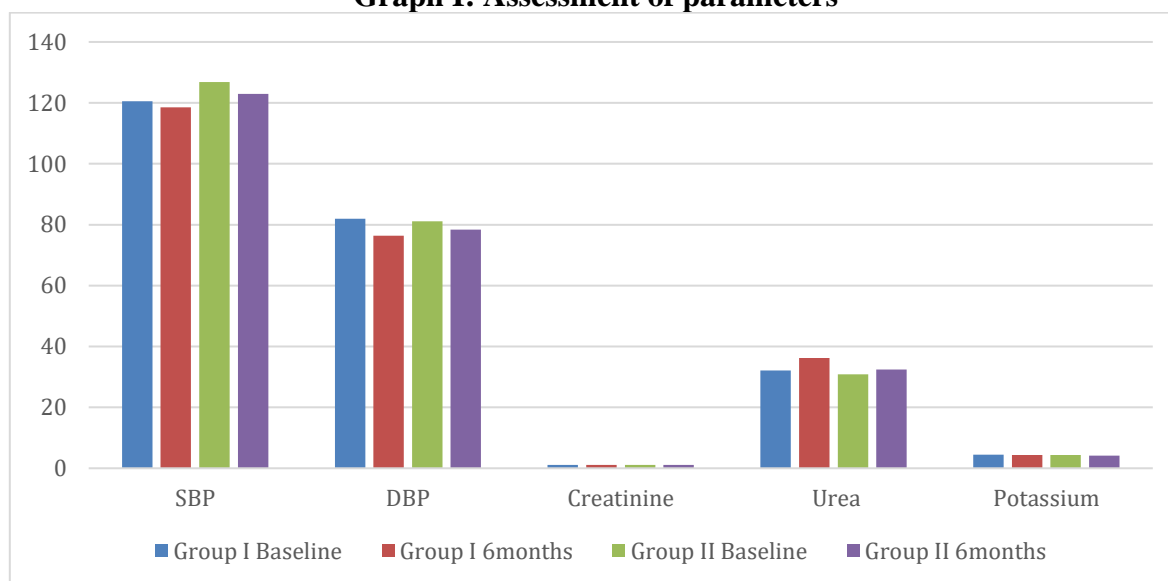
Graph I: Assessment of parameters

Table III: Comparison of 2D echo findings

Parameters	Group I		Group II		P Value
	Baseline	**6months**	**Baseline**	**6months**	
LVEF	23.4	28.1	32.4	25.9	0.04
LVIDD	6.7	6.2	5.4	5.3	0.02
LVISD	5.4	5.6	5.2	4.7	0.01
LV systole mass (gram)	216.7	210.5	208.4	20.1.4	0.92
LV diastole mass (gram)	238.4	230.1	231.3	219.5	0.82

Table III shows that at baseline and at 6 months, LVEF was 23.4 and 28.1 and 32.4 and 25.9 in group I and II respectively. LVIDD was 6.7 and 6.2 and 5.4 and 5.3. LVISD was 5.4 and 5.6 and 5.2 and 4.7 in group I and II respectively. LV systole mass (gram) was 216.7 and 210.5 and 208.4 and 20.1.4 in group I and II respectively. LV diastole mass (gram) was 238.4 and 230.1 and 231.3 and 219.5 in group I and II respectively. The difference was significant (P< 0.05).

Discussion

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Heart failure can have various causes. The most common cause of heart failure is a narrowing of the coronary arteries that supply blood to the heart muscle. This can lead to a heart attack, which damages the heart muscle and impairs its function.[7] Uncontrolled high blood pressure can cause the heart to work harder, leading to heart muscle thickening and stiffness over time. Cardiomyopathy refers to diseases of the heart muscle itself, which can weaken the heart and impair its pumping ability.[8] Cardiomyopathy can be caused by factors such as genetics, infections, alcohol abuse, or drug use. Malfunctioning heart valves can disrupt the flow of blood through the heart, leading to heart failure. Abnormal heart rhythms can cause the heart to pump ineffectively, leading to heart failure.[9] The present study was conducted to compare ACE inhibitors and ARNI (Sacubitril/Valsartan) in heart failure patients with reduced ejection fraction.

We found that group I had 22 males and 18 females and group II had 21 males and 19 females. The mean SBP at baseline and at 6 months was 120.5 and 118.5 in group I and 126.8 and 122.9 in group II respectively. DBP was 81.9 and 76.4 in group I and 81.1 and 78.4, creatinine was 1.07 and 1.09 in group I and 1.09 and 1.08 in group II. The mean urea level was 32.1 and 36.2 in group I and 30.9 and 32.4 in group II. The mean potassium level was 4.51 and 4.41 and 4.36 and 4.20 in group I and II at baseline and 6 months respectively. Sharma et al[10] included 240 patients, 120 each in ARNI and ACE group. All patients underwent 2 D echocardiography, six minutes walk test and functional class assessment at baseline and after follow up of 6 months. There was significant improvement in LVEF in ARNI group as compared to ACEI group (p value<0.05). Reduction in LVIDD and LVISD was also significant in ARNI group. Significant improvement in six- minute walk test was seen in ARNI group as compared to ACEI.

We found that at baseline and at 6 months, LVEF was 23.4 and 28.1 and 32.4 and 25.9 in group I and II respectively. LVIDD was 6.7 and 6.2 and 5.4 and 5.3. LVISD was 5.4 and 5.6 and 5.2 and 4.7 in group I and II respectively. LV systole mass (gram) was 216.7 and 210.5 and 208.4 and 20.1.4 in group I and II respectively. LV diastole mass (gram) was 238.4 and 230.1 and 231.3 and 219.5 in group I and II respectively. Rodil Fraile et al[11] analysed the improvement of the functional class and the 6 min walking test (6MWT) in patients with multiple pathologies and advanced heart failure. 65 multimorbidity patients with severe symptomatic HFrEF were initiated to receive sacubitril/valsartan. Mean age was 78.6 ± 7.4 years, and 68% were male. The Charlson co-morbidity index was 8 points. Seventy-four per cent had New York Heart Association (NYHA) Functional Class IV. After the treatment, patients were able to achieve 55.68 m or more on 6MWT, and 91% presented an improvement in the NYHA functional class. Sacubitril/valsartan, relieves symptoms and improves functional class prognostic risk of patients with advanced HFrEF and co-morbidity. Frey et al[12] enrolled 225 patients of heart failure. Out of these, 9.3% (n = 21) had a history of histologically confirmed cancer. Oncologic surgery was performed in 16 (76.2%) patients, 11 (52.4%) patients received previous antineoplastic therapy and 9 patients (42.9%) radiation. Sacubitril/valsartan was withdrawn in 3 of 21 patients (14.3%) because of dizziness (n = 2) or pruritus (n = 1). After a median follow-up of 12 months (range 1-34 months), NYHA functional class improved significantly from NYHA 3 to NYHA 2 (mean -0.6, p = 0.006) and left ventricular ejection fraction as assessed by echocardiography increased significantly from $26.8 \pm 5.4\%$ to $39.2 \pm 10\%$ (mean + 12%, CI 95% [8.4-16.4], p = 0.0004). NT-proBNP was significantly reduced (baseline median 2774 pg/ml, range 1441 - 12,982 vs follow-up 1266 pg/ml, range 199-6324, p = 0.009). There was no significant change in creatinine levels.

Conclusion

In this study comparing ACE inhibitors and ARNI in heart failure patients with reduced ejection fraction (HFrEF), both treatment groups showed improvements in several

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parameters. However, significant differences were observed in the improvement of left ventricular ejection fraction (LVEF), left ventricular internal dimensions (LVIDD and LVISD), and functional class.

The ARNI group demonstrated a greater improvement in LVEF compared to the ACE inhibitor group. This finding aligns with previous studies that have highlighted the superior efficacy of ARNIs in improving cardiac function in HFrEF patients. Additionally, ARNI therapy was associated with a significant reduction in LVIDD and LVISD, indicating favorable reverse remodeling effects.

Furthermore, the ARNI group showed a significant improvement in functional capacity, as assessed by the six-minute walk test, compared to the ACE inhibitor group. This improvement in exercise tolerance is an essential clinical outcome for heart failure patients and may indicate enhanced quality of life.

While both treatment groups demonstrated similar effects on blood pressure, renal function (creatinine, urea, and potassium levels), and left ventricular mass, the differences observed in cardiac function and functional capacity suggest a potential advantage of ARNIs over ACE inhibitors in HFrEF management.

Overall, these findings support the growing evidence that ARNIs, such as sacubitril/valsartan, offer superior benefits compared to ACE inhibitors in heart failure patients with reduced ejection fraction. However, further studies with larger sample sizes and longer follow-up periods are warranted to validate these results and assess long-term clinical outcomes and safety profiles.

Conflict of Interest: - None declared

Source of support: - Nil

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