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ORIGINAL RESEARCH

COMPARISON OF EFFECTIVENESS OF ISOSORBID DINITRATE/ HYDRALAZINE COMBINATION WITH SACUBITREL/ VALSARTAN IN CHF AMONG INDIAN PATIENTS

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ABSTRACT

Background: To compare the effectiveness of Isosorbid dinitrate/ hydralazine combination with Sacubitrel/ Valsartan in CHF in Indian patients.

Methods: One hundred ten CHF patients of both genders were divided into 2 groups of fifty- five each. Group I patients received Sacubitrel/ Valsartan and group II patients received Isosorbid dinitrate/ hydralazine. Effectiveness of both drug combination was compared.

Results: Clinical features recorded was ischaemic cardiomyopathy in 32 and 38 in group I and II patients respectively. LVEF found to be 29.1% and 29.4%. Medium B type natriuretic peptide level was 254 pg/ml and 255 pg/ml in group I and II patients respectively. NYHA functional class I was seen in 8 and 7, class II in 23 and 25, class III in 20 and 21 and class IV in 4 and 2 respectively. Medical history was diabetes seen in 21 and 9, hypertension in 17 and 14, atrial fibrillation in 11 and 12, stroke in 6 and 5 and myocardial infarction in 2 and 4 in group I and II patients respectively. SBP (mm Hg) was 126.8 and 124.6 and heart rate (beats/ min) was 70.2 and 74.6. Treatment given was digitalis in 42 and 52, B- blocker in 31 and 37, diuretic in 27 and 30 and mineralocorticoid antagonist in 13 and 16 patients in group I and II respectively. The difference was non- significant ($P>0.05$). Adverse events were hypotension in 6 and 2, serum creatinine >3.0 mg/dl seen in 2 and 4, serum potassium >5.5 mmol/l was seen in 5 and 9, angioedema in 6 and 8 and cough in 2 and 1 patients in group I and II respectively. The difference was significant ($P< 0.05$).

Conclusion: The combination of Sacubitrel/ Valsartan in CHF patients was found to be effective as compared to Isosorbid dinitrate/ hydralazine. However, large scale studies are required to substantiate the results obtained in this study.

Keywords: Sacubitrel/ Valsartan, Isosorbid dinitrate/ hydralazine, CHF

INTRODUCTION

Chronic heart failure (CHF), also known as congestive heart failure, is a long-term condition in which the heart is unable to pump blood effectively, leading to insufficient blood flow to meet the body's needs. This condition usually develops over time as the heart's pumping ability weakens.

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CHF can result from various underlying conditions that strain or damage the heart, such as coronary artery disease, hypertension (high blood pressure), myocardial infarction (heart attack), cardiomyopathy (disease of the heart muscle), valvular heart disease, and other cardiac or non-cardiac issues.[1]

Common symptoms include fatigue, shortness of breath (especially during physical activity or when lying down), persistent coughing or wheezing, fluid retention leading to swelling in the legs, ankles, or abdomen, and difficulty concentrating.[2] Morbidity is still rising. Over 5.7 million people in the USA have chronic heart failure (CHF), which results in 670,000 new cases each year and over USD 32 billion in medical costs and lost productivity. Currently, 4 types of HF are defined in actual guidelines: HF with reduced LVEF (< 40%; HFrEF), HF with mid-range LVEF (40% to 49%; HFmrEF), HF with preserved LVEF (≥ 50%; HFpEF), and HF with improved HF.[3]

By suppressing the renin-angiotensin-aldosterone system (RAAS) through AT1 receptor blockade and enhancing the natriuretic peptide system through neprilysin inhibition, sacubitril/valsartan (S/V; formerly known as LCZ696) is a novel form of pharmacotherapy that produces more effective neurohormonal modulation than can be achieved with RAAS inhibition alone.[4] Natriuretic peptide (NP) levels rise when neprilysin is inhibited, but vasoconstriction, aberrant growth, salt retention, and remodeling are all reduced.[5] To stop the neprilysin inhibitor from activating the RAAS, an ARB must be added. In the A-HeFT (African-American Heart Failure Trial), the addition of a combination pill of H-ISDN to optimal medical therapy was found to improve quality of life and to reduce HF-related hospitalizations and mortality rates.[6] We performed this study to compare the effectiveness of Isosorbid dinitrate/ hydralazine combination with Sacubitrel/ Valsartan in CHF in Indian patients.

MATERIALS & METHOD

This prospective, observational study comprised one hundred ten patients with CHF of both genders. We obtained approval from the ethical review committee. Patients' consent was obtained before starting the study. Patients with symptoms classified as class II, III, or IV by the New York Heart Association (NYHA), and an ejection fraction of 40% or less, a minimum of 150 pg of plasma B-type natriuretic peptide (BNP) or an N-terminal pro-BNP (NT-proBNP) level ≥600 pg per milliliter was required for the patients; alternatively, if the patients had been hospitalized for heart failure in the preceding year, a minimum of 100 pg of BNP were included in the study.

Data such as name, age, gender etc. was recorded. Patients were divided into 2 groups of fifty- five each. Group I patients received Sacubitrel/ Valsartan and group II patients received Isosorbid dinitrate/ hydralazine. Laboratory investigations consisted of white blood cell count, hemoglobin, sodium, blood urea nitrogen, serum creatinine, and B-type natriuretic peptide. Clinical features, findings, NYHA functional class, medical history, vitals, adverse events and treatment was recorded. The effectiveness of both drug combinations was compared. The results were compiled and subjected for statistical analysis using Mann Whitney U test. P value less than 0.05 was set significant.

RESULTS

Table I Baseline characteristics

Parameters	Variables	Group I	Group II	P value
Clinical features	Ischaemic cardiomyopathy	32	38	0.58
findings	LVEF (%)	29.1	29.4	0.86

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	Medium B type natriuretic peptide (pg/ml)	254	255	0.97
NYHA functional class	I	8	7	0.91
	II	23	25	
	III	20	21	
	IV	4	2	
Medical history	Diabetes	21	9	0.87
	Hypertension	17	14	
	Atrial fibrillation	11	12	
	Stroke	6	5	
	Myocardial infarction	2	4	
Vitals	SBP (mm Hg)	126.8	124.6	0.91
	Heart rate (beats/ min)	70.2	74.6	0.84
Treatment	Digitalis	42	52	0.72
	B- blocker	31	37	
	Diuretic	27	30	
	Mineralocorticoid antagonist	13	16	

Clinical features recorded was ischaemic cardiomyopathy in 32 and 38 in group I and II patients respectively. LVEF found to be 29.1% and 29.4%. Medium B type natriuretic peptide level was 254 pg/ml and 255 pg/ml in group I and II patients respectively. NYHA functional class I was seen in 8 and 7, class II in 23 and 25, class III in 20 and 21 and class IV in 4 and 2 respectively. Medical history was diabetes seen in 21 and 9, hypertension in 17 and 14, atrial fibrillation in 11 and 12, stroke in 6 and 5 and myocardial infarction in 2 and 4 in group I and II patients respectively. SBP (mm Hg) was 126.8 and 124.6 and heart rate (beats/ min) was 70.2 and 74.6. Treatment given was digitalis in 42 and 52, B- blocker in 31 and 37, diuretic in 27 and 30 and mineralocorticoid antagonist in 13 and 16 patients in group I and II respectively. The difference was non- significant (P>0.05) (Table I).

Table II Adverse events

Adverse events	**Group I**	**Group II**	**P value**
Hypotension	6	2	0.01
Serum creatinine >3.0 mg/dl	2	4	0.05
Serum potassium >5.5 mmol/l	5	9	0.04
Angioedema	6	8	0.72
Cough	2	1	0.28

Adverse events were hypotension in 6 and 2, serum creatinine >3.0 mg/dl seen in 2 and 4, serum potassium >5.5 mmol/l was seen in 5 and 9, angioedema in 6 and 8 and cough in 2 and 1 patients in group I and II respectively. The difference was significant (P< 0.05).

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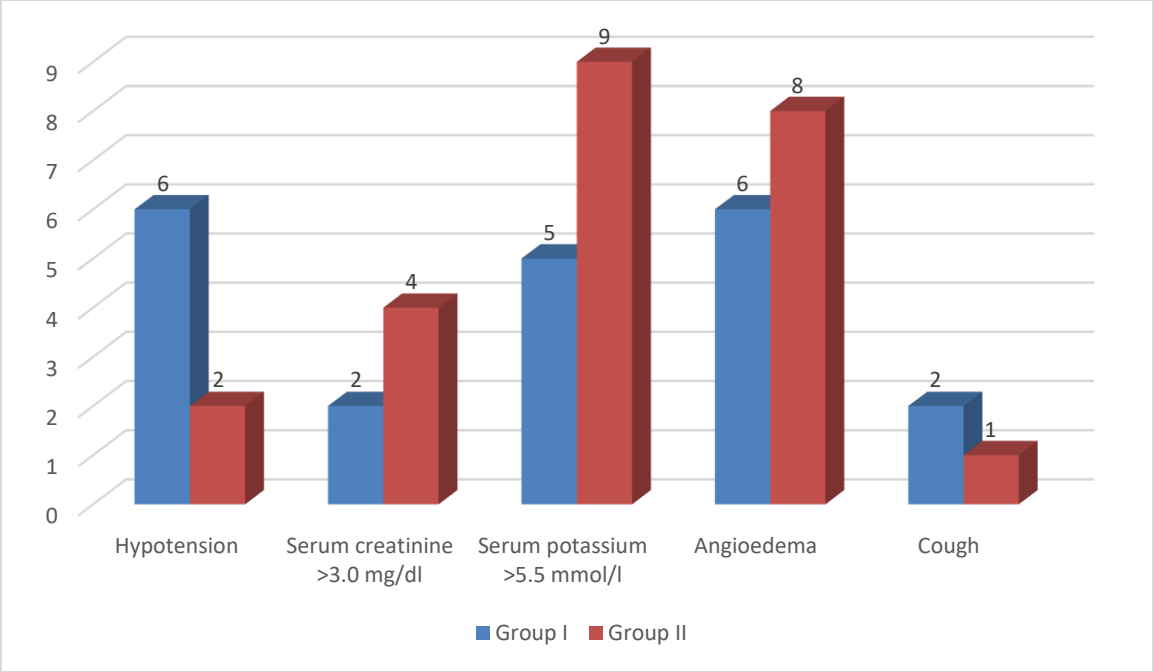

Graph I Adverse events

DISCUSSION

The combination of isosorbide dinitrate and hydralazine is a medication used in the treatment of heart failure, particularly in individuals with heart failure with reduced ejection fraction (HFrEF), a condition where the heart's pumping ability is compromised.[7] Isosorbide Dinitrate is a nitrate that dilates blood vessels (vasodilator), reducing the workload on the heart and improving blood flow.[8] Hydralazine is a direct-acting vasodilator that relaxes and widens blood vessels, reducing resistance to blood flow.[9] The isosorbide dinitrate/hydralazine combination is typically used in African American patients with heart failure who are symptomatic despite optimal medical therapy, including ACE inhibitors or angiotensin receptor blockers (ARBs) and beta-blockers.[10]At a 1-year follow-up, Farré et al[11] discovered that 8.8% of HF patients had been hospitalized for HF, while almost 30% had been hospitalized for other reasons. CHF is the most common reason for hospital stays for persons over 65, accounting for 1% to 2% of all hospital admissions each year. We performed this study to compare the effectiveness of Isosorbid dinitrate/ hydralazine combination with Sacubitrel/ Valsartan in CHF in Indian patients.

In our study, clinical features recorded was ischaemic cardiomyopathy in 32 and 38 in group I and II patients respectively. LVEF found to be 29.1% and 29.4%. Medium B type natriuretic peptide level was 254 pg/ml and 255 pg/ml in group I and II patients respectively. NYHA functional class I was seen in 8 and 7, class II in 23 and 25, class III in 20 and 21 and class IV in 4 and 2 respectively. Medical history was diabetes seen in 21 and 9, hypertension in 17 and 14, atrial fibrillation in 11 and 12, stroke in 6 and 5 and myocardial infarction in 2 and 4 in group I and II patients respectively. SBP (mm Hg) was 126.8 and 124.6 and heart rate (beats/ min) was 70.2 and 74.6. Treatment given was digitalis in 42 and 52, B- blocker in 31 and 37, diuretic in 27 and 30 and mineralocorticoid antagonist in 13 and 16 patients in group I and II respectively. Murray et al[12] compared the angiotensin receptor–neprilysin inhibitor LCZ696 with enalapril in patients who had heart failure with a reduced ejection fraction. Results showed that Enalapril increased these patients' chances of survival. In addition to prescribed medication. 914 patients (21.8%) in the

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LCZ696 group and 1117 patients (26.5%) in the enalapril group had experienced the primary outcome. 711 patients (17.0%) receiving LCZ696 and 835 patients (19.8%) receiving enalapril died in total (hazard ratio for death from any cause, of these patients, cardiovascular causes accounted for 558 (13.3%) and 693 (16.5%), respectively. LCZ696 decreased the symptoms and physical limits of heart failure and the risk of hospitalization for heart failure by 21% (P<0.001) when compared to enalapril. The percentage of patients experiencing hypotension was greater in the LCZ696 group.

Our results showed that adverse events were hypotension in 6 and 2, serum creatinine >3.0 mg/dl seen in 2 and 4, serum potassium >5.5 mmol/l was seen in 5 and 9, angioedema in 6 and 8 and cough in 2 and 1 patients in group I and II respectively. Ziaeian et al[13] evaluated the effectiveness of hydralazine–isosorbide dinitrate (H-ISDN) in African Americans with heart failure (HF) with reduced ejection fraction (HFrEF). They included 5,168 African-American patients with HF, with 15.2% treated with H-ISDN before index admission. After 18 months, there were 1,275 reported deaths (24.7%). The adjusted mortality rate at 18 months was 22.1% for patients receiving H-ISDN treatment and 25.2% for untreated patients.

CONCLUSION

The combination of Sacubitrel/ Valsartan in CHF patients was found to be effective as compared to Isosorbid dinitrate/ hydralazine. However, large scale studies are required to substantiate the results obtained in this study.

REFERENCES

1. Cole RT, Kalogeropoulos AP, Georgiopoulou VV, et al. Hydralazine and isosorbide dinitrate in heart failure: historical perspective, mechanisms, and future directions. Circulation 2011;123: 2414–22.
2. Carson P, Ziesche S, Johnson G, Cohn JN. Racial differences in response to therapy for heart failure: analysis of the vasodilator-heart failure trials. Vasodilator-Heart Failure Trial Study Group. J Card Fail 1999;5:178–87.
3. Yancy CW, Jessup M, Bozkurt B, et al. 2016 ACC/AHA/HFSA focused update on new pharmacological therapy for heart failure: an update of the 2013 ACCF/AHA guideline for the management of heart failure. J Am Coll Cardiol 2016;68: 1476–88.
4. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure of the European Society of Cardiology (ESC). Eur J Heart Fail 2016; 18:891–975.
5. Taylor AL, Ziesche S, Yancy C, et al. Combination of isosorbide dinitrate and hydralazine in blacks with heart failure [Erratum appears in N Engl J Med 2005;352:1276]. N Engl J Med 2004; 351:2049–57.
6. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013;62:e147–239.
7. Ellison GT, Kaufman JS, Head RF, Martin PA, Kahn JD. Flaws in the U.S. Food and Drug Administration's rationale for supporting the development and approval of BiDil as a treatment for heart failure only in black patients. J Law Med Ethics 2008;36: 449–57.

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8. Yancy CW, Fonarow GC, Albert NM, et al. Adherence to guideline-recommended adjunctive heart failure therapies among outpatient cardiology practices (findings from IMPROVE HF). Am J Cardiol 2010;105:255–60.
9. Golwala HB, Thadani U, Liang L, et al. Use of hydralazine-isosorbide dinitrate combination in African American and other race/ethnic group patients with heart failure and reduced left ventricular ejection fraction. J Am Heart Assoc 2013;2:e000214.
10. Farré N, Vela E, Clèries M . Real world heart failure epidemiology and outcome: a population-based analysis of 88,195 patients. PLoS One 2017; 12: e0172745.
11. Taylor AL, Ziesche S, Yancy C, et al. Combination of isosorbide dinitrate and hydralazine in blacks with heart failure [Erratum appears in N Engl J Med 2005;352:1276]. N Engl J Med 2004; 351:2049–57.
12. McMurray JJ, Packer M, Desai AS, et al., PARADIGM-HF Investigators and Committees. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med 2014;371: 993–1004.
13. Ziaeian B, Fonarow GC, Heidenreich PA. Clinical effectiveness of hydralazine–isosorbide dinitrate in African-American patients with heart failure. JACC: Heart Failure. 2017 Sep;5(9):632-9.