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Impact of Dyselectrolytemia on Heart Failure and their Long-Term Cardiovascular Outcomes: A Comparative Analysis

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Abstract

Introduction: One of the major causes of cardiovascular morbidity and mortality is heart failure (HF). It is very common in these patients to have an imbalance in their electrolytes and the acid–base levels, due to multiple factors. These acid base disorders are associated with the severity of HF and further contribute to poor long-term outcomes; hence this retrospective observational study was performed to evaluate the effect of alterations in the levels of serum sodium, potassium, magnesium and chloride on acute decompensated heart failure (ADHF) patients.

Methods: The hospital records were collected from November 2015 to May 2018 to identify patients of established discharge diagnosis of ADHF as per the Framingham Criteria. The admission and discharge levels of serum sodium, potassium, chloride and magnesium were collected, and their association with cardiac mortality was identified.

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Results: The average (mean) admission serum chloride levels were 99 +5.2 mEq/l and the average (mean) serum sodium levels were 128.9+6.7 meq/l. The mean serum chloride level at admission was directly correlated to the mean admission sodium level with $p < 0.001$. Mean admission serum potassium levels were 4.1+2.1 mEq/l and the mean serum magnesium levels were 1.2+0.7 meq/l; these were observed in 89.2% and 94.2 % of the patients respectively.

Conclusion: We observed an inverse correlation between the levels of serum sodium, chloride, potassium and magnesium, i.e; low levels of these ions were related to a high level of mortality in patients of acute decompensated cardiac failure.

Keywords

Acute Decompensated Heart Failure; Cardiac Failure; Dyselectrolemia; Potassium; Sodium.

Highlights

This is a retrospective observational study which was conducted at a tertiary care centre in Eastern India. The need for this study arose when many patients of acute decompensated heart failure (ADHF) were admitted in the cardiac wards and ICU of our hospital and they all had hyponatremia. On further examination, other electrolyte imbalances were also seen in those patients, hence this study was performed to look for the correlation between dyselectrolemia and cardiac failure in patients of ADHF.

Introduction

One of the major causes of cardiovascular morbidity and mortality is heart failure (HF), which is responsible for more than one million admissions per year in USA (United States of America), and it is also the commonest diagnosis at discharge among patients aged more than 65 years [1]. It has been observed that the relative incidence of HF is much less among females as compared to males, although they constitute around fifty percent of such cases, owing to their average prolonged life expectancy [2]. In such patients, a strong mortality predictor is the number of times he or she is admitted with acute decompensated heart failure (ADHF). The rates of mortality are as high as 20%, after discharge in these patients [3]. The prevalence and incidence of admissions due to HF have seen a threefold rise in the past 30 years, mainly due to the increase in number of elderly along with improvement in survival rates post MI (myocardial infarction), and a prolongation in survival of these patients with the advancements in medicine and device therapies [2].

It is very common in HF patients to have imbalance in their electrolytes and acid–base levels, due to multiple factors, like activation of various neural-humoral mechanisms, and a response to the drugs used to treat it like diuretics [2]. These acid base disorders reflect the severity of HF and thus further contribute to the poorer long-term outcomes and significant functional impairment [3]. The commonly seen

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electrolyte disturbances are hypochloremia, hyponatremia, hypomagnesemia and hypokalemia. The usual acid–base irregularities observed are pure metabolic alkalosis or it can also be seen in combination with respiratory alkalosis [4]. There are numerous mechanisms at play that give rise to these alterations. The reduced cardiac output can cause decreased blood flow in the renal system, with impaired excretion of electrolytes and water, and it leads to activation of renin-angiotensin mechanism, which can affect both - the electrolyte homeostasis and the cardiovascular system. These electrolyte disturbances are a very dangerous complication in patients with chronic or acute HF, and can also be hazardous due to the complications of therapy with, ACE inhibitors and/or cardiac glycosides [5]. Furthermore, reduction in serum sodium concentration has rarely been seen to occur in isolation, and it is the body's natural mechanism that to preserve the electroneutrality of plasma, an anion such as bicarbonate (HCO3-) or a chloride (Cl-) is subsequently reduced in relation to sodium (Na+) [6].

It has been observed that a patient is more prone to various drug toxicities in the acute phases of potassium deficiency, in contrast to chronic potassium deficiencies. These changes explain the clinical observations that acute hypokalemic states are related to a higher glycoside and diuretic sensitivity as compared to chronic potassium deficiency [6]. With potassium (K+), magnesium (Mg2+) is also known to influence the cardiovascular functions and it plays a vital role in the occurrence of arrhythmias. Magnesium is also essential for maintenance of potassium concentration in the intracellular fluid. Even though there are some conflicting data related to the prevalence of hypomagnesemia in chronic HF patients (value ranging from 7-37%), many researches have reported low concentrations of magnesium in these patients [7].

After an extensive literature search, we could not find a single study which has documented and compared the long-term outcomes of serum sodium, chloride, magnesium and potassium in ADHF patients. Hence, this study was conducted to assess the impact of hyponatremia, hypochloremia, hypokalemia and hypomagnesemia on CHF patients admitted a tertiary care centre in Southern India.

Materials and Methods

The hospital records were collected from November 2015 to May 2018 to identify patients of established discharge diagnosis of Acute Decompensated Heart Failure (ADHF), admitted at the Critical Care Unit at the Cardiology Department at our tertiary care center. Total 405 patients were identified and Framingham's criteria for diagnosis of heart failure was used.

To enhance the specificity of selection of patients with chronic heart failure, only those patients having a cardiac implantable electronic device like an ICD (implantable cardioverter-defibrillator) or patients on cardiac resynchronization therapy were included in the study. The presence of a cardiac resynchronization therapy device or an ICD was identified on history and examination, or if the patient underwent a procedure having implantation of a lead for single or a dual-chamber pacing ICD and/or if there was insertion of a pulse generator; or, if the same was confirmed on radiological examination.

Clinical, imaging, demographic and lab data, and a documented diagnosis were collected from medical records. Admission levels of serum sodium, chloride, magnesium and potassium were defined as serum

levels of these ions on the first blood drawn on day 1 of clincial presentation; discharge levels of all these ions were determined from the blood drawn on discharge day. The study was approved by the Institutional Ethical Committee vide letter no. IEC/PE/06/2026/24 dated 23/06/2018, and it conforms to the accepted ethical principles guiding human research as per as the Declaration of Helsinki.

Framingham Criteria for Heart Failure

Presence of two major or one major criterion with two minor criteria as follows was used [8]: -

Major criteria- rales, paroxysmal nocturnal dyspnea, radiographic evidence of cardiomegaly, distension of neck veins, acute pulmonary edema, hepatojugular reflux, weight loss of more than 4.5 kg in 5 days in response to treatment, S3 gallop or increased CVP (central venous pressure >16 cm H2O at right atrium).

Minor criteria- include hepatomegaly, dyspnea on exertion, bilateral ankle edema, nocturnal cough, reduction in vital capacity by one third from the maximum recorded, pleural effusion and tachycardia.

Inclusion criteria

- Patients having ADHF as clinical diagnosis
- B-type natriuretic peptide (BNP) level >100 pg/ml in 24 hours of hospitalization.

Exclusion criteria

- Patients not receiving loop diuretics during hospitalization
- Patients having a history of implantation of mechanical assisted device or a heart transplantation
- Patients on chronic hemodialysis
- Patients on renal-replacement therapy
- Patients not having a documentation of specific HF etiology.

Patients were followed up for a period of one year to look for mortality and its causes via telephonic conversation.

Definitions used in our study

- Hyponatremia - ≤135mg/dL
- Hypochloremia - ≤96mg/dL
- Hypokalemia - <3.5mg/dL
- Hypomagnesemia - <1.5mg/dL

Statistical methods

SPSS software was utilized for statistical analysis and P- value < 0.05 was considered as statistically significant.

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Results

Baseline characteristics

The Baseline characteristics of our demographic are depicted in Table 1. The mean age was 63.5 years. Majority of our patients were belonging to the elderly age group, and females and males were found to be equally distributed. The males had a significantly high mortality. Total follow-up duration was 1 year and mean time of follow-up was 11.5 months.

The commonest symptom was dyspnea (Figure 1) and the most commonly associated comorbidity was diabetes mellitus.

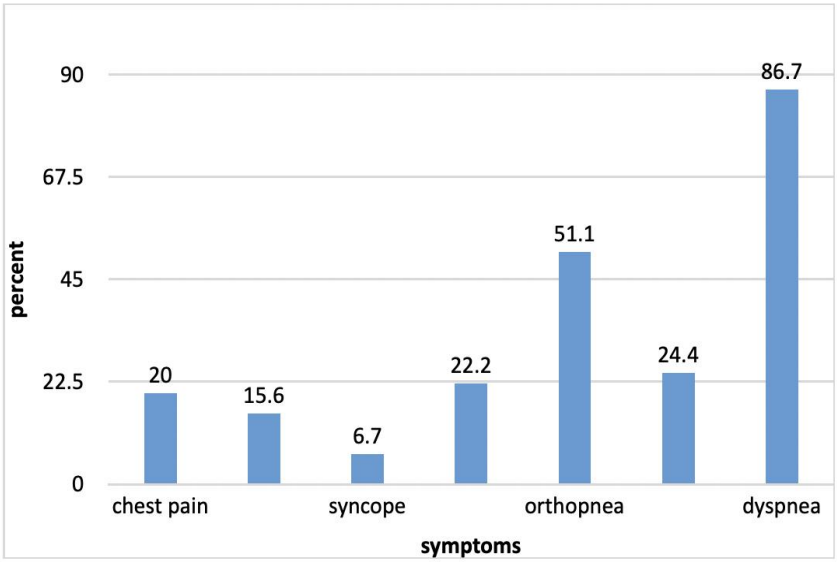

Figure 1: Symptomatology of the patients in our study group.

All of our patients received loop diuretics (Figure 2).

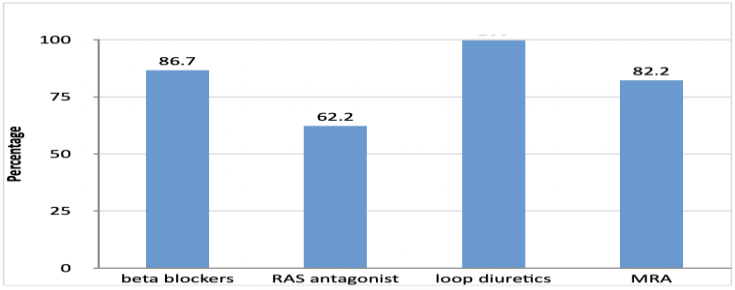

Figure 2: Drugs administered to the patients in our study.

Discussion

In this cohort of patients hospitalized for ADHF (acute decompensated heart failure) and electrolyte disturbances, we report numerous key findings which highlight the prognosis among them, based on the levels of serum sodium, chloride, potassium and magnesium. Firstly, the serum level of chloride was inversely and independently related to a higher risk of mortality. Secondly, the levels of sodium, chloride, potassium and magnesium modestly enhanced mortality prediction in ADHF patients, as the patients having lower levels of these ions had a poorer prognosis compared to the ones with normal levels. These results highlight the importance of these electrolytes on the prognosis of ADHF and emphasize that it provides a strong mortality prediction.

However, there are a few limitations present in our study. There's the risk of a selection bias for the patients undergoing treatment and evaluation of ADHF at various tertiary care centers. Moreover, our study did not display how we identified the patients having ADHF. In a similar way, the impact of levels of sodium, chloride, magnesium and potassium on rehospitalization of these patients was not be determined.

Sodium and chloride are both important ions in the ECF (extracellular fluid). A huge number of studies have reported that the sodium electrolyte disturbances are a predictor of poor prognosis in acute and chronic heart failure, but rarely any study has accounted for the levels of chloride, potassium or magnesium in their analysis [9]. Chloride is known as a much better predictor of cardiac outcomes as compared to serum sodium levels in heart failure, and the current dispute about the detrimental and beneficial effects of restriction of salt in HF patients might be related to its effect on the serum sodium-chloride homeostasis. Alterations in plasma volume, RAAS system (renin-angiotensin-aldosterone) and vasopressin secretion that are seen in exacerbation of heart failure are reported to be mediated by the levels of serum chloride and not by sodium levels [10]. Moreover, many studies in heart failure patients have found that serum chloride is inversely related to mortalities irrespective of the sodium level, hence its role as a potential prognostic marker in acute and chronic HF has been proposed [11,12].

Many studies have also shown that the mechanisms which cause reduction in serum sodium can also cause reduction in serum chloride [13], like impaired free water excretion which results from an increased vasopressin release, that is raised in patients with symptomatic HF, along with the multiple effects of excessive angiotensin II on the renal sodium and activation of neural thirst center as well as increased baroreceptor-mediated water retention. All these processes are directly and positively stimulated in heart failure [13]. As a result, a low chloride level might also be of dilutional nature. However, it can also point towards depletion of electrolytes, especially when the serum chloride is lower than the serum sodium levels, which occurs in diuretic-induced salt wasting where chloride is excreted whereas bicarbonate is retained in order to maintain electroneutrality [14]. Making this decision has many clinical implications when the clinician is providing decongestive cardiac therapy for patients in acute heart failure [15].

The cardiovascular outcomes and sodium levels have been analysed in many studies [16]. Patel et al depicted that the serum sodium level has a J-shaped relationship with the all-cause mortality in heart failure patents [17]. In these patients, level of sodium is associated with a higher mortality. As per,

hyponatremia is quite common in Turkish patients having HF, and serum sodium was found to be a significant and independent risk factor for raised mortality. [18]. Shorr et al.'s conducted research in which they showed that hyponatremia is directly proportional to the unfavorable outcomes in HF patients after discharge, which points to the probability that chronic hyponatremia plays a key role in pathology of acute and chronic HF [19]. Various other studies have also shown that a low chloride level in serum is related to adverse outcomes in the patients with acute [20-22] and chronic heart failure, both [23-25].

Along with sodium and chloride, other ions like potassium and magnesium have also been implicated in the occurrence of cardiac failure, and various studies [26-28] have been done to identify how their levels affect the cardiovascular system. Just as seen in other conditions like hypertension, myocardial infarction, kidney disease, the association between serum potassium (K+) concentration and the adverse cardiac failure outcome has been found to be a U-shaped graph, in which the low potassium level is related to poorer prognosis [26,29]. The RMP difference (resting transmembrane potential) is dependent on the extracellular and intracellular potassium concentration. Hypokalemia also increases the rate of depolarization in the cells, as well as its excitability and automaticity. Due to the fact that cardiac repolarization depends on the influx of potassium, a reduction in K+ levels increases the action potential and it prolongs the QT dispersion [30].

A low magnesium level is independently known to increase the risk of HF, but there's conflicting data on the association between outcomes of HF patients and the serum magnesium levels [31]. Another systematic review and meta-analysis showed that in heart failure patients, hypermagnesemia (serum magnesium level of more than 1.05 mmol/L) caused a higher risk of cardiovascular mortality, but the same was not seen in the case of hypomagnesemia [31]. An observational study used the data from ARIC cohort (Atherosclerosis Risk in Communities), and they concluded that a low magnesium level and a high phosphorus and calcium level was a risk factor for mortality in HF patients [32]. A prospective observational study conducted at a tertiary care ICU in India found that hypomagnesemia was significantly associated with adverse outcomes and higher mortality in critically ill patients [33].

Conclusion

We observed an inverse correlation among the levels of serum sodium, chloride, potassium and magnesium, i.e; low levels of these ions was associated with a high mortality in ADHF patients. To the best of our knowledge, an observational study which has examined the effects of serum sodium, chloride, potassium and magnesium, all in one cohort, for a long period of one year, has not been conducted in the Indian population. Hence, this study helps to fill the research gap and create a paradigm for further such studies to be done.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

What is already known?

Various studies have been conducted which have identified an inverse correlation between hyponatremia and hypochloremia and acute decompensated heart failure (ADHF). Other studies depict that

hyperkalemia leading to dysarrythmias leads to cardiac failure. Contrasting data is available regarding the effects of hyper and hypomagnesemia on ADHF.

What this Study Adds?

Our study reiterates the fact that hypochloremia and hyponatremia is a major predicting factor of mortality in patients of acute decompensated cardiac failure. Alongwith that, we have also compared the levels of magnesium and potassium in our patients and we found that hypokalemia and hypomagnesemia is also an independent mortality predictor in ADHF patients, in a large cohort of 405 patients. To the best of our knowledge, we could not find any other study that compares these four electrolyte imbalances in ADHF in single research, hence it aims to fill in the research gaps present in the literature.

Data Availability

All the data used in the study is available in the article sent for publication.

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