RESEARCH PAPER

Liver Function in Patients with Heart Failure on ARNI compared to those who are not on ARNI

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ABSTRACT

Background

Heart failure is the leading cause of morbidity and mortality and it affects multiple organs and systems. Liver failure and dysfunction is one of the common and major complications of HF. Angiotensin Receptor Neprilysin Inhibitor (ARNI) signifies the paradigm shift in the treatment of HF and it is shown to reduce the mortality and morbidity in Heart failure (HF) patients. But worries about the possible hepatotoxicity of ARNI have been arised, particularly in patients with pre-existing liver disease. Hence this present study is undertaken to assess the efficacy of ARNI on measures of liver function in patients with HFrEF compared to conventional therapy

Materials and Methods

This is a cross-sectional study. Around 65 patients with heart failure with reduced ejection fraction were recruited after obtaining informed consent and institutional ethical clearance. Patients with Symptomatic hypotension, estimated glomerular filtration rate < 30 mL/min/1.73 m2 ,history of serious side effects during treatment with ACEI or ARB,Patients with aspartate aminotransferase (AST) or alanine aminotransferase (ALT) exceeding twice the upper limit of normal, history of hepatic encephalopathy, oesophageal varices, or portacaval shunt were excluded from this study.

Results

In the present study showed that total bilirubin, AST, ALT, ALP, creatinine mean value is less in ARNI group compared to those who are not on ARNI. MELD – XI score was reduced in patients with ARNI treatment and it was found to be statistically significant (p=0.04).

Conclusion

Liver parameters and MELD – XI score was found to be better in HF patients with ARNI treatment when compared with patients without ARNI treatment. In conclusion, ARNI treatment is found to be beneficial for heart as well as liver parameters

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INTRODUCTION

Heart failure is the leading cause of morbidity and mortality in intensive care units all over the world. The patient with heart failure has the risk of 50% reduction in five year survival rate similar to the subjects with carcinoma (1). Heart failure is a complex disease affecting multiple organs such as heart, liver, kidney, lungs etc. Heart failure (HF) is caused by either systolic or diastolic dysfunction or both which results in reduced cardiac output (CO) and hypoperfusion (2, 3). The encumbrance of heart failure is continuously escalating. In 2020, around 6.7 million individuals with 20 years and above had HF and the level is projected to increase by 8.5 million by 2030 (4).

Liver dysfunction is one of the major complications of heart failure. Reduction of CO leads to central venous pressure elevation and reduction of arterial perfusion which eventually leads to passive hepatic congestion and liver injury (5). Past researchers have shown that the derangement of liver parameters were associated with increased risk of morbidity and mortality in heart failure patients (6).

(MELD-XI) score was used to evaluate the prognosis and severity in patients with liver disease MELD-XI score was shown to be associated with a risk for adverse cardiovascular events in relatively small numbers of HF patients

Neurohormonal therapy plays a vital role in treating HF since half of patients will have reduced ejection fraction (7, 8). Angiotensin Receptor Neprilysin Inhibitor (ARNI) signifies the paradigm shift in the treatment of HF (9). Sacubitril/valsartan, the first agent to be approved in a new class of drugs called angiotensin receptor neprilysin inhibitors (ARNIs). ARNI has shown to reduce the morbidity and mortality in patients with HFrEF compared to traditional ACEIs or ARBs alone (10).

Despite its proven efficacy, concerns about the potential hepatotoxicity of ARNI have been raised, particularly in patients with preexisting liver disease or compromised liver function. Hence this present study is undertaken to assess the efficacy of ARNI on measures of liver function in patients with HFrEF compared to conventional therapy.

Materials and Methods

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This cross sectional study was conducted using medical records from Saveetha medical college spanning from October 2022 to April 2024. Around 65 patients with heart failure with reduced ejection fraction were recruited after obtaining informed consent and institutional ethical clearance.

65 Patients with HFrEF on ARNI were matched with HFrEF patients on conventional therapy based on age, gender, and baseline liver function were included

Patients with Symptomatic hypotension, estimated glomerular filtration rate < 30 mL/min/1.73 m2 ,history of serious side effects during treatment with ACEI or ARB,Patients with aspartate aminotransferase (AST) or alanine aminotransferase (ALT) exceeding twice the upper limit of normal, history of hepatic encephalopathy, oesophageal varices, or portacaval shunt were excluded from this study.

Results

Data was analysed with the help of SPSS Statistics for windows, version 16.0. Frequency analysis and chi Square test were used for categorical variables, mean and standard deviation were used for numerical variables. Students T test is performed to determine the association between the Liver function on those with & without ARNI

Table 1: Comparison of Liver function test and ARNI treatment in HFrEF patients by student t test

Liver function test parameter	ARNI Treatment Yes Mean ± SD N=37	ARNI Treatment No Mean ± SD N=28	t - value	p – Value
AST	31.05 ± 15.09	34.89 ± 17.01	- 0.752	0.455 (ns)
ALT	31.05 ± 15.09	27.35 ± 17.01	0.925	0.358 (ns)
ALP	98.35 ± 52.3	119.1 ± 44.0	1.933	0.05**
Total protein	6.49 ± 0.81	6.72 ± 0.63	- 1.088	0.281 (ns)
Albumin	3.2 ± 0.73	3.4 ± 0.57	- 1.401 1	166 (ns)
Total bilirubin	0.60 ± 0.32	0.73 ± 0.38	- 1.551	126 (ns)
Creatinine	0.89 ± 0.20	0.91± 0.20	- 3.97	0.693 (ns)

Table 1 shows the comparison of liver function test and ARNI treatment. All the liver parameters except ALT is reduced in patients with ARNI treatment.

Table 2: Demographic data of patients with heart failure in this study

Demographic data and treatment on heart failure	Frequency N =65	Percent N=100
Age		
≤ 60	35	54%
>60	30	46%
Gender		
Male	40	61.5%
Female	25	38.5%
Treatment		
ARNI		
Yes	37	57%
No	28	43%

Table 2 shows the demographic data of the subjects in this study.

Table 3: Comparison of MELD – XI score in patients with and without ARNI treatment

ARNI Treatment	MELD – XI score ≤12.6 value N (%)	MELD – XI score ≥12.7 N (%)	Total N (%)	X2 - Value	p-value
Yes	21 (70)	16 (45.7)	37 (56.9)	3.884	0.04**
No	09 (30)	19 (54.3)	28 (43.1)		
Total	30 (46.2)	35 (53.8)	65 (100)		

Table 3 shows that MELD – XI score was reduced in patients with ARNI treatment and it was found to be statistically significant (p=0.04).

Discussion

Patients with heart failure with reduced ejection fraction are prone to derangements of liver parameters and dysfunction. Liver dysfunction is one of the major complications of heart failure. Reduction of CO leads to central venous pressure elevation and reduction of arterial perfusion which eventually leads to passive hepatic congestion and liver injury.

Past studies have shown that reduced cardiac index is associated with elevated liver parameters such as AST, ALT and total bilirubin (11, 12).

In the present study showed that total bilirubin, AST, ALT, ALP, creatinine mean value is less in ARNI group compared to those who are not on ARNI. But values were not very significant.

Suzuki K et.al, also found similar results like the present study (13). They have found that the conventional measures of liver function were significantly improved in the sacubitril/valsartan group compared. In this study, ALT was found to be higher in patient with ARNI treatment and Suzuki et.al, also clarified that higher ALT was related to a lower risk of CV events (13).

MELD-XI score has been considered as the predictive value for the risk of the primary endpoint, hospitalization, CV death and all-cause death, after adjusting for demographics, CV comorbidities in heart failure patients, In this study, MELD – XI score was reduced in patients with ARNI treatment and it was found to be statistically significant

(p=0.04). Van Deursen VM et.al, showed that improvement of HF by sacubitril/valsartan may have improved cardiac performance and reduced right atrial pressure leading to decrease the hepatic congestion and thereby improves the liver function (14).

Major findings of the present study are as follows: (i) among the conventional measures of liver function, ALP showing significant predictive value (ii) measures of liver function and the MELD-XI score were improved by sacubitril/valsartan compared with conventional therapy

Conclusion

Liver function in patients and MELD- XI on ARNI for heart failure is better compared to those who are not on ARNI which can be significant if more number of patients is included in study

Limitation

Even though treatment with ARNI may have beneficial effects on measures of liver function in these patients, sample size needs to be increased to consider liver function parameters as a significant predictor for Heart failure prognosis

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