Prognostic Value of Serum Sodium and Chlorine Level in Acute Decompanse Heart Failure

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Abstract: Acute heat failure is a significant reason of morbidity and mortality that is commonly seen in the emergency department. In our study, we aimed to investigate the effectiveness of serum sodium and chloride levels for predicting the prognosis of the patients with acute decompensated heart failure. Our study has been conducted in Health Sciences University Emergency Medicine Department Ankara Health Application and Research Center Emergency Clinic (SBÜ Acil Tıp ABD Ankara SUAM Acil Tıp Kliniği) between 1.12.2018 and 1.12.2019 after receiving ethics committee's approval. Our study is a prospective, observational clinical trial. 120 patients older than 18 years old with informed consent who admitted to emergency department with the diagnoses of acute heart failure and acute decompensation of chronic heart failure were included without any exclusion criteria. The cases included in our study were divided into 3 groups; the patients who had got treated in the emergency department and discharged from the hospital, the patients who were hospitalized in cardiology clinic and the patients who were hospitalized in intensive care unit. Serum sodium and chloride levels in blood samples were compared when these 3 groups of patients were admitted to the emergency department. 48.3% (n:58) of patients were discharged from the hospital while 26.7% (n:32) of patients were hospitalized and 25% (n:30) of patients were hospitalized in intensive care unit. The patients with serum chloride levels below than 98.5 mmol/l needed longer hospitalization while no significant correlation between serum sodium levels and hospitalization ratio was detected. Lower serum chloride level is a valuable indicator for evaluating the prognosis and predicting the need of hospitalization of the patients who were admitted to the emergency department with acute heart failure. There was no correlation between the serum sodium levels and prognosis and the need for hospitalization.

Keywords: acute heart failure, chloride, sodium

Akut Dekompanse Kalp Yetmezliğinde Serum Sodyum ve Klor Seviyesinin Prognostik Değeri

Özet: Akut kalp yetmezliği acil servislerde sık karşılaşılan önemli bir morbidite ve mortalite nedenidir. Biz yapmış olduğumuz bu çalışma ile akut dekompanse kalp yetmezliği olan hastalarda hastaneye yatış veya taburculukta serum sodyum ve klor düzeyinin etkinliğini araştırmayı amaçladık. Çalışmamız SBÜ Acil Tıp ABD Ankara SUAM Acil Tıp Kliniğinde 1.12.2018 ile 1.12.2019 tarihleri arasında etik kurulu onayı alınarak yapıldı. Çalışmamız prospektif, gözlemsel bir klinik çalışma olarak gerçekleştirildi. Çalışmaya acil servisimize başvuran akut kalp yetmezliği ve kronik kalp yetmezliğinin akut dekompanzasyonu tanılı aydınlatılmış onamı alınan, 18 yaşın üzerindeki dışlama kriteri olmayan 120 hasta dahil edildi. Çalışmamıza dahil edilen hastalar acil servisten tedavi alıp taburcu olanlar, servise yatış yapılanlar ve yoğun bakım yatışı yapılanlar olarak 3 gruba ayrılmıştır. Bu 3 grubun acil servise başvurduğu sırada alınan kan örneklerindeki serum sodyum ve klor düzeyleri

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karşılaştırılaştırılmıştır. Hastaların % 48,3'ü (n:58) acil servisten taburcu olurken, % 26,7'sine (n:32) servis yatışı, % 25'ine (n:30) yoğun bakım yatışı yapıldı. Klor değeri 98,5 mmol/L ve altında olan hastaların daha çok hastaneye yatış ihtiyacı olduğu tespit edilirken, sodyum değeri ile hastaneye yatış arasında herhangi bir anlamlı ilişki tespit edilememiştir. (p=0,041; p=0,810) Servis ve yoğun bakım yatışı yapılan hasta grupları arasında sırasıyla sodyum ve klor değerlerinin ortancası 136 – 137,5 mmol/L, 97,5 – 97,5 mmol/L olup herhangi bir anlamlı farklılık izlenmedi. (p=0,949; p=0,938). Akut kalp yetmezliği ile acil servislere başvuran hastaların yatış ihtiyacını öngörmede ve prognoz değerlendirmesinde düşük serum klor seviyesi değerli bir göstergedir. Sodyum seviyesi ile yatış ihtiyacı ve prognoz arasında herhangi bir ilişki yoktur.

Anahtar kelimeler: akut kalp yetmezliği, klor, sodyum

INTRODUCTION

Heart failure: accompanied with dyspnea, low exercise toleration, chronic fatigue which are the result of constructional and functional cardiac abnormalities, is a disease which has a high ratio of mortality and morbidity (Walls et al., 2017). Acute heart failure is defined as acute worsening of heart failure symptoms and findings. Decompensated heart failure could also be called as acute pulmonary edema (Heidenreich et al., 2013; Degertekin et al., 2012). Heart failure is a disease with a poor prognosis, the 5-year survival rate of patients with heart failure is 50%. Advanced age, exercise intolerance, plasma levels of norepinephrine and natriuretic peptide, anemia, renal dysfunction, hyponatremia, higher troponin levels, ischemic ECG findings are related with poor prognosis in patients with heart failure (Weintraub et al., 2010; Benjamin et al., 2019). In our study we aimed to find the relationship between the serum sodium and chloride levels of the patients who were admitted to our emergency service with acute worsening of heart failure symptoms and the hospitalization or discharge of the patients.

MATERIAL and METHODS

Study Population and Study Protocol

Our study was conducted between 1.12.2018 and 1.12.2019 in Ankara Training and Research Hospital emergency room as a prospective, observation-based clinical research set. It was conducted according to the latest version of Helsinki Declaration and Good Clinical Practice Directives. Our study was approved from the ethical committee of Ankara Training and Research Hospital.

Although acute heart failure diagnosis could be given with basic clinical features, we chose to include the patients with acute heart failure and acute decompensation of chronic heart failure according to the heart failure guidelines published in 2016 by European Society of Cardiology.

1- One or more of the following must exist with NT-pro BNP≥300 ng/L;
- one of the following: coronary artery disease, hypertension, cardiotoxic drug usage, diuretic drug usage
- orthopnea/paroxysmal nocturnal dyspnea
- one of the following: hearing crepitant rales in physical examination, existence of edema in bilateral lower extremities, murmur, jugular venous dilatation, lateral translocation of cardiac apex beat
- any ECG abnormalities

2- Acute worsening or acute onset of heart failure symptoms and findings

The patients who were included to our study were divided into three groups as patients who were discharged, patients who were hospitalized in clinical ward and patients who were hospitalized in

intensive care units and needed inotropic medication and/or mechanical ventilation support. The serum sodium and chloride levels of the patients of these three groups when they were admitted to the emergency service were compared, and the serum sodium and chloride levels of the hospitalized patient group and discharged patient group were compared.

The laboratory tests of the patients who were included in our study had been done by the emergency service laboratory of Ankara Training and Research Hospital and the corrected serum sodium levels regarding the serum glucose concentration were calculated by ourselves. The arterial blood pressure was recorded as mean arterial blood pressure. Vital signs, serum sodium, chloride, calcium, troponin levels and blood gas analysis of the patients were recorded when they were admitted to the emergency service. Roche E411, Roche Cobas 6000 with 5th generation highly sensitive Troponin T kits and ion selective electrolyte kits were used for measurements of serum chloride, sodium and troponin. Cut off values were determined as the kits' references. More than 50% rise at 99th percentile on troponin values at 0 and 3rd hour were considered as significant.

Study inclusion criteria
- Patients with acute heart failure
- Patients with acute decompensation of chronic heart failure
- Patients who are older than 18 years of age and gave informed consent

Study exclusion criteria
- Pregnancy
- <18 years of age
- Patients who did not want to be included to the study
- Patients who did not sign the informed consent form
- Conditions that affect the serum sodium and chloride levels:
    - Septic shock
    - Renal failure with etiology other than heart failure
    - Chronic renal failure
    - Inappropriate ADH syndrome
    - Diabetes Insipidus
    - Patients who were hospitalized due to infectious diseases
    - Ascites with acute liver failure or chronic liver failure
    - Nephrotic edema
    - Clinical conditions which cause dehydration such as burns, trauma, bleeding, enteritis, pancreatitis, acute abdomen were excluded

Statistical Analysis
Data were analyzed with SPSS 22.0 analysis software. Definitive statistics were presented as mean (±), standard deviation, median (min, max), distribution of frequency and percentage. Compatibility to normal distribution of variables were analyzed with visual (histogram) and statistical methods (Kolmogorov-Smirnov/Shapiro-Wilk). Pearson chi-square, Mann Whitney U test, Independent-sample t test, Kruskal-Wallis variance analysis, One-way analysis of variance, Tukey test, Spearman test were used as statistical methods. Value of statistically significance was accepted as $p < 0.05$. According to the performed power analysis with 50 patients for each of the groups of patients with normal levels of serum sodium and chloride and lower levels of serum sodium and chloride, we obtained 0.05 error margin, 0.99 statistical power and 1.7 effect size.

RESULTS

One hundred twenty patients were included in our study. Age, sex, and outcome (hospitalization, intensive care unit or discharge) of the patients are shown in Table 1.

Table 1. Age and sex distribution of included patients.

	Number of participants	(%)
Age group (n=120)		
< 65 years of age	24	20.0
> 65 years of age	96	80.0
Sex (n=120)		
Male	52	43.3
Female	68	56.7
Outcome (n=120)		
Discharge	58	48.3
Hospitalization	32	26.7
Intensive Care Unit	30	25.0

The area under the curve was calculated as 0.614 (p=0.032) in ROC curve analysis of chloride levels according to the outcome (hospitalization or discharge) (Figure 1). Sensitivity (54.8%) and specificity (63.8%) were determined regarding the kits that were whose cut-off value for chloride is 98.5 mmol/L.
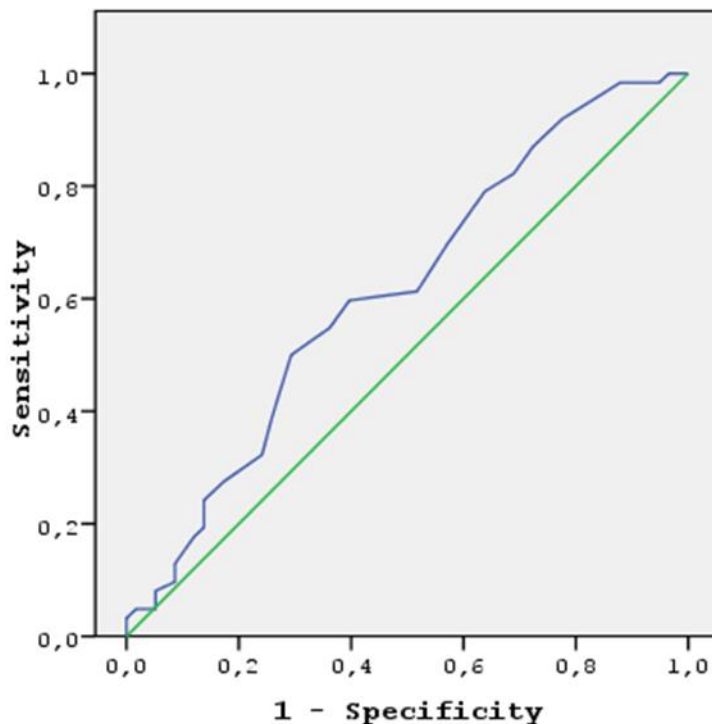

Figure 1. ROC curve analysis of chloride levels according to the outcome.

The patients with chloride levels lower than 98.5 mmol/L had more hospitalization rate and this found to be statistically significant (p=0.041). There was no significant relationship between sodium, chloride and calcium levels of the hospitalized patients and hospital area which the patients needed to be followed in (clinical ward or intensive care unit). Distribution of hospitalization status and where the patients were hospitalized at, clinical ward or ICU, according to the sodium, chloride and calcium levels of the participants are shown in Table 2.

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Table 2. Distribution of hospitalization status.

	Hospitalization Status				Clinical Ward or ICU			
	Discharge		Hospitalization		Clinical Ward		ICU	
	Number	(%)	Number	(%)	Number	(%)	Number	(%)
Sodium value	**n=120**				**n=62**			
≤135 mmol/L	24	47.1	27	52.9	15	55.6	12	45.4
≥136 mmol/L	34	49.3	35	50.7	17	48.6	18	51.4
		p=0.810				p=0.585		
Chloride value	**n=120**				**n=62**			
≤98.5 mmol/L	21	38.2	34	61.8	18	52.9	16	47.1
≥98.6 mmol/L	37	56.9	28	43.1	14	50	14	50
		p=0.041				p=0.818		
Calcium value	**n=117**				**n=62**			
≤8.79 mg/dL	24	42.9	32	57.1	17	53.1	15	46.9
≥8.80 mg/dl	33	54.1	28	45.9	13	46.4	15	53.6
		p=0.224				p=0.605		

Three (2.5%) of the participants were found to be deceased when we evaluated the mortality and recurrent admission to the hospital of the patients who were included to our study. One (0.8%) of the participants was admitted to the emergency service when we evaluated the recurrent hospital admission in one month period. Mortality and recurrent hospitalization rates were low and not statistically significant.

DISCUSSION

The main goal of the study was detecting the availability of serum sodium and chloride levels in deciding hospitalization and prognosis of the patients with acute heart failure. Also, we tried to find the answer whether is there any relationship between serum sodium and chloride levels and ICU admission.

Gheorghiade et al. reviewed data from OPTIMIZE-HF (The Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) which included 48612 patients from 259 hospitals. They evaluated the patients with acute heart failure after discharge from hospital in 90 days. The rate of hospitalization and requirement of inotrope medication were higher in hyponatremic patients.

Hospitalization duration and mortality rate were detected higher on decompensated heart failure patients with low serum sodium level in a study by Klein et al. (2005) which included 949 patients.

The relationship between low serum sodium levels and higher rate of mortality and recurrent hospital admission was detected as statistically significant in the study of Park et al. (2016) which included 1650 patients from eight centers.

Mohan et al. (2013) scanned patients who had hyponatremia and were hospitalized for this reason between the years 1999 and 2004 from United States National Health and Nutrition Examination Survey database and researched hyponatremia's effect on mortality rate. 38% of the patients who were hospitalized for heart failure with hyponatremia died in this study and this was statistically significant. Kearney et al. (2002) reviewed data from UK-HEART (The United Kingdom Heart failure Evaluation and Assessment of Risk Trial) which included all the hospital's data between December 1993 and April 1995. Low serum sodium levels were found to affect the mortality rate of the patients with heart failure when they analyzed data of the 553 patients with heart failure who had been hospitalized. According to the study, low serum sodium levels were found to increase the risk of terminal chronic heart failure.

We found that the patients with hyponatremia had higher hospitalization rate, even though this situation was not found statistically significant (p=0.810). Also, hyponatremia was not found to be a determinant factor in hospitalization at intensive care unit and was found to be statistically insignificant (p=0.585). We could not conduct a statistical analysis about relationship between serum sodium levels and mortality due to the low mortality rate (2.5%) in our study.

Serum chloride levels below than 96 meq/L was related with higher mortality rate independent of serum sodium levels in a study by Grodin et al. (2015), which included 1318 patients with heart failure between July 2008 and December 2013 at Cleveland Clinic. Grodin et al. (2016), researched the patients who had coronary angiography in Cleveland Clinic between the years of 2001-2006 retrospectively and they analyzed 1260 patients who got heart failure diagnosis in follow up. In the results of analysis, they noticed that the patients with low serum chloride levels had significantly increased risk of mortality than the patients with normal or high serum chloride levels.

Serum chloride levels of the 2033 patients who had been hospitalized for heart failure were recorded at the beginning and serum chloride levels of 1960 patients were recorded after 14th day of hospitalization in the study by Ter Maaten et al. (2016) reviewing the data from PROTECT (Placebo-controlled Randomized Study of the Selective A1 antagonist Rolofylline for Patients Hospitalized with Acute Decompensated Heart Failure and Volume Overload to Assess Treatment Effect on Congestion and Renal Function) trial. There was a significant relationship between lower serum chloride levels and hospitalization for acute heart failure. Hypochloremia that persisted or occurred in the duration of 14 days was related with lower survival rate.

Grodin et al. (2018), reviewed the data from the TOPCAT (Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist) trial. They analyzed 942 patients hospitalized for heart failure and their serum chloride levels. Lower serum chloride levels was not found to be significantly variable in hospitalization of the patients. But lower serum chloride levels had significant relationship with increased mortality rate of cardiovascular diseases and death by all causes.

Zhang et al. (2018), found a negative correlation between the serum chloride levels and long-term mortality in their study that included 1021 heart failure patients between October 2009 and December 2011. In the statistical analysis made with ROC curve, the cut off value for chloride to predict mortality was found as 102.8 mmol/L.

Patients with chloride levels below than 98.5 mmol/L had increased risk of hospitalization when we analyzed serum chloride levels of the 120 patients who were included to our study (p=0.041). But there was no significant relationship between serum chloride levels and ICU admission or clinical ward

admission (p=0.818). We could not conduct a statistical analysis about the relationship between serum chloride levels and mortality due to the low mortality rate (2.5%) in our study.

CONCLUSION

Low serum chloride level is a significant indicator that predicts need for hospitalization of acute decompensated heart failure patients who were admitted to the emergency service. But that is not possible to say the same thing about low serum sodium levels according to the results of our study.

Limitation

The rate of mortality and recurrent hospital admission for heart failure were low in our study so we could not conduct any statistical analysis between serum sodium, chloride levels and mortality rate or recurrent hospital admission rate. This situation was a big limitation for our study.

Conflict of Interest: There is no conflict of interest among the authors.

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