Introduction

Congestive heart failure represents a perfect clinical setting for the development of electrolyte abnormalities, thus electrolyte disturbances are a common complication. Central hemodynamic derangements in this condition result in renal dysfunction caused by decreases in renal blood flow and glomerular filtration rate activation of the renin-angiotensin-aldosterone axis enhanced sympathetic nervous system tone with increased release of various neurohormones (catecholamines, vasopressin, and vasoactive intestinal polypeptide); and elevation of other substances (atrial natriuretic peptide, endothelin, and prostaglandins) influencing fluid- electrolyte balance and vasoactivity ***(Jao et al., 2010).***

Therapies, especially diuretic agents, used to treat heart failure can greatly influence fluid and electrolyte balance. In CHF, electrolyte disturbances can do the most harm. A significant electrolyte abnormality (hypokalemia or hypomagnesemia), may evoke near-syncope, syncope, malignant dysrhythmias, or death because of the arrhythmogenic milieu (including diseased, ischemic, and stressed myocardium; elevated catecholamines; or arrhythmogenic drugs). Thus electrolyte abnormalities in CHF represent more than a simple laboratory finding and their management more than a casual therapeutic exercise ***(Jao et al., 2010).***

The most commcn electrolyte abnormalities in chronic CHF are hyponatremia, hypokalemia, and hypomagnesemia. Because their respective mechanisms for development, clinical significance, and management approaches differ, each abnormality is need to be discussed,with the understanding that they can occur together and that one often complicates the clinical and laboratory courses of the other ***(Jao et al., 2010).***

In acute decompensated heart failure the degree of hyponatremia often parallels the severity of cardiac dysfunction and is further exacerbated by any reduction in glomerular filtration rate and arginine vasopressin dysregulation. Even modest improvement of hyponatremia may have survival benefits. Although management of hyponatremia in acute decompensated heart failure has traditionally focused on improving cardiac function and fluid restriction, the magnitude of improvement of serum sodium is fairly slow and unpredictable ***(Jao et al., 2010).***

Maintenance of normal potassium homeostasis has become an increasingly important limiting factor in the therapy of heart failure with the application of loop diuretics and digoxin, hypokalemia has become a frequent and feared side effect of treatment. Low serum K^+ in HF may be also a marker of increased neurohormonal activity and disease progression. To gain the maximum benefit from treatment, we need to individualize drug use and carefully monitor electrolytes ***(Bielecka-Dabrowa et al., 2011).***

Magnesium deficit is a frequent electrolyte disorder in patients with CHF occurring either as an isolated disturbance on in association with other acid–base and electrolyte abnormalities. Several interrelated mechanisms are implicated in its pathogenesis. The distin s ction between magnesium deficiency (reversible by nutritionalupplements) and the various types of magnesium depletion, which require specific measures, is of great value in the management of the magnesium deficit in CHF patients. Clinicians should be aware of the incidence and related pathophysiology of hypomagnesemia in CHF patients since its early detection and appropriate treatment may inhibit its arrhythmiogenic potential ***(Milionis et al., 2002).***

Aim of the Work

The aim of this work is to highlighting the role of electrolyte disturbances (hyponatremia, hypokalemia, hypomagnesemia) in prognosis and management of CHF

Chapter (1):

PATHOPHYSIOLOGY OF ELECTROLYTE DISTURBANCES IN CONGESTIVE HEART FAILURE: HYPONATREMIA, HYPOKALEMIA, HYPOMAGNESEMIA

Introduction

Congestive heart failure (CHF) is a complex clinical syndrome, characterized by multiple metabolic alterations. Hyponatremia, hypokalemia, and hypomagnesemia are the most common electrolyte disorders of CHF. These electrolyte disturbances are not commonly encountered in mild to moderate ventricular dysfunction and compensated cardiac failure. The decrease in cardiac output (CO) leads to a reduction in renal blood flow, with impairment of renal excretion of water and electrolytes, and causes the activation of several neurohomonal responses which affect both cardiovascular homeostasis and electrolyte balance. Diuretics can depress the serum concentration of cation via direct renal tubular effects and stimulation of the reninangiotensin-aldosterone axis (RAAS) and vasopressin (VP) release ***(CAS et al., 1995).***

Pathophysiology of congestive heart failure

General overview:

CHF is a complex clinical syndrome characterized by dysfunction of the left, right, or both ventricles and the resultant changes in neurohormonal regulation and accompanied by effort intolerance, fluid retention, and shortened survival. It is often a terminal stage of heart disease, occurring after all reserve capacity and compensatory mechanisms of the myocardium and peripheral circulation have been exhausted ***(Hunt et al., 2005).***

Heart failure (HF) results from myocardial dysfunction that impairs the heart's ability to circulate blood at a rate sufficient to maintain the metabolic needs of peripheral tissues and various organs. It follows myocardial damage when the compensatory hemodynamic and neurohormonal mechanisms are exhausted and results from the loss of a critical amount of functioning myocardium due to acute myocardial infarction (MI), prolonged cardiovascular stress (hypertension, valvular disease), toxins (eg, alcohol abuse), or infection; in some cases, there is no apparent cause (idiopathic cardiomyopathy) ***(Hunt et al., 2005).***

Definition of heart failure:

HF is a chronic disease characterized by the inability of the heart to pump an adequate amount of blood to achieve the demand of the different organ systems. Once diagnosed,

medication is required for the rest of the patient's life to improve their life quality and survival ***(Dallas et al., 2006).***

Aetiology of HF:

Table (1): Causes of heart failure *(Baldasseroni et al., 2002)*

Causes of heart failure	%
• Ischaemic heart disease	40%
• Dilated cardiomyopathy	32%
• Valvular heart disease	12%
• Hypertension	11%
• Other 1- Viral myocarditis 2- Infiltrations of the muscle (amyloidosis) 3- HIV cardiomyopathy 4- Connective tissue diseases (SLE) 5- Abuse of drugs(alcohol and cocaine) 6- Pharmaceutical drugs chemotherapeutic agents 7- Arrhythmias	5%

HIV (human immunodeficiency virus) SLE (systemic lupus erythromatosis)

Pathophysiology of heart failure:

CHF arises as an abnormality in cardiac structure, function, rhythm, or conduction. HF often occurs in elderly patients who have multiple comorbid conditions (eg, angina, HTN, DM, and chronic lung disease) ***(McMurray et al., 2005).***

CHF not only an inability of the heart to maintain adequate oxygen delivery; it is also a systemic response attempting to compensate for the inadequacy.Determinants of CO (heart rate and stroke volume) as shown in (Fig. 1).

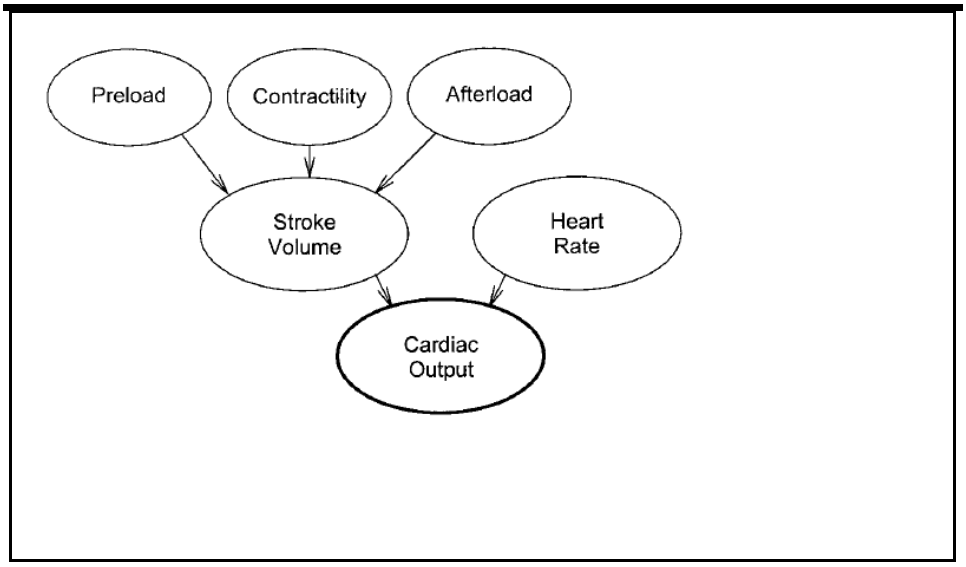


Figure (1): The determinants of cardiac output *(Figueroa, 2006).*

Stroke volume

Is further determined by the preload, contractility, and afterload. These variables are important in understanding the pathophysiologic consequences of HF and treat it. The preload characterizes the volume that the pump is given to send forward, the contractility characterizes the pump, and the afterload determines what the heart must work against ***(Brausnwald, 1998)***.

- **Preload**

Expressed as the end-diastolic pressure/ volume of the left ventricle and is assessed by measuring the right atrial pressure. The preload is not only depend on intravascular volume; it is also influenced by any restriction to ventricular

filling.An increased positive pleural pressure]dynamic hyperinflation in chronic obstructive pulmonary disease (COPD)[can reduce right-atrial pressure (which equals central venous pressure minus pleural pressure) and thus reduce ventricular filling. The cardiac pump is a muscle and will respond to the volume it is given with a determined output. If volume increases, the amount pumped out in a normal physiologic state will increases, to a determined plateau; this relationship is described by the Frank-Starling law as shown (Figs. 2 and 3) ***(Brausnwald, 1998)***.

Diastolic function is determined by 2 factors: the elasticity or distensibility of the left ventricle, which is a passive phenomenon, and the process of myocardial relaxation, which is an active process that requires metabolic energy. Relaxation of the myocardium occurs in early diastole, and the "untwisting" of the left ventricle is an active process that produces a suction effect that augments left-ventricular filling. Loss of normal left ventricular distensibility or relaxation by either structural changes (left-ventricular hypertrophy) or by functional changes (ischemia) impairs ventricular filling (preload) ***(Brausnwald, 1998)***.

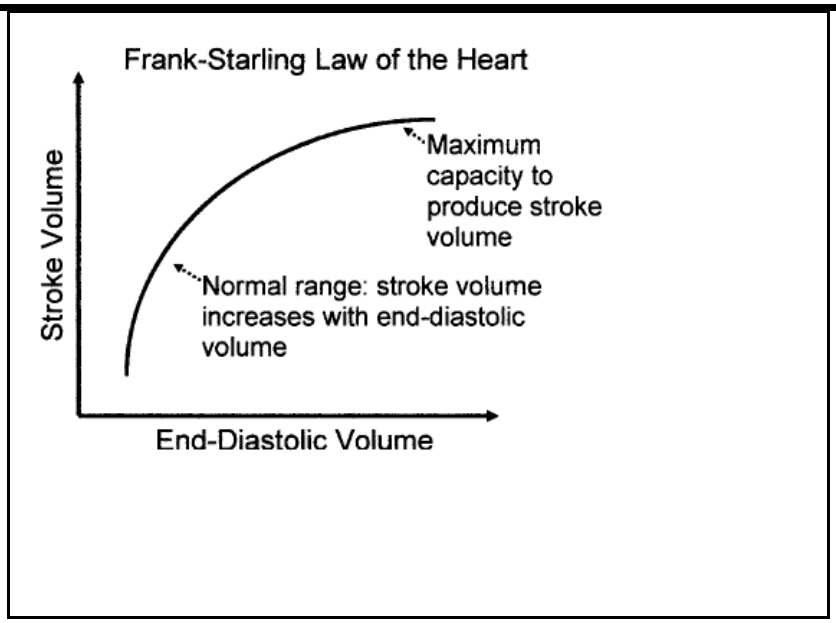


Figure (2): **The Frank-Starling law of the heart:** the ventricular volume increases and stretches the myocardial muscle fibers, the stroke volume increases, up to its maximum capacity.After that point, increasing volume increases pulmonary capillary pressure (and pulmonary congestion), without increasing the stroke volume or cardiac output. The mechanism is the length-force relationships of muscle contraction ***(Figueroa, 2006).***

The exercise intolerance seen with diastolic dysfunction largely from the impairment of ventricular filling, which elevates left-atrial pressure and pulmonary venous pressure and causes pulmonary congestion. Additionally, inadequate CO during exercise results in poor perfusion of skeletal muscles, especially the leg muscles and the accessory muscles of respiration ***(Kitzman, 2005).***

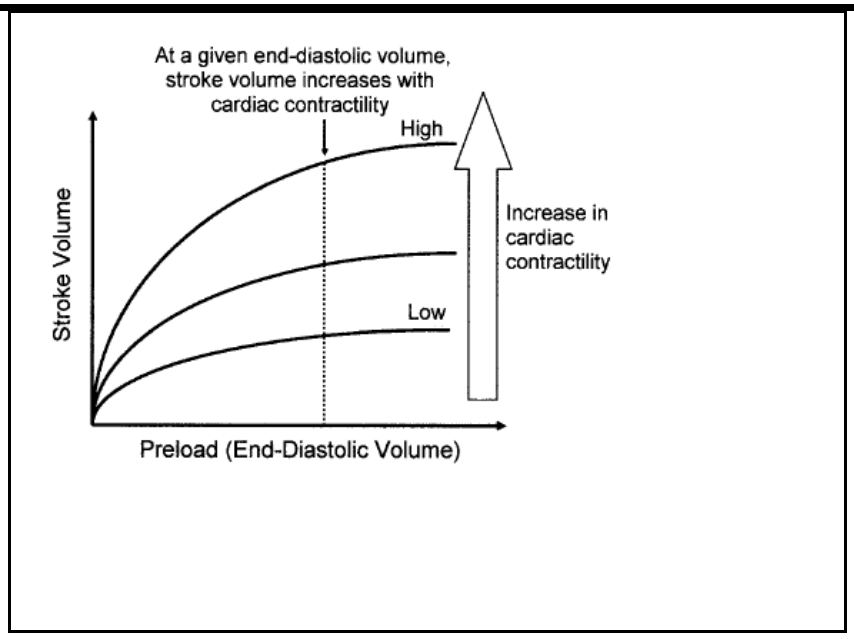


Figure (3): **Series of Frank-Starling curves:** demonstrates that at any given preload (end-diastolic volume), increases in contractility will increase stroke volume (volume of blood ejected from the ventricle with each beat) ***(Figueroa, 2006).***

- **Cardiac contractility:**

Represents the muscular pumping of the heart and is commonly expressed as the ejection fraction. The heart will respond to the same preload with different stroke volumes, depending on inherent characteristics of the heart. A heart with normal systolic function will maintain an ejection fraction of over 50–55%. A previous myocardial infarction may result in nonfunctioning myocardium that will impair contractility. Ischemic myocardial tissue can be nonfunctioning (hibernating) but revitalized by surgical or medical therapy directed at ischemic heart disease ***(Choudhury et al., 2002).***

- **Afterload**

Is the load that the pump has to work against, which is usually clinically estimated by the mean arterial pressure. The normal CO is relatively insensitive to afterload up to 140 mm Hg. However, the afterload represents not only the vascular resistance but also the wall tension and intrathoracic pressure that the myocardium must work against.these 3 variables are impaired in the patient with CHF ***(Brausnwald, 1998)*.**

Pathophysiology of neurohumoral system:

If CO falls, either the heart rate or stroke volume must change in order to maintain perfusion. If stroke volume cannot be maintained,heart rate must increase to maintain CO. The pathophysiology behind CHF includes a structural abnormality and cardiovascular response to poor perfusion with the activation of the neurohumoral system ***(Jessup et al., 2007)***.

Activation of RAAS attempts to increase preload by stimulating retention of salt and H2O, vasoconstriction (afterload), and augmenting cardiac contractility. Initially, this response will suffice, but prolonged activation results in loss of myocytes. The stressed myocardium undergoes remodeling and dilation ***(Eichhorn et al., 1996)***.

This process also has detrimental effects on the functioning of the lungs, kidneys,, blood vessels. Remodeling also results in additional cardiac decompensation from complications, including mitral regurgitation(from valvular

annulus stretching),and cardiac arrhythmias from (atrial remodeling) ***(Jessup et al., 2007).***

CHF patient as the elevated end-diastolic pressure leads to pulmonary edema and dyspnea. Patients presentation can greatly differ, depending on the chronicity of the disease, most patients experience dyspnea when pulmonary-artery occlusion pressure exceeds 25 mm Hg. However, the patient with longstanding CHF can tolerate filling pressure up to 40 mm Hg ***(Gehlbach et al., 2004).***

The lung provides multiple mechanisms to avoid the consequences of pulmonary edema. Initially, as pressure increases, pulmonary capillaries are recruited and increase capacitance to deal with the added volume. As pressure continues to increase, volume can be diverted from the alveoli to the interstitium. At this point, by action of pressure gradients, fluid will form in the interlobular septae and the perihilar region. CHF is associated with increased venous capacitance and lymphatic drainage of the lung. As a result, crackles are often absent, even in the setting of elevated pulmonary capillary pressure. Continued sodium retention results in peripheral edema and, ultimately, development of pleural effusions The long-term response to elevated pulmonary venous pressure includes interstitial fibrosis with of the alveolar membrane. Thus, severe, chronic HF can result in interstitial fibrosis and a restrictive lung disease ***(Malik et al., 2000).***

With acute decompensation, the pulmonary capillary membrane may succumb to increased pressure, with shearing of the capillary and release of fluid, protein, and occasionally red blood cells into the alveoli. The lungs' response will include cough ***(Gehlbach et al., 2004).***

Pathophysiology of hyponatremia in CHF

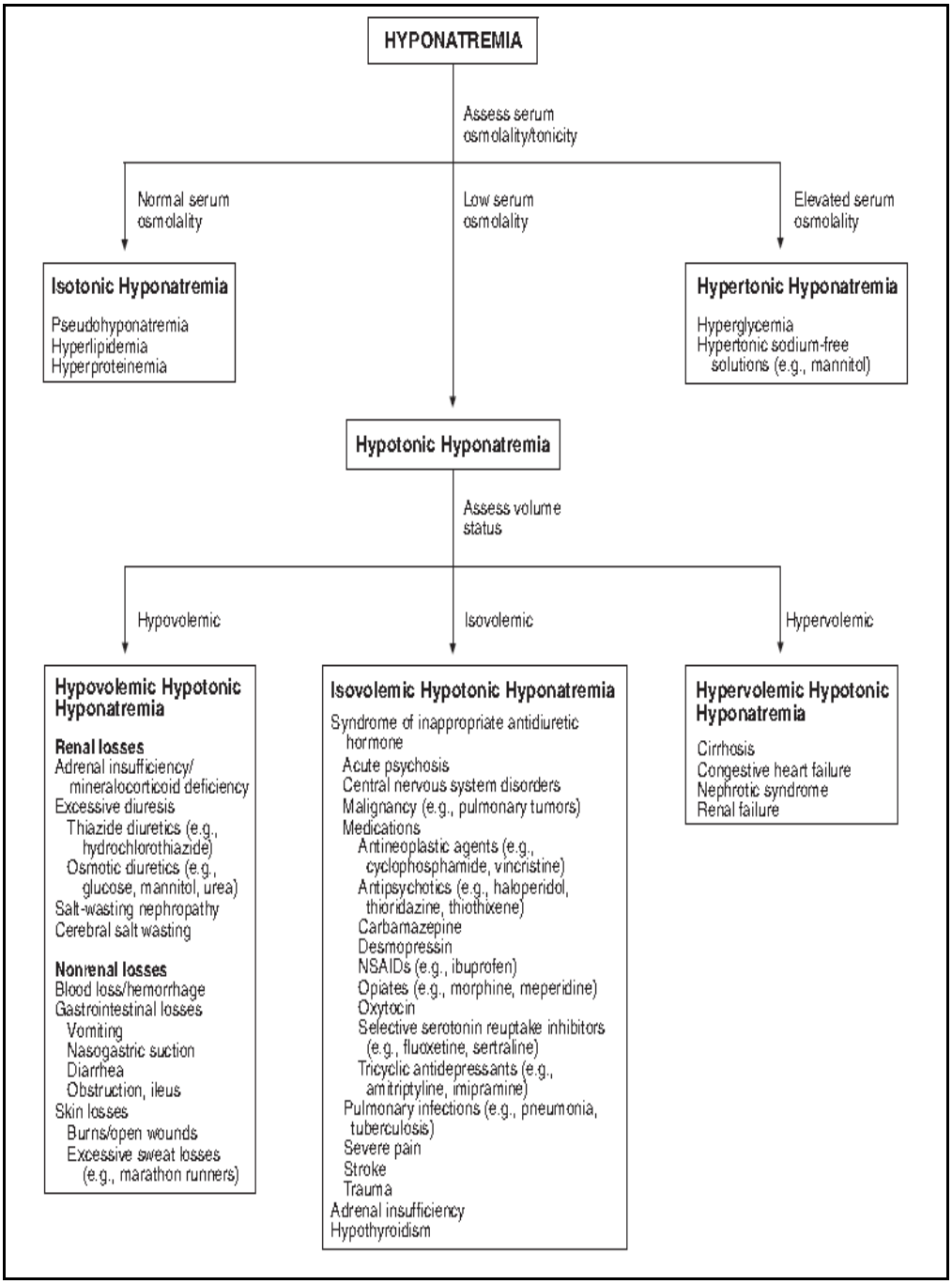
General overview:

Although HF manifests primarily with cardiopulmonary symptoms, hyponatremia is very common in this patient population. In fact, hyponatremia is present in over 20% of patients admitted to hospital with HF.Not only is it a common occurrence, but it has repeatedly been shown to be a marker of increased mortality in the HF population. Both the maladaptive neurohormonal and renal changes as well as diuretic treatment of HF contribute to the development of hyponatremia ***(Goldberg et al., 2006).***

Definition of hyponatremia:

Hyponatremia is defined as a decrease in the serum sodium concentration to a level below 136 mmol per liter ***(Gennari, 1998).***

Aetiology of hyponatremia:



NSAIDs = nonsteroidal antiinflammatorydrugs.

Figure (4): Etiology of hyponatremia ***(Michael et al., 2005)***