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Original Article

Role of thiamine supplementation in patients with heart failure – An Indian perspective

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ABSTRACT

Background: Heart failure (HF) is a leading cause of mortality worldwide. Despite numerous therapeutic maneuvers, the prognosis remains dismal. Thiamine is an important vitamin, essential in energy formation inside the cells. Subclinical deficiency is very common in HF patients. Thiamine supplementation in such cases may improve cardiac function.
Objectives: To assess the effect of thiamine supplementation on cardiac parameters and functional capacity in HF patients.
Methods: A total of 40 HF patients with NYHA Class II and III symptoms were divided into two groups of twenty each. One group received thiamine and another placebo. Cardiac parameters (ESV, EDV, and EF) and functional capacity (6MWT) were measured at the start of the study, at 1 week and after 4 weeks.
Results: After 1 week of intervention in Thiamine group, ESV decreased by a mean of 6.45 ml and 6MWT improved by 27.67 m, EDV decreased by 7.1 ml and EF improved by 1.56%. In Placebo group, EDV increased by 0.93 ml and ESV and EF remained almost unchanged. 6MWT improved from 261.11 ± 49.96 to 275.78 ± 62.60 m ($p = 0.01$). After 4 weeks in Thiamine group, ESV decreased by 8.09 ml and EF increased by 18.65% and 6MWT by 55.35 m. In Placebo group, EDV increased by 5.25 ml and ESV decreased by 6.03%. EF and 6MWT did not show any significant change.
Conclusion: Thiamine supplementation improves cardiac function and may prove to be an important part of HF treatment regimen particularly in India given the high prevalence of thiamine deficiency.

1. Introduction

Heart failure (HF) is a clinical syndrome that occurs in patients who, because of an inherited or acquired abnormality of cardiac structure and/or function, develop a constellation of clinical symptoms (dyspnea and fatigue) and signs (edema and rales) that lead to frequent hospitalizations, a poor quality of life, and a shortened life expectancy.[1] Heart failure is classified into two categories: 1. HF with a reduced Ejection fraction (EF) (Systolic Failure); 2. HF with preserved EF (Diastolic Failure).

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HF is a burgeoning problem worldwide, which affects almost 23 million people.[2] The prevalence of HF follows an exponential pattern, rising with age, and affects 6–10% of people older than 65 years. Despite many recent advances in the evaluation and management of HF, the development of symptomatic HF still carries a poor prognosis. Community-based studies indicate that 30–40% of patients die within 1 year of diagnosis and 60–70% die within 5 years, mainly from worsening HF or as a sudden event (probably because of a ventricular arrhythmia).

The recommended pharmacological therapy includes the use of angiotensin converting enzyme inhibitors, angiotensin receptor blocker, beta-blockers, diuretics, and aldosterone antagonists.[3] Additional non-pharmacological measures, such as cardiac resynchronization therapy, implantable cardioverter defibrillators, and exercise training, have shown beneficial outcomes in quality of life, morbidity, and/or mortality of HF patients.

The impact of heart failure and its treatment on specific nutrient requirements is unknown. Anorexia, malnutrition, advanced age, and frequent hospitalization are all factors that have been identified as contributing to increased risk of nutrient deficiencies in patients with congestive heart failure.[4] Furthermore, diuretic medications used for management of fluid overload have been linked with biochemical and clinical markers of thiamine deficiency suggesting inappropriate diuretic induced losses of water-soluble vitamins in this population.

Thiamine is a water-soluble vitamin that plays an important role as a coenzyme in carbohydrate metabolism.[5] Through the addition of magnesium and ATP, thiamine is converted to thiamine pyrophosphate by the enzyme thiamine pyrophosphokinase. As the metabolically active form of thiamine, thiamine pyrophosphate serves as a cofactor for pyrophosphate dehydrogenase complex and for transketolase, both key mediators of energy-substrate metabolism. Thiamine deficiency results in decreased ATP production and increased cellular acidosis on a metabolic level.[6] Thiamine itself is stored in the body in only small amounts and cannot be produced endogenously. Adequate nutritional intake through diet (whole grains, legumes, and nuts) or supplements is therefore critical in preventing deficiency.

Thiamine deficiency causes cardiovascular and neurological damage that presents clinically as Beriberi. When the circulatory system is predominantly involved (Wet Beriberi), patients predominantly present with high-output biventricular heart failure, peripheral vasodilatation, volume overload, tachycardia, and wide pulse pressure, as well as relative depression of left ventricular function with low ejection fraction.

Given the proposed role of thiamine deficiency in HF, several small studies have been conducted to examine the clinical utility of supplementation. The known effects of thiamine deficiency on the heart suggest that supplementation may be of therapeutic benefit if examined in large HF trials. This assumes importance because thiamine supplementation is inexpensive and devoid of significant side effect.

Because of the above-mentioned reasons, a study entitled ''EFFECT OF THIAMINE SUPPLEMENTATION IN HEART FAILURE'' was conducted to assess the effect of thiamine supplementation in CHF.

2. Aims and objectives

To study the effect of thiamine supplementation in heart failure patients with functional class II and III, irrespective of thiamine status, on:

1. Cardiac parameters (ESV, EDV, and EF).
2. Functional capacity (6MWT)

3. Material and methods

The study entitled ''EFFECT OF THIAMINE SUPPLEMENTATION IN HEART FAILURE'' was conducted in the Department of Cardiology, Sheri Kashmir Institute of Medical Sciences (SKIMS), J&K, India; it is a tertiary care hospital catering to the healthcare needs of about a population of 10 million. A total of 40 patients with heart failure of NYHA class II and III symptoms were included in the study.

3.1. *Inclusion criteria*

All patients with New York Heart Association (NYHA) functional class II & class III Heart failure with ejection fraction less than 50% due to (1) Chronic ischemic heart disease, (2) Idiopathic dilated cardiomyopathy, (3) Valvular heart disease.

The diagnosis of heart failure was made using Framingham Criteria requiring two major or one major and two minor criteria.

3.2. *Exclusion criteria*

1. CHF Class I and IV
2. LVEF $>$ 50%
3. More than 65 years of age
4. Creatinine $>$2 mg/dl
5. Malignancies
6. Chronic Obstructive Pulmonary Disease (COPD)
7. Orthopedic problems
8. Anemia (hemoglobin $<$ 12 g/dl)
9. Recent thiamine or multivitamin supplements

3.3. *Principle of the method*

Baseline investigations, including complete blood count, renal function test, and liver function test, were done in all patients and only those patients with hemoglobin more than 12 g/dl and normal creatinine were included in the study.

At the start of the study each of the 40 patients underwent echocardiography (to calculate End-diastolic volume (EDV) and End-systolic volume (ESV) by Simpson method), Six-minute walk test (6MWT), and blood pressure and pulse rate measurement. This was a double-blind randomized study where patients were randomized to oral thiamine 100 mg/day or placebo based on a computer generated randomization. Both the capsules, thiamine and placebo, were physically similar to avoid bias. Drug compliance was ensured strictly by calling patients every week and handing over medication