Introduction

Decomponsated congestive heart failure is the most common cause of hospitalization among patients with congestive heart failure it results from new onset of left ventricular systolic dysfunction or, more often exacerbation of chronic heart failure ***(Kunshen liu et al., 2006).***

Over the past decade many advances in management of decompensated congestive heart failure have been achieved, however the overall outcome remains discouraging, the predominant symptoms in such patient are dyspnea, fatigue and dependent oedema which are associated with pulmonary venous congestion, raised venous pressure and low cardiac output ***(Lucas et al., 2000).***

Accordingly, the rapid relief of symptoms achieved by intra venous administration of diuretics, vasodilators, and positive inotropics agents to decrease cardiac filling pressure and increase cardiac output remain the primary goal ***(Gupta et al., 2005).***

Prednisone, glucocorticoids that has renal specific vasodilator properties, can increase renal plasma flow and Glomerular Filtration Rate with no changes in glomerular filtration faction ***(Gupta et al., 2005).***

In addition glucocorticoid may have important regulatory effects on natriurtic peptides and their receptors ***(Baylisc et al., 1978).***

In previous study, we found that prednisone had potent diuretic effects in patients with stable congestive heart failure, and could restore renal function and elicit patients with refractory diuretic resistance ***(Nevskaia et al., 1977)***

Aim of the Work

The aim of this study is to determine the effect of prednisone, added to conventional treatment of patients with decompensated congestive heart failure, refractory to conventional care, on congestive symptoms and improvement of clinical state.

Heart Failure

Introduction:

Heart failure (HF) remains the only common cardiovascular syndrome increasing in prevalence and incidence. Despite significant advances in pharmacological and device therapies, morbidity and mortality for those afflicted with HF remains high ***(Hunt, 1995).***

Epidemiology:

Definition:

Given pathophysiological and clinical heterogeneity, it is not surprising that there is not yet any firm consensus definition of the clinical syndrome of HF. Over the past several decades, basic and clinical research elucidating the complex and continuous interplay of adaptive and maladaptive myocyte, myocardial extracellular matrix, hemodynamic, biochemical, energetic, genetic, neurohormonal, renal, pulmonary, skeletal muscle,vascular endothelial alterations and adaptations in HF has rendered consensus definition even more challenging ***(Katz, 2003).***

Other Definitions of Heart Failure:

A pathophysiological state in which an abnormality of cardiac function is responsible for the failure of the heart to pump

blood at a rate commensurate with the requirements of the metabolizing tissues ***(Eugene Braunwald, 1980).***

Heart failure is the state of any heart disease in which, despite adequate ventricular filling, the heart's output is decreased or in which the heart is unable to pump blood at a rate adequate for satisfying the requirements of the tissues with functional parameters remaining within normal limits ***(Denolin et al., 1983)***

Heart failure is a complex clinical syndrome that can result from any cardiac disorder that impairs the ability of the ventricle to eject blood ***(Packer, 1999).***

Heart failure is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood *ACC/AHA Consensus Guidelines, 2001* ***(Hunt, 1995).***

Classification:

Heart failure may be classified as either predominantly systolic or diastolic. Almost all instances of systolic HF also exhibit diastolic abnormalities; most instances of diastolic HF also exhibit systolic abnormalities, usually inadequate systolic functional reserve ***(Angeja and Grossman, 2003).*** The cardiomyopathies have traditionally been classified as either dilated, restrictive, or hypertrophic ***(Dec and Foster, 1994).***

Other Classification:

A. Clinical classification:

Table (1): Classification and common clinical characteristics of patients with acute heart failure.

Clinical Classification	Symptom Onset	Signs and Symptoms	Hemodynamics	Other Diagnostics
I Acute decompensated congestive heart failure	Usually gradual	Peripheral edema (often significant), dyspnea, usually well-perfused extremities	SBP: Low normal/high	CXR: Normal or mild interstitial edema, possible pleural effusion
			CI: Low normal/high	
			PCWP: Mildly increased	
II Acute heart failure with hypertension/hypertensive crisis	Often very rapid	Dyspnea, altered mental status, possible oliguria/anuria	SBP: High (>180/100 mm Hg)	CXR: Normal or interstitial edema
			CI: Usually normal	
			PCWP: >18 mm Hg	
III Acute heart failure with pulmonary edema	Rapid or gradual	Severe dyspnea, tachypnea, tachycardia	SBP: Low normal	SaO_2: <90%
				CXR: Alveolar edema
IVa Cardiogenic shock/low output syndrome	Usually gradual	Evidence of hypoperfusion; oliguria	SBP: Low normal	
			CI: Low, <2.2 liters/min/m^2	
			PCWP: >16 mm Hg	
IVb Severe cardiogenic shock	Often rapid	Marked hypoperfusion; oliguria/anuria	SBP: <90 mm Hg	Usually in presence of severe
			CI: Very low, <1.8 liters/min/m^2	LV systolic dysfunction
			PCWP: >18 mm Hg	

Table (1): Continued.

Clinical Classification	Symptom Onset	Signs and Symptoms	Hemodynamics	Other Diagnostics
V High output failure	Rapid or gradual	Well-perfused extremities; often tachycardic	SBP: Variable	
			CI: Increased	
			PCWP: Normal or increased	
VI Right-sided acute heart failure	Rapid or gradual	Edema, markedly elevated neck veins, often poor perfusion, but clear lungs	SBP: Low	CXR: often clear lung fields with evidence of pulmonary hypertension; BNP may be elevated in pulmonary embolus
			CI: Low	
			PCWP: Low	

BNP = B-type natriuretic peptide; CI=cardiac index; CXR=chest x-ray; PCWP= pulmonary capillary wedge pressure; SBP= systolic blood pressure.

(Nieminen et al., 2005)

B. Functional Classification of Heart Failure

Table (2): New York Heart Association (NYHA) Classification of Cardiac Disease.

Functional Capacity	Objective Assessment
Class I	Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitations, dyspnea, or anginal pain.
Class II	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
Class III	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
Class IV	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present, even at rest. If any physical activity is undertaken, discomfort is increased.

(Modified from New-York Heart Association: Diseases of the Heart and Blood Vessels, Nomenclature and Criteria for Diagnosis. 6th ed. Boston, Little Brown, 1964, p 114).

Pathophysiology of Heart Failure

Neurohormonal Mechanisms:

Some experts have suggested that HF should be viewed as a neurohormonal model, in which HF progresses as a result of the overexpression of biologically active molecules that are capable of exerting deleterious effects on the heart and circulation ***(Mann and Bristow, 2005).***

Neurohumoral Effects of Heart Failure:

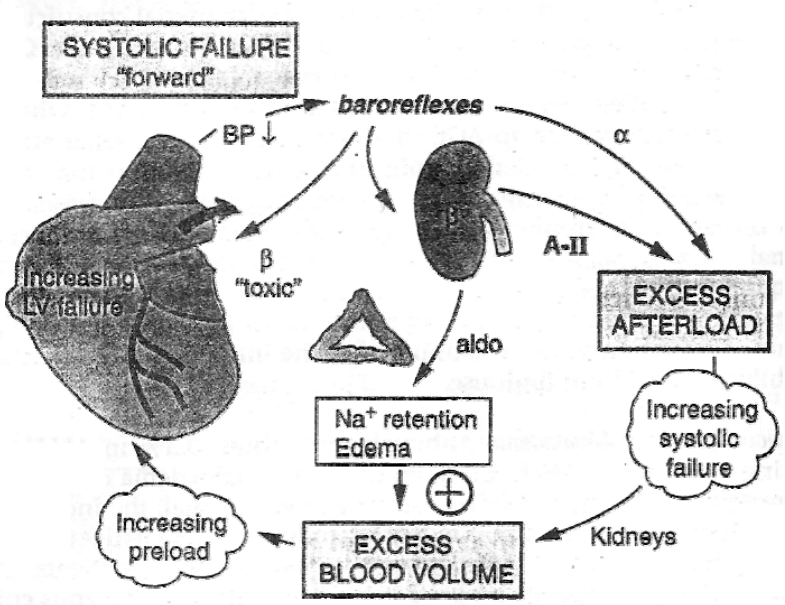

Figure (1): Neurohumoral adaptation in heart failure. The crucial consequence of LV failure is the inability to maintain a normal blood pressure and normal organ perfusion. As a result of reflex baroreflex activation and excess adrenergic stimulation, there is alpha **(a)** mediated peripheral vasoconstriction that increases the afterload and leads to increased LV failure. Excess alpha **(a)** adrenergic stimulation leads to peripheral vasoconstriction. Furthermore, excess β-adrenergic stimulation promotes renin release with increased vasoconstrictive angiotensin-1I *(A-Il)* and release of aldosterone. Increasing preload and afterload leads to increasing LV failure ***(Opie, 2005.)***

1-Activation of the sympathetic nervous system:

The decrease in cardiac output in HF activates the sympathetic nervous system, which occurs early in the course of HF. In HF patients inhibitory input from baroreceptors and mechanoreceptors decreases and excitatory input increases with a resultant loss of heart rate variability and increased peripheral vascular resistance ***(Floras, 2003).***

As a result of the increase in sympathetic tone, there is an increase in circulating levels of NE, a potent adrenergic neurotransmitter. As HF progresses there is a significant decrease in the myocardial concentration of NE. The mechanism responsible for cardiac NE depletion in severe HF is not clear and may relate to an "exhaustion" phenomenon resulting from the prolonged adrenergic activation of the cardiac adrenergic nerves in HF ***(Floras, 2003).***

Although NE enhances both contraction and relaxation and maintains blood pressure, myocardial energy requirements are augmented, which can intensify ischemia when myocardial O_2 delivery is restricted. The augmented adrenergic outflow from the central nervous system may also trigger ventricular tachycardia or even sudden cardiac death, particularly in the presence of myocardial ischemia. Thus activation of the sympathetic nervous system provides short-term support that has the potential to become maladaptive in the long term ***(Floras, 2003).***

2-Activation of the renin-angiotensin system:

The presumptive mechanisms for RAS activation in HF include renal hypoperfusion, decreased filtered sodium reaching

the macula densa in the distal tubule, and increased sympathetic stimulation of the kidney, leading to increased renin release from a juxtaglomerular apparatus. Renin cleaves four amino acids from circulating angiotensinogen, which is synthesized in the liver, to form the biologically inactive decapeptide angiotensin I. Angiotensin-converting enzyme (ACE) cleaves two amino acids from angiotensin I to form the biologically active octapeptide (1-8) angiotensin II ***(Schrier & Abraham, 1999 and Floras, 2003).***

Angiotensin II has several important actions that are critical to maintaining short-term circulatory homeostasis. However, the sustained expression of angiotensin II is maladaptive and leads to fibrosis of the heart, kidneys, and other organs. Angiotensin II can also lead to worsening neurohormonal activation by enhancing the release of NE from sympathetic nerve endings, as well as stimulating the zona glomerulosa of the adrenal cortex to produce aldosterone. The sustained expression of aldosterone may exert harmful effects by provoking hypertrophy and fibrosis within the vasculature and the myocardium, thus contributing to reduced vascular compliance and increased ventricular stiffness ***(Schrier and Abraham, 1999).***

3- <u>Neurohormonal alterations of renal function</u>:

One signature of advancing HF is increased salt and water retention by the kidneys. This can be explained by the concept of decreased "effective arterial" blood volume, which postulates that despite blood volume expansion in HF, inadequate cardiac output sensed by baroreceptors in the vascular tree leads to sustained

activation of the sympathetic nervous and the renin-angiotensin systems ***(Schrier and Abraham, 1999).***

4-<u>Neurohormonal alterations in the peripheral vasculature:</u>

In patients with HF the complex interactions between the autonomic nervous system and local autoregulatory mechanisms tend to preserve circulation to the brain and heart while decreasing blood flow to the skin, skeletal muscles, splanchnic organs, and kidneys. This intense visceral vasoconstriction during exercise helps to divert the limited cardiac output to exercising muscle but contributes to hypoperfusion of the gut and kidneys ***(Eichhorn and Bristow, 1996).***

The vasoconstricting neurohormones activate counter-regulatory vasodilator responses including release of natriuretic peptides, NO, bradykinin, adrenomedullin, apelin, and vasodilating prostaglandins PGI_2 and PGE_2. Under normal circumstances the continuous release of NO (endothelium-derived relaxing factor) from the endothelium counteracts the vasoconstricting factors and allows for appropriate vasodilatory responses during exercise ***(Mann, 2005).***

However, as HF advances there is loss of endothelial-mediated vasodilatory responsiveness, which contributes to the excessive peripheral arterial vasoconstriction that is emblematic of advanced HF ***(Mann, 2005).***

***Stages of Heart Failure*:**

HF should be viewed as a continuum that is comprised of four interrelated stages (Fig. 2):

Stage A: includes patients who are at high risk for developing HF, but without structural heart disease or symptoms of HF (e.g., patients with diabetes or hypertension).

Stage B: includes patients who have structural heart disease but without symptoms of HF (e.g., patients with a previous myocardial infarction [MI] and asymptomatic LV dysfunction).

Stage C: includes patients who have structural heart disease who have developed symptoms of HF (e.g., patients with a previous MI with shortness of breath and fatigue).

Stage D: includes patients with refractory HF requiring special interventions (e.g., patients with refractory HF who are awaiting cardiac transplantation). A simplified algorithm for approaching patients with HF is illustrated in Figure 1.

(Jessup and Brozena, 2003)

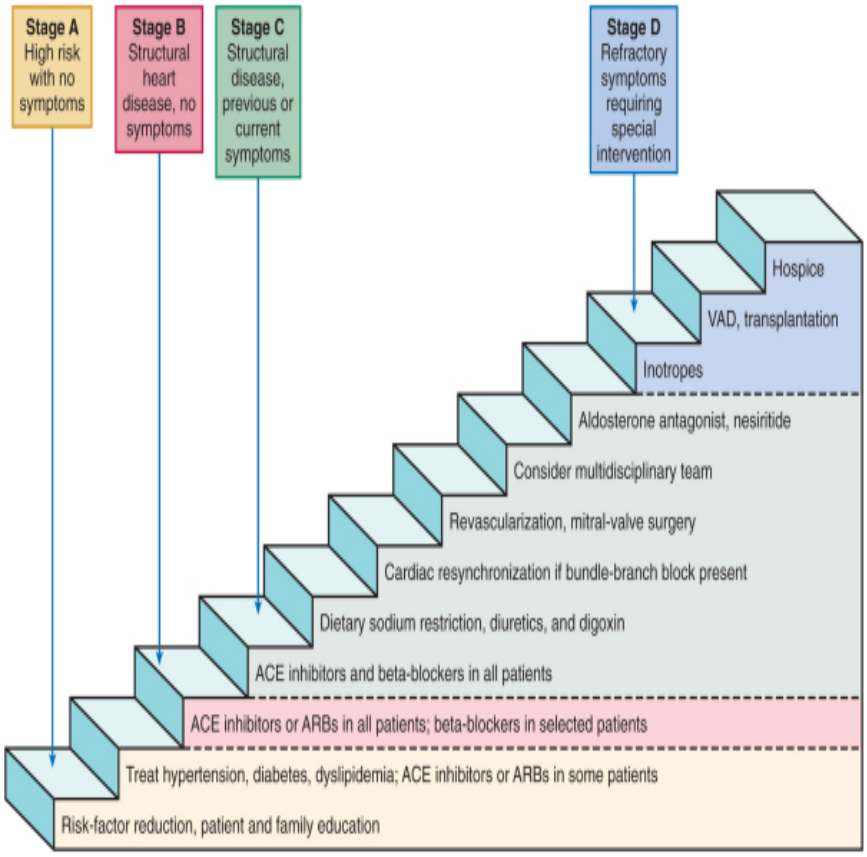

Figure (2): Stages of heart failure and treatment options for systolic heart failure. Patients with stage A heart failure are at high risk for heart failure but do not have structural heart disease or symptoms of heart failure. This group includes patients with hypertension, diabetes, coronary artery disease, previous exposure to cardiotoxic drugs, or a family history of cardiomyopathy. Patients with stage B heart failure have structural heart disease but have no symptoms of heart failure. This group includes patients with left ventricular hypertrophy, previous myocardial infarction, left ventricular systolic dysfunction, or valvular heart disease, all of whom would be considered to have New York Heart Association (NYHA) class I symptoms. Patients

with stage C heart failure have known structural heart disease and current or previous symptoms of heart failure. Their symptoms may be classified as NYHA class I, II, III, or IV. Patients with stage D heart failure have refractory symptoms of heart failure at rest despite maximal medical therapy, are hospitalized, and require specialized interventions or hospice care. All such patients would be considered to have NYHA class IV symptoms. ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; VAD = ventricular assist device ***(Jessup and Brozena 2003).***

Diagnostic Criteria of Heart Failure

Table (3): Diagnostic criteria for heart failure (HF) in population-based studies.

Framingham Criteria[*]			
Major Criteria	***Minor Criteria***	***Major or Minor Criteria***	
Paroxysmal nocturnal dyspnea or orthopnea	Ankle edema, night cough	Weight loss >4.5 kg in 5 days in response to treatment	
Neck-vein distention	Dyspnea on exertion		
Rales	Hepatomegaly		
Cardiomegaly	Pleural effusion		
Acute pulmonary edema, S_3 gallop	Vital capacity decreased one third from maximal capacity		
Increased venous pressure (>16 cm H_2O)	Tachycardia (rate >120/min)		
Hepatojugular reflux			
NHANES Criteria[†]			
Category	*Criteria*		
History	Dyspnea		
		On level ground?	1
		On climbing?	1
		Do you stop for breath when walking at an ordinary pace?	2
		Do you stop for breath	2