#### ORIGINAL RESEARCH

# ASSESSMENT OF EFFECTS OF TORSEMIDE ON NYHA FUNCTIONAL CLASS AND HOSPITALISATION IN PATIENTS OF CHF: AN OBSERVATIONAL STUDY

## <sup>1</sup>Dr. Vinita Bharti, <sup>2</sup>Devendra Kumar Katiyar

<sup>1</sup>Associate Professor, T.S.Misra Medical College & Hospital, Amausi, Lucknow, Uttar Pradesh, India

<sup>2</sup>Professor, Department of Pharmacology, KGMU, Lucknow, Uttar Pradesh, India

## **Correspondence:**

Associate Professor, T.S.Misra Medical College & Hospital, Amausi, Lucknow, Uttar Pradesh, India

Email: vinitashivmani@gmail.com

#### **ABSTRACT**

Background: To assess the effects of torsemide on NYHA functional class and hospitalisation in patients of CHF.

Materials & methods: Detailed clinical history, physical examination and diagnostic tests mainly electrocardiogram (ECG), chest X-ray and whenever necessary echocardiography was carried out in all the patients. 50 subjects were enrolled in the present study. Only those patients were enrolled who received torsemide orally in the dose of 10 mg once a day. All the findings were recorded in Microsoft excel sheet and were analysed by SPSS software.

Results: At baseline, 14 percent, 36 percent, 38 percent and 12 percent of the patients were of NYHA class I, II, III and IV respectively. At the end of the study, 22 percent, 44 percent, 24 percent and 10 percent of the patients were of NYHA class I, II, III and IV respectively. A significant improvement was seen in terms of NYHA class. 12 percent of the patients required hospitalization in the present study.

Conclusion: Torsemide leads to greater improvement in NYHA functional class. Thus; torsemide appears to be a reasonable alternative.

Key words: Chronic heart failure, Torsemide

#### INTRODUCTION

Heart failure is the end result of a number of different pathophysiological processes in which there is injury to the heart with loss or impairment of functioning myocardial cells.5 Compensatory neurohormonal mechanisms are activated in order to maintain adequate cardiac function and tissue perfusion. Activation of the sympathetic nervous system increases heart rate and cardiac contractility, while activation of the renin–angiotensin– aldosterone system increases sodium reabsorption and water retention. Although these responses are

initially beneficial, prolonged overstimulation of the sympathetic nervous system and reninangiotensin-aldosterone system results in maladaptive cardiovascular remodelling.<sup>1-3</sup>

Chronic heart failure (CHF) is a burgeoning problem worldwide with > 20 million people affected. The pathophysiology of CHF is very complex. The symptoms like dyspnoea, orthopnoea and fatigue often limit the exercise capacity and hamper Quality of Life (QoL) in these patients. Many patients with advanced HF attach greater significance to QoL than they do to duration of life. Moreover, worse QoL is associated with hospital readmission and death in patients of HF.Reduction in mortality in this condition has been achieved by treatment with vasodilators, in particular, angiotensin converting enzyme inhibitors (ACE inhibitors), however volume overload is a common clinical syndrome in patients with CHF and is responsible for two- third of CHF related hospital admissions. Because patients with CHF avidly retain sodium and fluid, management with high ceiling or loop diuretic is often necessary. Torsemide is a loop diuretic that belongs to the pyridine -sulfonylurea class. It received approval for use in the united states in 1993. The effect of torsemide is dosedependent. The maximum effective dose is the dose required to attain maximum sodium excretion. Hence; the present study was conducted for assessing the effects of torsemide on NYHA functional class and hospitalisation in patients of CHF.

#### **MATERIALS & METHODS**

The present study was conducted for assessing the effects of torsemide on NYHA functional class and hospitalisation in patients of CHF.Inclusion criteria for the present study included: Male and female patients of chronic heart failure with age of at least 18 years and those who required diuretic therapy. The diagnosis of CHF and its categorisation into particular NYHA functional classwas done.

Detailed clinical history, physical examination and diagnostic tests mainly electrocardiogram (ECG), chest X-ray and whenever necessary echocardiography was carried out in all the patients. 50 subjects were enrolled in the present study. Only those patients were enrolled who received torsemide orally in the dose of 10 mg once a day. All the findings were recorded in Microsoft excel sheet and were analysed by SPSS software.

### **RESULTS**

Mean age of the patients was 53.6 years. Majority proportion of the patients of both the study groups were males. Significant proportion of the patients of the present study were urban residence. At baseline, 14 percent, 36 percent, 38 percent and 12 percent of the patients were of NYHA class I, II, III and IV respectively. At the end of the study, 22 percent, 44 percent, 24 percent and 10 percent of the patients were of NYHA class I, II, III and IV respectively. A significant improvement was seen in terms of NYHA class. 12 percent of the patients required hospitalization in the present study.

NYHA class	Baseline		End of study		p- value
	Number	Percentage	Number	Percentage	
I	7	14	11	22	0.001
II	18	36	22	44	(Significant)
III	19	38	12	24	
IV	6	12	5	10	
Total	50	100	50	100	

Table 1: Comparison of pre-treatment and post-treatment NYHA class

#### DISCUSSION

Chronic heart failure (CHF) is a progressive syndrome that results in a poor quality of life for the patient and places an economic burden on the health care system. Despite advances in the control of cardiovascular diseases such as myocardial infarction (MI), the incidence and prevalence of CHF continue to increase.1 An accurate estimate of disease burden is difficult to gather because of the vast number of patients with asymptomatic left ventricular (LV) dysfunction. As the population ages, there is an epidemiological shift toward a greater prevalence of clinical heart failure with preserved LV function, the so-called stiff-heart syndrome. In fact, heart failure with preserved systolic function may account for up to two-thirds of cases in patients older than 70 years.<sup>5-8</sup>

Torasemide (torsemide) is a high-ceiling loop diuretic which acts on the thick ascending limb of the loop of Henle to promote rapid and marked excretion of water, sodium and chloride. Like furosemide (frusemide), its major site of action is from the luminal side of the cell. Torasemide is at least twice as potent as furosemide on a weight-for-weight basis, produces equivalent diuresis and natriuresis at lower urinary concentrations and has a longer duration of action, allowing once-daily administration without the paradoxical antidiuresis seen with furosemide. Torasemide also appears to promote excretion of potassium and calcium to a lesser extent than furosemide. In trials of up to 48 weeks' duration in patients with mild to moderate essential hypertension, torasemide, administered as a single daily dose, has been shown to achieve adequate blood pressure control reaching steady-state within 8 to 12 weeks. Those patients not responding initially have generally responded to a doubling of the dose. The present study was conducted for assessing the effects of torsemide on NYHA functional class and hospitalisation in patients of CHF.

Mean age of the patients was 53.6 years. Majority proportion of the patients of both the study groups were males. Significant proportion of the patients of the present study were urban residence. At baseline, 14 percent, 36 percent, 38 percent and 12 percent of the patients were of NYHA class I, II, III and IV respectively. At the end of the study, 22 percent, 44 percent, 24 percent and 10 percent of the patients were of NYHA class I, II, III and IV respectively. In a study by Gupta et al addition of torsemide to standard therapy with ACEIs and β blocker in patients with left ventricular systolic dysfunction who were not congested was not associated with significant change in measures of QoL or other surrogate markers of prognosis compared to placebo. This suggests that effect of diuretics on QoL in HF patients is due to relief of congestive symptoms. <sup>10</sup>

In the present study, a significant improvement was seen in terms of NYHA class. 12 percent of the patients required hospitalization in the present study. In a TORIC study, authors evaluated 1377 CHF patients with NYHA functional class II- III under real life situations with wide inclusion criteria and few exclusion criteria. It demonstrated that torsemide was significantly more efficacious than frusemide/ other diuretics in improving NYHA functional class. The proportion of patients showing a functional improvement of at least 1 grade in NYHA functional class was significantly greater in the torsemide group than in frusemide/ other diuretic group. Torsemide was also more efficacious than frusemide alone in improving NYHA functional class. Another study by Muller et al comparing frusemide and torsemide showed that NYHA functional class improved in both groups. However, when considering individual changes in NYHA functional classes 40.2 % of torsemide treated patients improved by at least one NYHA functional class, 38.5 % were unchanged and 21.3 % worsened, respectively. Figures in frusemide treated patients were 30.7 % improved, 46.5 % unchanged and 22.8 % worsened. The overall trend for improvement was only significant in torsemide but not in frusemide treated patients.

#### **CONCLUSION**

Torsemide leads to greater improvement in NYHA functional class. Thus; torsemide appears to be a reasonable alternative.

#### REFERENCES

- 1. Nanayakkara S, Kaye DM. Management of heart failure with preserved ejection fraction: a review. Clin Ther 2015;37:2186-98.
- 2. Pfeffer MA, Claggett B, Assmann SF, Boineau R, Anand IS, Clausell N, et al. Regional variation in patients and outcomes in the treatment of preserved cardiac function heart failure with an aldosterone antagonist (TOPCAT) trial. Circulation 2015;131:34-42.
- 3. Rector TS. Kubo SH, Cohn JN. Validity of the Minnesota Living With Heart Failure Questionnaire as a Measure of Therapeutic Response to Enalapril or Placebo. Am J Cardiol. 1994; 71: 1106-07
- 4. Rector TS, Cohn JN: Assessment of Patient Outcome With The Minnesota living With Heart Failure Questionnaire Reliability an Validity during A Randomised, Double Blind, Placebo Controlled Trial of Pimobendan. Am Heart J. 1992; 124: 1017-25.
- 5. Rector TS, Johnson G, Dunkman B, Farrell L, Smith B, et al. Evaluation By Patients With Hydralazine Plus Isosorbide Dinitrate on Enalapril Compared With Hydralazine Plus Isosorbide Dinitrate on Quality of Life, U-HeFT II. Circulation. 1993; 87: 71-77.
- 6. Kubo S, Gollub S, Bourge R, rahko P, Cobb F, Jessup M, et al.Beneficial Effects of Pimobendan on Exercise Tolerance and Quality of Life in Patients With Heart Failure. Results of a Multicenter trial. Circulation. 1992; 85: 142-49.
- 7. Briancon S, Alla F, Mejat F, Guillemin F, Villemot JP, Mertes PM, et al. Measurement of Functional Inability and Quality Of Life in Cardiac Failure. Transcultural Adaptation and Validation of the Goldman, Minnesota and Duke Questionnaire. Arch Mal Coeur Vaiss. 1997; 90: 1577-85.

- 8. Solomon SD, Zile M, Pieske B, Voors A, Shah A, Kraigher-Krainer E, et al. The angiotensin receptor neprilysin inhibitor LCZ696 in heart failure with preserved ejection fraction: a phase 2 double-blind randomised controlled trial. Lancet 2012;380:1387-95.
- 9. Hopper I, Samuel R, Hayward C, Tonkin A, Krum H. Can medications be safely withdrawn in patients with stable chronic heart failure? Systematic review and meta-analysis. J Card Fail 2014;20:522-32.
- 10. Gupta S, Waywell C, Gandhi N, Clayton N, Keevil B, Clark Al, et al.The Effects of Adding Torasemide to Standard Therapy on Peak Oxygen Consumption, Natriuretic Peptides, and Quality of Life in Patients with Compensated Left Ventricular Systolic Dysfunction. Eur J Heart Fail. 2010; 12 (7): 746-52.
- 11. Muller K, Gamba G, Jaquet F, Hess B. Torsemide Vs. furosemide in primary care patients with chronic heart failure NYHA II to IV. Efficacy and quality of life. Eur J Heart Fail. 2003; 5(6): 793-801.
- 12. Cosin J, Diez J. Torasemide in chronic heart failure: results of the TORIC study. Eur J Heart Failure. 2002; 4: 507 –13.