

Diagnostic Usefulness of the Urinary Na/K Ratio and Serum Chloride in Children with Decompensated Heart Failure

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

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List of Contents

Title	Page No.
List of Tables	i
List of Figures	iv
List of Abbreviations	vi
Introduction	1
Aim of the Work.....	12
Review of Literature	
📖 Heart Failure in Pediatrics	13
📖 Diuretics & Diuretic Resistance	37
📖 Electrolyte Abnormalities in Heart Failure	51
Subjects and Methods	64
Results	78
Discussion	112
Summary	132
Conclusion.....	137
Recommendations	138
References	139
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table (1):	Common signs and symptoms of heart failure in children	18
Table (2):	Showing comparison between Modified Ross classification and NYHA classification	18
Table (3):	Scoring system for grading CHF in infants:	20
Table (4):	Drugs used in pediatric heart failure	30
Table (5):	Showing differences between Aquaretics and Diuretics	35
Table (6):	Basic data of the included patients	78
Table (7):	Diagnosis of the patients included	79
Table (8):	Clinical data of the studied patients on admission and follow up	80
Table (9):	Chest x ray of the patients on admission and follow up	81
Table (10):	Serum electrolytes and acid base status on admission and follow up	82
Table (11):	Renal function and Urinary parameters in the studied patients on admission and follow up	83
Table (12):	Demographic data and anthropometric measures of patients requiring Furosemide infusion and those kept on interval dosing	84
Table (13):	Clinical and radiological data of the patients on furosemide infusion versus those maintained on interval dosing	85

List of Tables (Cont...)

Table No.	Title	Page No.
Table (14):	Serum electrolyte of the patients on furosemide infusion versus those maintained on interval dosing	86
Table (15):	Urinary parameters of patients on Furosemide infusion versus those maintained on interval dosing	87
Table (16):	Parameters of diuretic response in the two groups	89
Table (17):	demographic data and anthropometric measures in patients with or without hypochloremia.....	91
Table (18):	Relation between hypochloremia and Diuretic dose	92
Table (19):	Change of furosemide therapy after admission in patients with or without hypochloremia.....	93
Table (20):	Comparison of clinical and radiological features of patients with or without hypochloremia on presentation and follow up	95
Table (21):	Showing comparison of serum electrolytes, acid base status and renal parameters of patients with or without hypochloremia on presentation and follow up.....	96
Table (22):	Showing comparison of urinary electrolytes and Urinary parameters of patients with or without hypochloremia on presentation and follow up	97

List of Tables (Cont...)

Table No.	Title	Page No.
Table (23):	Comparison of diuretic response in patients with or without hyponatremia	99
Table (24):	Correlation between serum chloride and demographic data, clinical, laboratory changes and different parameters for assessment of diuretic response	102
Table (25):	Demographic and anthropometric measures in patients with or without hyponatremia	104
Table (26):	Showing diuretics use in patients with or without hyponatremia	105
Table (27):	Clinical and radiological data in patients with or without hyponatremia	106
Table (28):	Showing serum electrolytes, acid base status and renal parameters in patients with or without hyponatremia	107
Table (29):	Urinary electrolytes in patients with or without hyponatremia	108
Table (30):	Showing measures of diuretic response in patients with or without hyponatremia	109
Table (31):	Comparison of diuretic response in patients with normal versus abnormal serum electrolytes	110

List of Figures

Fig. No.	Title	Page No.
Figure (1):	CXR showing "egg on side" heart with enlargement of the cardiac silhouette with narrowing of the superior mediastinum.....	23
Figure (2):	Chest radiograph showing Total Anomalous Pulmonary Venous Return (TAPVR).....	24
Figure (3):	Electrocardiogram of patient with anomalous left coronary artery from the pulmonary artery (ALCAPA).....	25
Figure (4):	Hyponatremia in heart failure	53
Figure (5):	Hypokalemia in heart failure.....	61
Figure (6):	Diagnoses of the patients included in the study.	79
Figure (7):	Bar chart comparing relation serum chloride at day 1 and day 3.....	86
Figure (8):	Bar chart comparing net fluid output at day 3 admission with or without Furosemide infusion.	88
Figure (9):	Box plot showing significantly less change in Na/K ratio with furosemide infusion.....	90
Figure (10):	Box plot showing significantly less change in body weight in patients with furosemide infusion.	90
Figure (11):	Bar chart comparing dose of furosemide in normal and hypochloremic patients.	92
Figure (12):	Bar chart comparing chloride status in patients on furosemide infusion or shots.	94

List of Figures (Cont...)

Fig. No.	Title	Page No.
Figure (13):	Comparing Net fluid out put/40 mg furosemide in Hypochloremic and Normochloremic patients.....	98
Figure (14):	Showing that hypochloremic group had more negative change in Na/K ratio denoting poorer diuretic response.....	100
Figure (15):	Showing that hypochloremic group needed more cumulative dose of furosemide denoting poorer diuretic response.....	100
Figure (16):	Showing that hypochloremic group had less change in body weight/40 mg furosemide denoting poorer diuretic response.	101
Figure (17):	Box plot showing relation between cumulative diuretic dose and different electrolyte abnormalities.	111
Figure (18):	Box plot showing relation between Change in bodyweight /total diuretic dose and different electrolyte abnormalities.	111

List of Abbreviations

Abb.	Full term
<i>ACEI</i>	<i>Angiotensin Converting Enzyme Inhibitor</i>
<i>ACHF</i>	<i>Advanced Chronic Heart Failure</i>
<i>ADH</i>	<i>Anti Diuretic Hormone</i>
<i>ADHF</i>	<i>Acute Decompensated Heart Failure</i>
<i>AHF</i>	<i>Acute heart failure</i>
<i>ALCAPA</i>	<i>Anomalous left coronary artery from the pulmonary artery</i>
<i>ANP</i>	<i>Atrial Natriuretic Peptide</i>
<i>AQP2</i>	<i>Aquaporin 2</i>
<i>ARBs</i>	<i>Angiotensin II Receptor Blockers</i>
<i>AS</i>	<i>Aortic Stenosis</i>
<i>ASD</i>	<i>Atrial Septal Defect</i>
<i>ATP</i>	<i>Adenosine triphosphate</i>
<i>AVP</i>	<i>Arginine Vasopressin</i>
<i>BMI</i>	<i>Body Mass Index</i>
<i>BNP</i>	<i>Brain Natriuretic Peptide</i>
<i>BUN</i>	<i>Blood Urea Nitrogen</i>
<i>BW</i>	<i>Body Weight</i>
<i>CAVC</i>	<i>Common Atrioventricular canal</i>
<i>CHD</i>	<i>Congenital Heart Disease</i>
<i>CHF</i>	<i>Congestive Heart Failure</i>
<i>CKD</i>	<i>Chronic kidney disease</i>
<i>CL</i>	<i>Chloride</i>
<i>COA</i>	<i>Coarctation of Aorta</i>
<i>COP</i>	<i>Cardiac output</i>
<i>CRT</i>	<i>Cardiac Resynchronization Therapy</i>
<i>CTR</i>	<i>Cardiothoracic ratio</i>
<i>CXR</i>	<i>Chest X Ray</i>
<i>DCM</i>	<i>Dilated Cardio Myopathy</i>
<i>ECG</i>	<i>Electro Cardio Gram</i>

List of Abbreviations (Cont...)

Abb.	Full term
<i>ECMO</i>	<i>Extra Corporeal Membrane Oxygenation</i>
<i>EF</i>	<i>Ejection Fraction</i>
<i>EPHESUS</i>	<i>Eplerenone Heart Failure Efficacy and Survival Study</i>
<i>EVEREST</i>	<i>Efficacy of Vasopressin Antagonist in Heart Failure Outcome Study with Tolvaptan</i>
<i>GFR</i>	<i>Glomerular Filtration Rate</i>
<i>GLDH</i>	<i>Glutamate Dehydrogenase</i>
<i>h</i>	<i>Hour</i>
<i>H</i>	<i>Hydrogen</i>
<i>HF</i>	<i>Heart Failure</i>
<i>HFNEF</i>	<i>Heart Failure with Normal Ejection Fraction</i>
<i>HFREF</i>	<i>Heart Failure with Reduced Ejection Fraction</i>
<i>HIV</i>	<i>Human Immunodeficiency Virus</i>
<i>ICD</i>	<i>Implantable Cardioverter Defibrillator</i>
<i>ISE</i>	<i>Ion Specific Electrode</i>
<i>IV</i>	<i>Intravenous</i>
<i>IVS</i>	<i>Intact Ventricular Septum</i>
<i>K</i>	<i>Potassium</i>
<i>LV</i>	<i>Left Ventricle</i>
<i>LVEDD</i>	<i>Left Ventricular End Diastolic Diameter</i>
<i>LVESD</i>	<i>Left Ventricular End Systolic Diameter</i>
<i>MI</i>	<i>Myocardial infarction</i>
<i>Na</i>	<i>Sodium</i>
<i>NAD</i>	<i>Nicotinamide Adenine Dinucleotide</i>
<i>NADH</i>	<i>Nicotinamide Adenine Dinucleotide Dehydrogenase</i>
<i>NADPH</i>	<i>Nicotinamide Adenine Dinucleotide Phosphate</i>
<i>NCC</i>	<i>Na-Cl Co transporter</i>
<i>NKCC2</i>	<i>Sodium-Potassium-Chloride Co transporter</i>
<i>NKCC2</i>	<i>Sodium-Potassium-Chloride Co transporter</i>

List of Abbreviations (Cont...)

Abb.	Full term
<i>NO</i>	<i>Nitric Oxide</i>
<i>NT BNP</i>	<i>N- Terminal Brain Natriuretic Peptide</i>
<i>NYHA</i>	<i>New York Heart Association</i>
<i>PCT</i>	<i>Proximal Convoluted Tubule</i>
<i>PCWP</i>	<i>Pulmonary capillary wedge pressure</i>
<i>PDA</i>	<i>Patent Ductus Arteriosus</i>
<i>PVC</i>	<i>Poly Vinyl Chloride</i>
<i>RAAS</i>	<i>Renin Angiotensin Aldosterone System</i>
<i>Sa O2</i>	<i>Oxygen saturation</i>
<i>SCD</i>	<i>Sudden Cardiac Death</i>
<i>Sig</i>	<i>Significance</i>
<i>SNS</i>	<i>Sympathetic Nervous System</i>
<i>SPSS</i>	<i>Statistical package for social science</i>
<i>TAPVC</i>	<i>Total Anomalous Pulmonary Venous Connection</i>
<i>TAPVR</i>	<i>Total Anomalous Pulmonary Venous Return</i>
<i>TGA</i>	<i>Transposition of Great Arteries</i>
<i>UOP</i>	<i>Urine output</i>
<i>WRF</i>	<i>Worsened Renal Function</i>
<i>V2R</i>	<i>vasopressin type 2 receptor</i>
<i>VAD</i>	<i>Ventricular Assist Device</i>
<i>VEC</i>	<i>Extracellular volume</i>
<i>VSD</i>	<i>Ventricular Septal Defect</i>
<i>WNKs</i>	<i>With No Lysine Kinases</i>
<i>Wt</i>	<i>Weight</i>

ABSTRACT

Objective: Comparing diuretic efficacy between high dose furosemide as a continuous infusion and bolus injections in children with congenital left to right shunts presenting with decompensated chronic heart failure.

Outcome measures: Diuretic efficacy of furosemide therapy assessed by net fluid output /40mg furosemide, change in Na/K ratio and change in body weight/40 mg furosemide in children with acute on top of chronic heart failure.

Patients and methods: The study included twenty six (26) patients, median age 0.75 years (range 0.42-1.2 years) with congenital left to right shunts presenting with normal ejection fraction heart failure. Two urine samples were collected from patients on admission and at day 3 of admission for immediate assay of urinary Na and K.

Results: Thirteen patients (50%) were on continuous furosemide infusion versus thirteen (50%) that were kept on furosemide bolus injections. Patients on Furosemide infusion had significantly prolonged Capillary refill time and worse ROSS classification on admission and on follow up. On assessment of the diuretic response in the two groups we have found that patients on furosemide infusion had decreased Na/K ratio ($P=0.017$), increased furosemide dose ($P=0.018$), had less change in body weight($P=0.000$) in relation to the diuretic dose and less fluid output ($p=0.081$).

Conclusion: Augmentation of furosemide therapy in the form of infusion rather than interval dosing in patients with heart failure is not always associated with an equivalent increase in diuresis and may not benefit the patient.

Key words: Pediatric, heart failure, diuretic resistance, furosemide infusion

Abbreviations: ADHF: Acute Decompensated Heart Failure, CHF: Chronic Heart Failure, CTR: Cardiothoracic Ratio, CXR: Chest x ray, HF: Heart Failure, K: Potassium, Na: Sodium, NYHA: New York Heart Association, SSPS: Statistical package for social science, UOP: Urine output.

INTRODUCTION

Hear failure (HF) is a major clinical issue, which imposes a heavy social and economic burden on health care systems. In fact, it directly causes approximately 1 million hospital admissions every year in Adults in the United States (*Roger et al., 2013*).

Fluid overload, clinically evident as systemic and/or pulmonary congestion, represents the most frequent cause of hospitalization in this clinical setting, plays a central role in the progression of HF and has a major negative prognostic impact (*Dupont et al., 2011*).

Adequate control of systemic congestion along with maintenance and improvement of renal function represents a key target of patient management in HF (*Greene et al., 2013*). On these grounds, current guidelines suggest that decongestion should be attempted through diuretic therapy. Diuretics, essentially loop diuretics, are utilized in more than 90% of patients with HF to obtain an increase in urinary output, dyspnea relief and weight loss (*Ponikowski et al., 2016*).

Diuretic treatment of systemic and pulmonary congestion can be ineffective in some patients with HF – a condition commonly referred to as diuretic resistance or refractoriness. However, the lack of an operational definition makes it difficult to define the exact incidence of this problem. It is thought that

about one third of patients with HF, especially in the phase of acute decompensation, may present with apparent diuretic refractoriness (*Voors et al., 2014*).

Lower chloride (CL) levels are linked to reduced loop diuretic response. Hypochloremic patients have a greater relative wasting of chloride compared with sodium(Na), whereas renal free water clearance does not seem to be impaired, suggesting that depletion rather than dilution may be the responsible mechanism (*Hanberg et al., 2016*).

Adult studies have demonstrated that hypochloremia is associated with neurohormonal activation and diuretic resistance with chloride depletion as a candidate mechanism. Sodium-free chloride supplementation can be associated with increases in serum chloride and changes in several cardiorenal parameters as aminoterminal pro B-type natriuretic peptide which decreases with chloride supplementation and the blood urea nitrogen to creatinine ratio which increases with chloride supplementation (*Hanberg et al., 2016*).