Comparative Study between Fractional Excretion of Sodium and Fractional Excretion of Urea in Differentiating Prerenal from Renal Acute Kidney Injury in ICU Patients with Circulatory Shock

Thesis

Submitted for Partial Fulfillment of the Master Degree In in Anesthesia and Intensive Care and Pain Management

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2019

Acknowledgement

First and foremost, I feel always indebted to ***God,*** the Most Kind and Most Merciful.

I'd like to express my respectful thanks and profound gratitude to ***Prof. Dr. Sherif Wadie Nashed Sargious,*** Professor of Anesthesia and Intensive Care and Pain Management, Faculty of Medicine – Ain Shams University, for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.

I am also delighted to express my deepest gratitude and thanks to ***Dr. Mahmod Hassan Mohamed Hassan,*** Assistant Professor of Anesthesia and Intensive Care and Pain Management, Faculty of Medicine – Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.

I am deeply thankful to ***Dr. Sameh Ahmed Refaat Mostafa,*** Lecturer of Anesthesia and Intensive Care and Pain Management, Faculty of Medicine – Ain Shams University, for her great help, active participation and guidance.

I would like to express my hearty thanks to all ***My Family*** for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients participated in this study.

Dr. George Saad Rizk Saad

Dedication

To The Soul of My Late Professor

Professor Dr. Mahmoud Hassan Mohamed Hassan

He was a great source of knowledge and experience; he was the corner stone of this work

Our great thanks for his encouragement and patience

May Allah bless his Soul

List of Contents

List of Tables

List of Figures

List of Abbreviations

Abbr.	Full term
ACE	Angiotensin-Converting Enzyme
ARF	Acute Renal Failure
ATN	Acute Tubular Necrosis
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
D5W	Dextrose in Water
ESRD	End-Stage Renal Disease
FELi	Fractional Excretion of Trace Lithium
FENa	Fractional Excretion of Sodium
FEUA	Fractional Excretion of Uric Acid
FEUrea	Fractional Excretion of Urea
GFR	Glomerular Filtration Rate
KDIGO	Kidney Disease Improving Global Outcomes
RFI	Renal Failure Index
ROC	Receiver Operating Characteristic
SCr	Serum Creatinine
SD	Standard Deviation
UNa	Urinary Sodium
UO	Urine Output

INTRODUCTION

The rate of acute kidney injury (AKI) in Intensive Care Units is 5% and if it was a part of multiple organ disease the rate of death increases up to 50% ***(Kirwan, 2015).***

Prerenal acute renal injury accounts for 30–40% of cases of decreased urine output in ICU and it is easy to solve this problem by correcting the underlying disorder, but prolonged or severe prerenal insult may proceed to oliguric renal acute renal injury ***(Abernethy and Lieberthal, 2012).***

There is big difference in the results between patients who suffer prerenal insult and those who have renal injury as prerenal insult is a representation of the physiological hemodynamic response to the decreased circulatory volume ***(Uchino et al., 2005).***

Early diagnosis of either type of them leads to proper management and better prognosis ***(Westhuyzen, 2003).*** Depending only on the fluid challenge test to differentiate between them may lead to fluid overload in renal acute injury ***(Westhuyzen 2003, Fahimi 2009).***

Different clinical chemistry tests have been used to distinguish prerenal from renal injury as urine analysis, osmolarity, specific gravity, urinary sodium level, urinary to plasma creatinine ratio and blood urea to plasma creatinine ratio but they all aren't sensitive and specific enough ***(Jayasundera and Macnab, 2012).***

Fractional excretion of sodium (FENa) is one test that showed reasonable specificity and sensitivity and it is defined as the percentage of Na+ filtered by the kidney which is not reabsorbed and excreted in the urine. The medical principle is that in cases of decreased glomerular filtration rate as in hypovolemia, reabsorption of Na+ from renal tubules increases so FENa in cases of prerenal acute kidney insult is decreased ***(Jayasundera and Macnab, 2012).***

Also FENa is a simple laboratory test; it is influenced by lots of medications and medical conditions. As example; diuretics increase sodium secretion so FENa is falsely high and norepinephrine decreases sodium excretion so FENa is falsely low ***(Bacic et al., 2005, Van Biesen et al., 2005).***

As most patients in ICU receives diuretics or norepinephrine as a part of their medication due to their

shock and AKI, results of FENa tests are not accurate in those patients ***(Lattanzio et al., 2009).***

Urea is not affected by diuretic therapy or epinephrine used in these cases as it is dependent on passive forces so Fractional Excretion of Urea (FEUrea) can be used as an alternative to FENa ***(Carvounis et al., 2012).***

The goal of this study was to compare FENa and FEUrea in differentiating renal from prerenal acute renal injury, and to observe the effect of diuretics on both of them which was not specifically studied before especially in patients with AKI complicating circulatory shock.

AIM OF THE WORK

Comparison between FENa and FEurea in differentiating renal from prerenal acute kidney injury in circulatory shock, and the effect of diuretics on their handling.

REVIEW OF LITERATURE

Circulatory shock refers to an abnormality of the circulatory system in which there is inadequate tissue perfusion because of a relatively or absolutely inadequate cardiac output. The causes are divided into four groups: **hypovolemic shock**, an inadequate volume of blood to fill the vascular system; **distributive, vasogenic**, or **low-resistance shock**, an increase in the size of the vascular system produced by vasodilation in the presence of a normal blood volume; **cardiogenic shock**, inadequate heart output as a result of myocardial abnormalities; and **obstructive shock**, inadequate cardiac output as a result of blood flow obstruction in the lungs or heart.

Diagnosis of circulatory shock is made on the following criteria:

First, systemic arterial decreased blood pressure is usually present, but the degree of this decrease may be only moderate, especially in patients with chronic increased blood pressure. Typically, in adults, the systolic arterial pressure is

below 90 mm Hg or the mean arterial pressure is less than 70 mm Hg, with associated increased heart rate

Second, there are clinical signs of decreased tissue perfusion, which are obvious through the three systems of the body: cutaneous (skin that is cold and clammy, with vasoconstriction and bluish discoloration, findings that are most evident in low-flow states), renal (urine output of <0.5 ml /kg/hr.), and neurologic (changed mental state, which typically includes disorientation and confusion).

Third, increased serum lactate level is typically found, indicating abnormal oxygen metabolism in tissues. The normal blood lactate level is nearly 1 mmol / L, but the level is increased (>1.5 mmol per liter) in acute failure of circulatory system.

Types of shock:

Shock is classified into four major types depending on the responsible cause: low volume, cardiogenic, obstructive, and distributive shock ***(ATLS Student Course Manual, 2018).***

1. Hypovolemic Shock

Hypovolemic shock is characterized by hypotension; a rapid, thready pulse; cold, pale, clammy skin; intense thirst; rapid respiration; and restlessness or, alternatively, torpor. Urine volume is markedly decreased. However, none of these findings is invariably present. Hypovolemic shock is commonly subdivided into categories on the basis of cause. The use of terms such as "hemorrhagic shock," "traumatic shock," "surgical shock," and "burn shock" is of some benefit because although there are similarities among these various forms of shock, there are important features that are unique to each.

In hypovolemic and other forms of shock, inadequate tissue perfusion leads to increased anaerobic glycolysis, with the production of large amounts of lactic acid. In severe cases, the blood lactate level rises from a normal value of about 1mmol/L to 9 mmol/L or more. The resulting lactic acidosis depresses the myocardium, decreases peripheral vascular responsiveness to catecholamines, and may be severe enough to cause coma.

A decrease in pulse pressure or mean arterial pressure decreases the number of impulses ascending to the brain from the arterial baroreceptors, resulting in an increased vasomotor discharge. The resulting vasoconstriction is generalized, sparing only the vessels of the brain and the heart. The coronary vessels are dilated because of the increased myocardial metabolism secondary to an increase in heart rate. Vasoconstriction in the skin accounts for the coolness and pallor, and vasoconstriction in the kidneys accounts for the shutdown in renal function.

The immediate cardiac response to hypovolemia is tachycardia. With more extensive loss of volume, tachycardia can be replaced by bradycardia. With very severe hypovolemia, tachycardia reappears. Bradycardia may be due to the unmasking of a vagally mediated depressor reflex, perhaps related to limiting blood loss. Vasoconstriction in the kidney reduces glomerular filtration. This reduces water loss, but it reaches a point at which nitrogenous products of metabolism accumulate in the blood (**prerenal azotemia**). If hypotension is prolonged, there may be severe renal tubular damage, leading to acute kidney injury. The fall in blood pressure and the decreased O2-carrying power of the blood