THE EFFECTIVENESS OF ENTERAL TABLE SALT IN HYPONATREMIA AT THE KENYATTA NATIONAL HOSPITAL CRITICAL CARE UNIT

A DISSERTATION IN PART FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF DEGREE OF MASTER OF MEDICINE IN ANAESTHESIA, UNIVERSITY OF NAIROBI

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DECLARATION

I**, Dr. Mohammed Yahya Rashid**, declare that the work contained herein is my original idea and has not been presented at any other place to the best of my knowledge.

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DEDICATION

To my parents, Prof. Rashid M. Mzee and Zalikha Muhammad Sabur, whose support, guidance and unconditional love have brought me this far.

To my beloved wife, Faiza Abdirahim and daughter Swafiya: my joy and strength.

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ABBREVIATIONS

ACTH: Adrenocorticotrophic Hormone

ADH: Antidiuretic Hormone

ANP: Atrial Natriuretic Peptide

BNP: Brain Natriuretic Peptide

CVVH: Continous Veno-Venous Hemofiltration

FeNa: Fractional Excretion of Sodium

ODS: Osmotic Demyelination Syndrome

SIADH: Syndrome of Inappropriate Antidiuretic Hormone secretion

SLEDD: Slow Low-Efficiency Daily Dialysis

SPSS: Statistical Package for the Social Scale

OPERATIONAL DEFINITIONS

Effectiveness: Percentage of patients with normal sodium levels within 48 hours of enteral table salt administration for hyponatremia.

Hypernatremia: Sodium level above 155mmol/L

Hypertonic saline: 3% sodium chloride

Hyponatremia: Sodium level below 135mmol/L

ABSTRACT

Introduction: Hyponatremia, defined as serum sodium level of less than 135mEq/L [1], is the most common electrolyte abnormality in hospitalised patients. It is estimated to occur in 2-4% of hospitalised patients and in 15-30% of critically ill patients [2]. Mortality for patients with acute hyponatremia is quoted as high as 50% while that of chronic hyponatremia at 10-20%[3,4].

The principles of management of hyponatremia might not be applicable in many CCU cases creating the dilemma of what to do in situations where fluid cannot be restricted or the underlying condition is not responding to treatment fast enough. This together with the inconsistent supply of hypertonic saline and the unavailability of the newer drugs and slow sodium tablets has resulted in the use of enteral table salt in correcting hyponatremia at our KNH CCU set up[5-10].

There is paucity of data on enteral table salt as the sole agent in correcting hyponatremia especially in the critical care set up. In the management of syndrome of inappropriate ADH secretion (SIADH), Binu et al[11] and Rose BD[12] describe the use of oral salt and furosemide but not in a critical care setup, neither do they discuss the effectiveness. Another case report by Karen et al [13] also describes the use of oral sodium in hyponatremia but in an outpatient set up and does not discuss its effectiveness.

Objective: The primary objective was to determine the effectiveness of enteral table salt in correcting hyponatremia at the Kenyatta National Hospital Main Critical Care Unit. The secondary objective was to determine the safety or associated side effects of enteral table salt at the Kenyatta National Hospital Main Critical Care Unit.

Research Methodology: This was a prospective observational study. Patients with hyponatremia where table salt had been prescribed were included in the study. Serial plasma sodium levels were analyzed from the moment the table salt was prescribed using a standardized analyzer. Associated side effects were also documented as well as changes in the patients' clinical status. The study utilised 40 consenting adult patients who fit the inclusion criteria during the course of their treatment. Data was entered into and managed in Microsoft Excel 2013 data entry sheet pre-coded to reflect the design of the data collection tool. Data cleaning was done continuously during data collection and the final dataset was exported to SPSS version 21.0 statistical software for analysis. The study findings were presented using tables and graphs.

Findings: 32 patients (80%) had normal sodium levels after 1 or 2 days of table salt administration while 4 patients (10%) had hypernatremia and 4 patients (10%) persisted with hyponatremia despite 2 days of table salt administration. This translates to 90% effectiveness in correcting hyponatremia within 48 hours. Of the 80% with normal sodium levels, 65% were corrected within 24 hours while the remaining 15% required 48 hours of table salt administration.

The overall mean change in sodium levels was 6.8mmol/L. The overall mean change in sodium levels per 104meq/L (equivalent to sodium content in 1 tea spoon of salt) intake of sodium was

1.7mmol/L. The average dosing frequency was 2.25 tea spoons of salt per day (ranging from 1 to 4 tea spoons of table salt per day).

Only 1 patient (2.5%) developed diarrhoea and 2 patients (5%) had deteriorating consciousness. No patient experienced any of the other associated side effects namely; Nausea/Vomiting, Convulsions, Abnormal posturing/Movement and Nystagmus.

Conclusion: We, therefore, conclude from our findings that enteral table salt is 90% effective in correcting hyponatremia in the critical care set up. We also conclude that it is relatively safe.

CHAPTER ONE: INTRODUCTION

1.0 Background Information

Sodium is the principal extracellular cation. It is responsible for the generation of action potentials in muscle and nerves. Pathological increase or decrease of total body sodium is associated with corresponding changes in plasma and extracellular volume. Hyponatremia and hypernatremia result from relative excesses or deficits of water respectively. Regulation of sodium is by the renal and endocrine systems. Aldosterone, atrial natriuretic peptide (ANP) and antidiuretic hormone(ADH) amongst other effectors control the total body sodium[3].

Normal serum sodium is within the ranges of 135 to 155meq/L. Hyponatremia, defined as serum sodium concentration of less than 135mEq/L [1], is the most common electrolyte abnormality in hospitalised patients. It is estimated at 2-4% of hospitalised patients and 15-30% of critical care patients[2]. In the majority of hyponatremic patients, total body sodium may be normal or increased. The commonest clinical associations of hyponatremia include post operative patients, intracranial diseases, malignancies, drugs including medications and pulmonary diseases[3]. The mortality for patients with acute hyponatremia is quoted as high as 50% while mortality for chronic hyponatremia at 10-20%[4].

Low serum sodium indicates excess total body water per solute in the absence of hyponatremia associated with normal or increased tonicity. This is otherwise known as dilutional hyponatremia. In normal individuals, this would trigger a compensatory mechanism to excrete the excess water and restore balance. In persistent hyponatremia there is a pathological inability to excrete the excess water. Dilutional hyponatremia is seen in three clinical situations where the extracellular volume is low, normal or high[5].

Hyponatremia may present with minor signs like decreased mentation and nausea or more severe symptoms including deteriorating of consciousness, seizures, stupor, coma, hyponatremic encephalopathy and osmotic demyelination syndrome[5,14,10].

Evaluation of hyponatremia includes assessment of serum sodium concentration, serum osmolality, urine sodium, urine osmolality, urine to sodium electrolyte ratio, fractional excretion of sodium, serum uric acid and urea concentrations, acid-base and potassium balance, hormonal profiles, saline infusion test and imaging modalities chest x-ray, computerised tomography scan and magnetic resonance imaging.

The management of hyponatremia is determined by the severity of the hyponatremia, acuteness of onset, presence or absence of symptoms, volume status and the etiology of the hyponatremia[5, 6,7,8] . Severe or symptomatic hyponatremia is rapidly corrected with hypertonic saline while mild to moderate, asymptomatic or chronic hyponatremia is managed by total body water correction and treatment of underlying causes amongst other newer medications. However this might not be practical in many CCU cases creating the dilemma of what to do in situations where fluid cannot be restricted (patients on endogastric feeds, total parenteral nutrition or high fluid state requirement) or the underlying condition is not responding to treatment fast enough. This together with the inconsistent supply of hypertonic saline (with its feared complication) and the newer drugs has resulted in the use of enteral table salt in correcting most cases of hyponatremia at KNH CCU.

1.1 Research Questions

1. What is the effectiveness of enteral table salt in correcting hyponatremia at the Kenyatta National Hospital Main Critical Care Unit.
2. What are the associated side effects of enteral table salt in correcting hyponatremia at the Kenyatta National Hospital Main Critical Care Unit.

1.2 Research Objectives

The general objective of this study was to determine whether enteral table salt is effective in correcting hyponatremia at the Kenyatta National Hospital Main Critical Care Unit.

1.2.1 Specific Objectives

1. To determine the effectiveness of enteral table salt in correcting hyponatremia at the Kenyatta National Hospital Main Critical Care Unit.
2. To determine the safety or associated side effects of enteral table saltat the Kenyatta National Hospital Main Critical care Unit.

1.3 Justification

The KNH CCU Protocol does not provide a comprehensive guide on management of hyponatremia, neither does it include the role of enteral table salt yet it is routinely used.

The recognised modes of correcting hyponatremia include fluid restriction in normovolemic and hypervolemic hyponatremias, parenteral normal saline in hypovolemic hyponatremia andparenteral hypertonic saline otherwise known as 3% Saline in severe or symptomatic hyponatremia.

At the Kenyatta National Hospital Intensive Care Unit, the supply of hypertonic saline is inconsistent and slow sodium tablets are not readily available hence the use of enteral table salt has been the norm. Most cases of hyponatremia are not severe or symptomatic hence hypertonic saline is not indicated. Fluid restriction cannot be practically applied because most patients' nutritional requirements are administered in fluid states which cannot be restricted due to the compromise on caloric intake and other nutrients.

However there is limited data to support the use of enteral table salt, as the sole agent, in correcting hyponatremia especially in the critical care set up.
This study therefore aimed to assess the effectiveness ofenteral table salt in correcting hyponatremia in the critical care set up.

1.4 Study Assumptions

The study assumed that the primary physician prescribed the adequate amount of enteral table salt for correcting hyponatremia.
The study assumed that the subjects had a normal enteral absorptive capability.
The study assumed that table salt was administered by the primary nurses as prescribed by the primary physician.

CHAPTER TWO: LITERATURE REVIEW

PhysiologicalRole of Sodium

Sodium is the principal extracellular cation. It is responsible for the generation of action potentials in muscle and nerves. Pathological increase or decrease of total body sodium is associated with corresponding changes in plasma and extracellular volume. Hyponatremia and hypernatremia result from relative excesses or deficits of water respectively. Regulation of sodium is by the renal and endocrine systems. Aldosterone, atrial natriuretic peptide (ANP) and antidiuretic hormone(ADH) control the total body sodium[3].

2.0 Regulation of sodium balance and extra cellular fluid

Extracellular fluid (ECF) volume is directly proportional to the total body sodium content hence a positive sodium balance increases ECF and vice versa. The net sodium balance is equal to the total sodium intake (170 mEq/d for adults) minus renal and extrarenal losses with the kidneys playing a crucial role in sodium regulation by excretion.In absence of pathology, urinary sodium concentration reflects effective intravascular volume.

There are multiple mechanisms involved in regulating ECF and sodium and they work in co-ordination or independently. These mechanisms involve volume sensors and volume change effectors.

ECF and total body sodium are tied to each other; this regulation is achieved via sensors that detect changes in the effective intravascular volume. Baroreceptors are the principal volume receptors. Since blood pressure is the product of cardiac output and peripheral vascular resistance, changes in intravascular volume or preload affect cardiac output and eventually blood pressure. Baroreceptors located at the carotid sinus and afferent renal arterioles function as sensors of intravascular volume. Blood pressure changes at the carotid sinus modulate sympathetic activity and ADH secretion while changes at the afferent renal arterioles modulate the rennin-angiotensin-aldosterone system. ADH release is also modulated by stretch receptors in the atrias.

Effectors of volume change eventually alter urinary sodium excretion. Increase in effective intravascular volume increase urinary sodium excretion while decrease in effective intravascular volume decrease urinary sodium excretion. The mechanisms involved include the following:

Renin–Angiotensin–Aldosterone system; the secretion of renin increases formation of angiotensin II which increases the secretion of aldosterone. Aldosterone enhances the reabsorption of Sodium in the distal renal tubules. Angiotensin II is also a vasoconstrictor and potentiates the actions of norepinephrine, it is also involved in sodium reabsorption in the proximal renal tubules.

Antidiuretic Hormone (ADH); ADH has less effects on sodium excretion despite playing a major role in maintaining extracellular volume in situations of decreased effective intravascular volume.

Atrial Natriuretic Peptide (ANP); ANP is secreted by both atrias following distension. Its main actions include arterial vasodilation and urinary sodium and water excretion at the level of the collecting tubules. ANP is also inhibits renin and aldosterone secretion and also antagonizes ADH.

Brain Natriuretic Peptide (BNP); BNP is secreted by the ventricles in response to ventricular overdistention. It is markedly increased in acute congestive cardiac failure resulting in dillutional hyponatremia.

Glomerular Filtration Rate (GFR) and Plasma Sodium Concentration; GFR is directly proportional to intravascular volume. Expansion of intravascular volume increases sodium excretion and vice versa hence maintaining a constant intravascular volume in absence of kidney pathology.

Tubuloglomerular Balance; the amount of sodium reabsorbed in the proximal tubules is controlled within narrow limits. This tubuloglomerular balance is influenced by the rate of renal tubular flow and changes in peritubular capillary hydrostatic and oncotic pressures.

Sympathetic Nervous System Activity; Sympathetic activity increases sodium reabsorption in the proximal tubules and also mediates vasoconstriction reducing renal blood flow. The cardiorenal reflex from stimulation of the left atrial stretch receptors antagonizes this sympathetic renal tone maintainaing a constant ECF volume.

Pressure Natriuresis; Pressure diuresis is independent of hormonal or neural mechanisms. Elevation ofblood pressure results in increased urinary sodium excretion and vice versa[15].

2.1 Introduction to Hyponatremia

Hyponatremia is defined as serum sodium of less than 135mEq/L[1], is the most common electrolyte abnormality in hospitalised patients. It is estimated at 2-4% of hospitalised patients and 15-30% of critical care patients[2].No local data is available on hyponatremia in the critical care set up. In the majority of hyponatremic patients, total body sodium may be normal or increased. The commonest clinical associations of hyponatremia include post operative patients, intracranial diseases, malignancies, drugs including medications and pulmonary diseases[3]. The mortality for patients with acute hyponatremia is quoted as high as 50% while mortality for chronic hyponatremia at 10-20%[4].

Hyponatremia used to be classified as pseudohyponatremia and true hyponatremia. Pseudohyponatremia was an artefact associated with the use of flame photometry which is nowadays an obsolete technique for measuring plasma sodium in hyperlipidemic or hyperprotinemic patients. Direct potentiometry which is the current analytic method directly measures sodium without interference by lipids and proteins[3].

2.2 Classification of hyponatremias

Low plasma sodium indicates excess total body water per solute in the absence of hyponatremia associated with normal or increased tonicity. This is otherwise known as dilutional hyponatremia. In normal individuals, this would trigger a compensatory mechanism to excrete the excess water and restore balance. In persistent hyponatremia there is a pathological inability to excrete the excess water. Dilutional hyponatremia is seen in three clinical situations where the extracellular volume is low, normal or high[5].

Hyponatremia with Decreased Extracellular Volume

Contracted extracellular volume leads to vigorous water retention mediated primarily by ADH release[15]. This is stimulated by atrial stretch receptors and thirst with resultant increased water intake. In such situations, urinary sodium excretion is low and with the resultant increased water intake and retention, the total body water is increased to a greater extent than the reduced amount of solute[16,17,18]. A few exceptions where the urine sodium excretion may be normal or high as a result of both sodium and water loss in urine include adrenal insufficiency, diuretic use and salt loosing nephropathies[5]. Adrenal insufficiency results in excessive permeability of the collecting tubules to water due to lack of cortisol and failure of ADH suppression by low plasma osmolarity. Thiazide diuretics impair sodium and potassium transport at the distal convoluted tubules potentiating the effects of ADH[14,19,18].

Hyponatremia with Increased Extracellular Volume

Hyponatremia with hypervolemia is seen in congestive cardiac failure, nephrotic syndrome, cirrhosis, protein-losing enteropathy and pregnancy. These disorders are associated with increased extracellular volume and the inability to maintain normal intravascular volume. The low intravascular volume, despite the high extracellular volume and total body water, triggers ADH release and the resultant hyponatremia[16,17,18,19,20, 21].

Hyponatremia with Normal Extracellular Volume

Hyonatremia with normovolemia is seen in the syndrome of inappropriate ADH release (SIADH)[19,21,22,23,24,25], psychogenic water ingestion[26,27,28] and decreased solute intake[29]. Decreased solute intake limits the maximum volume of water that can be excreted despite maximum urine dilution. Low protein intake also generates little urea for excretion.

Normovolemic hyponatremia is more commonly seen with SIADH as a result of ADH release in response from a variety of disorders but primarily from pulmonary and CNS pathologies. The pulmonary pathologies include malignancy, tuberculosis, pneumonia, chronic obstructive pulmonary diseases, respiratory failure and mechanical ventilation. The CNS pathologies include encephalitis, status epilepticus, brain tumours, meningitis, head trauma and stroke. The actual mechanism of ADH release in the above disorders remains unclear. Certain drugs have also been associated with SIADH including chemotherapeutics, chlorpropramide, nicotine, tricyclic antidepressants, serotonin reuptake inhibitors and opioids[19,21,22,23,24,25].

Hyponatremia without Hypertonicity

Hyponatremia without hypotonicity was a condition seen in patients with severe hyperprotenemia or hypertriglyceridemia when plasma sodium was measured by flame photometry, now an obsolute method replaced by the use of ion specific sodium electrodes[3,5].

Hyponatremia with Hypertonicity

In this paradoxical condition, hyponatremia is associated with decreased rather than increased total body water. It is commonly seen with hyperglycemia, mannitol infusion and radiopaque contras agents. Both glucose and mannitol add osmoticaly active molecules to the extracellular compartment with resultant water movement from the intracellular to the extracellular compartment. Osmolality increases but plasma sodium falls because of the additional water in the extracellular space[5].

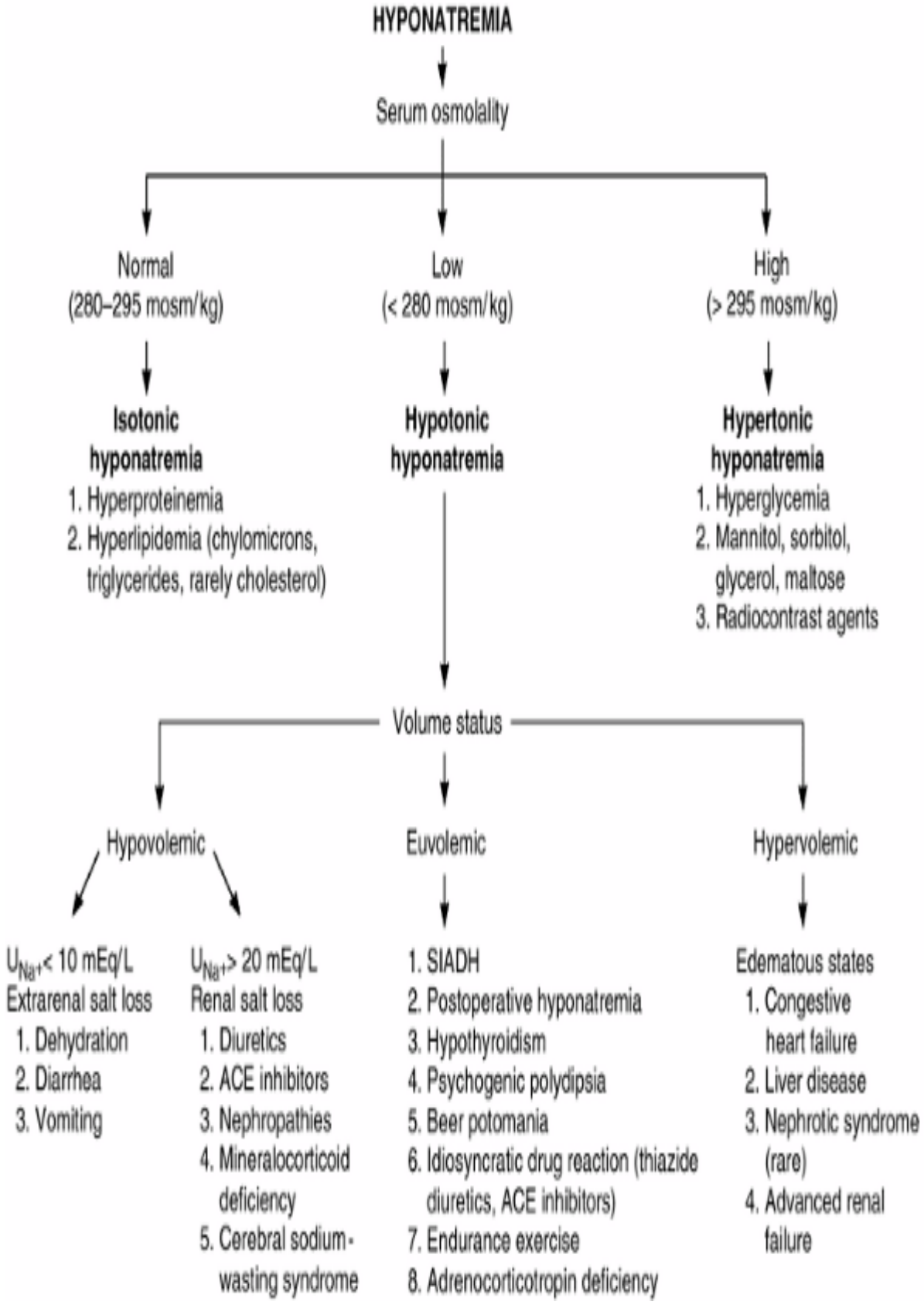

Figure 1: Classification of Hyponatremias [3-5, 15]

2.3 Signs and symptoms of hyponatremia

The rate of change of hyponatremia plays a major role in symptomatology[9]. A rapid fall is associated with more severe acute changes[30]. Hyponatremia with associated hypo osmolality is often asymptomatic until plasma sodium falls below 125meq/L[31]. The symptoms may be minor like decreased mentation or severe including deteriorating conscious levels, seizures, nausea, vomiting, stupor and coma[14]. Severe symptoms are more likely to occur with marked hyponatremia of below 115meq/L in acute setting[32] or 110meq/L in chronic hyponatremia[33] or with rapid deterioration of plasma sodium levels in either of the two[9]. Hyponatremic encephalopathy has been described as a syndrome of opisthotonos, respiratory depression, impaired responsiveness, incontinence, hallucinations, decorticate posturing and seizures[5].

Osmotic demyelination syndrome has been associated with both severe hyponatremia and rapid correction of hyponatremia possibly as a result of adaptation in certain regions of the brain[10]. It often occurs 2 to 6 days after the correction of severe hyponatremia but may also be seen before or during the correction of hyponatremia[9,10]. It may present as locked in syndrome. Associated corticobulbar or corticospinal signs include weakness, spastic quadriparesis, dysphonia and dysphagia. Imaging modalities, CT scan may show radioluscent areas, or a decreased T1-weighted MRI intensity is evident of myelinosis in the central pons and other regions of the brain[5].

Hypovolemic hyponatremic patients may have signs of volume depletion like tachycardia, hypotension, decreased skin turgor or overt weight loss while those with hypervolemic hyponatremia may present with oedema and weight gain.

2.4 Laboratory evaluation of hyponatremia

Serum sodium

The ideal method is direct potentiometry by ion specific electrodes. Pseudohyponatremia (falsely low sodium with normal plasma osmolarity) used to occur when flame photometry was used, now an obsolute method in most clinical laboratories[1,23,34,35]

Serum osmolality

It should be ideally measured by an osmometer, if not available then random blood sugar, serum triglyceride and serum protein could be helpful in differentiating between true, pseudo

and translocational hyponatremia[1,18,23,12]. When blood sugar is less than 300mg/dl, hyperglycemia has minimal interference on serum sodium concentration, above that for each mg increase in blood glucose serum sodium decreases by 1.6 meq/L[36,37]. When serum triglycerides are above 100mg/dl, for every 500mg/dl increase in serum triglycerides, serum sodium falls by 1meq/L. When serum protein is above 8gm/dl, for every 1gm/dl increase in serum protein, serum sodium falls by 4meq/L[38].

Urine sodium

Measurement of urine sodium helps determine the source of sodium loss as either renal or non renal. It is also useful in distinguishing between euvolemic and hypervolemic hyponatremia where clinical assesment of volume status is in accurate[18,19,39,40]. In hypovolemic patients normal saline infusion should supress ADH release and promote the excretion of dillute urine. If a patient has SIADH then ADH supression will not occur and urine osmolality will remain elevated despite the saline infusion[38].

Urine osmolality

Urine osmolality is useful in distinguishing between impaired and normal water excretion in hyponatremia[39]. In impaired water excretion urine osmolality is >150mosm/kg indicating an inability to excrete free water commonly as a result of excess ADH[23,38].

Urine to serum electrolyte ratio

This is the sum of urine sodium plus potassium concentrations divided by the serum sodium concentration. In the management of hyponatremia with fluid restriction, a ratio of <0.5 indicates high urine electrolyte free water hence adequate fluid restriction while a ratio of>1 indicates hypertonic urine hence fluid restriction is not sufficient and other measures should be implimented to correct the hyponatremia[41].

Fractional excretion of sodium(FENa)

This provides a more accurate assesment of volume status than urine sodium alone as it corrects for the effect of urine volume variations on the urine sodium. A FENa <0.1% would represent hypovolemic hyponatremia while >0.1% would represent hypervolemic and normovolemic hyponatremia[38].

Serum uric acid and urea concentrations

Serum uric acid and urea may provide a clue as to the cause of the hyponatremia. Low serum uric acid and urea can be seen with SIADH, hypopituitarism, hypervolemia and thiazide diuretics while normal serum uric acid and urea may be seen with hypovolemia [38,39,42,43,44].

Acid-base and potassium balance

The pH status and potassium levels may be helpful in determining the cause of the hyponatremia as per the associations below:

. Normal acid base and potassium- SIADH

. Metabolic acidosis and hypokalemia-Diarrhea and laxative abuse

. Metabolic alkalosis and hypokalemia-Diuretic use or vomiting

. Mild metabolik alkalosis and normal potassium-hypopituitarism[39, 45,46,47].

Hormonal profiles

Pregnancy is associated with downward resetting of serum osmolality (and serum sodium) owing to human chorionic gonadotrophin-induced release of the hormone relaxin[48].Hyponatremia is also associated with primary or secondary adrenal insufficiency andhypothyroisism[49,50]. ACTH, ACTH stimulation tests, thyroid hormone profile and a pregnancy test may also be relevant in identifying the cause of hyponatremia.

Saline infusion

Infusion of normal saline with monitoring of serum sodium for upto 8 hours. This would improve hypovolemic hyponatremia while normovolemic and hypervolemic hyponatremia will worsen hence its use as a diagnostic test in identifying the type of hyponatremia[38].

Other investigations

ECGmay show non ischaemic ST elevation associated with hyponatremia. CT Scan and MRI brain imaging may show CNS pathologies that may be the cause of the hyponatremia.

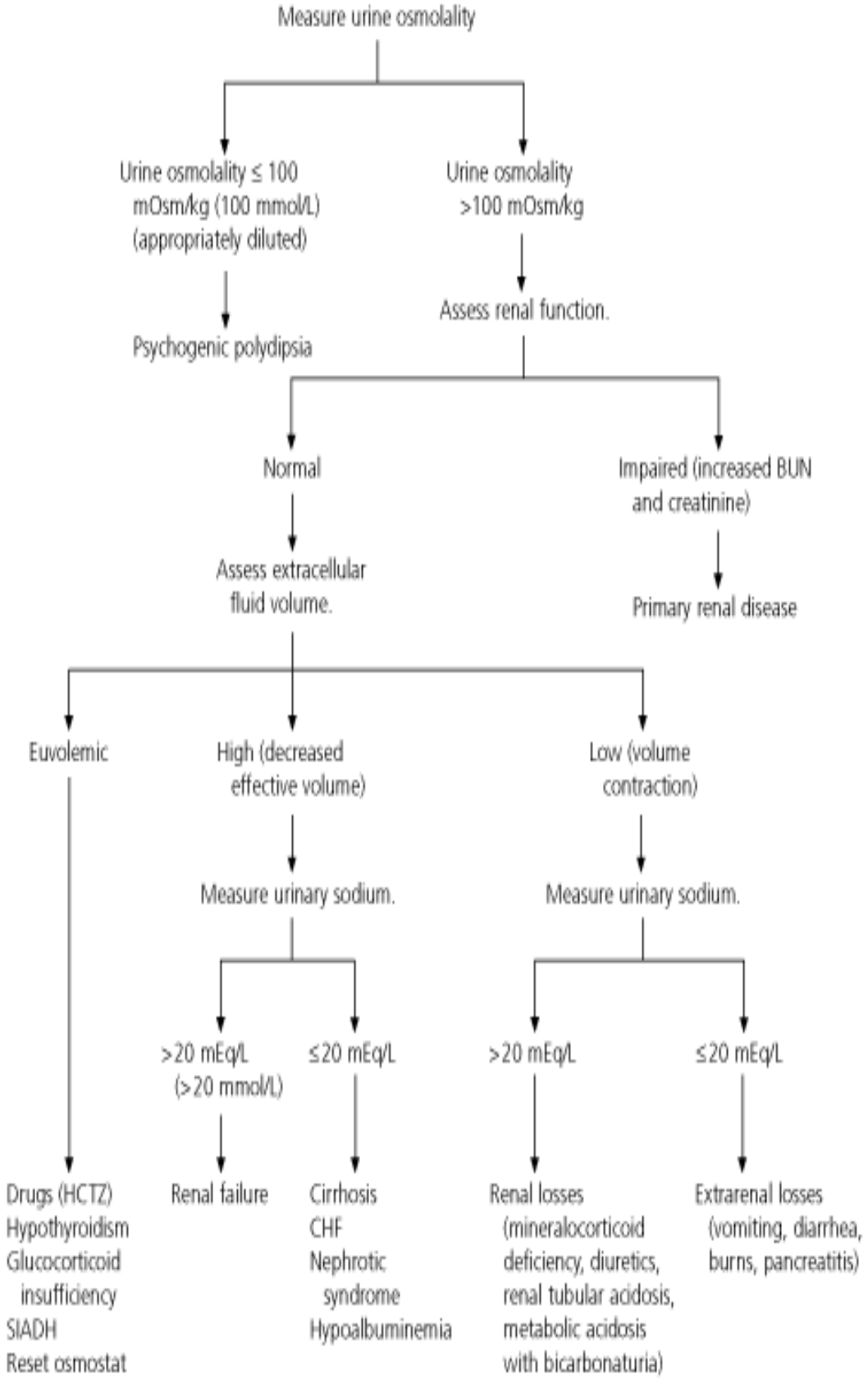

Figure 2: Laboratory Evaluation of Hyponatremias [3-5, 15]

2.5 Treatment of hyponatremia

The management of hyponatremia is determined by the severity of the hyponatremia, acuteness of onset, presence or absence of symptoms, volume status and the etiology of the hyponatremia[5,6,7,8] . For mild hyponatremias(>120meq/L), asymptomatic or chronic patients aggressive management is not required.

Establish the Need for Rapid or Aggressive Correction

Patients presenting with severe symptoms like altered mental status and convulsions and those with severe hyponatremia (110meq/L) even if asymptomatic would require rapid and aggressive sodium correction[5,6,7,8,31].

Patients with acute hyponatremia are often symptomatic. Such patients have not had time for brain adaptation to occur hence the high risk of brain herniation necessitating rapid correction. Recommended treatment is Hypertonic saline bolus of 100mls over 10 minutes up to three times or until acute symptoms subside. The aim is to raise serum sodium by 4-6mmol/ to prevent brain herniation[1].

In chronic hyponatremia patients are generally asymptomatic not necessitating rapid or aggressive correction. However if the patients develop severe hyponatremia(125meq/L) or become symptomatic the aggressive therapy is indicated as for acute hyponatremia and vasopressin antagonists may also be used[1,6,8].

Patients with mild symptoms like dizziness, forgetfulness and gait disturbances should be treated with less aggressively. If the urine to serum electrolyte ratio is <0.5 then fluid restriction alone is adequate but if the ratio is >1then salt tablets and a loop diuretic may be added. Vasopressin antagonists without fluid restriction may also be adequate[38].

In patients at low risk of ODS (acute hyponatremias), a maximum of 10 to 12 mmol/L increase in serum sodium per day is recommended while in those at high risk of ODS(chronic hyponatremias), a maximum of 8mmol/L per day is the recommended[1].
1ml/kg of hypertonic saline(3% saline) is estimated to raise the serum sodium by 1meq/L nevertheless frequent measurement is necessary[38].

Determine the Water Excess

This can be determined by relating the current measured sodium to total body water then substituting 140meq/L for normal sodium as follows[5,51]:

$$\text{TBW (L)} = \text{normal TBW (L)} \times \frac{140}{[\text{Na}]}$$

For a 70kg man with a normal total body water of 0.6L/Kg would be 42L. If the sodium is 110meq/L TBW would be:

$42 \times 140 \div 110 = 53.5$ L

Hence the water excess would be:

$53.5 \text{ L} - 42 \text{ L} = 11.5$ L

If the desired corrected sodium is 125meq/L, so as to avoid too-rapid correction then the estimated water excess to be corrected would be:

$53.3 \text{ L} - (42 \times 125 \div 110) = 5.8$ L

Correct the Underlying Problem

Hypovolemic hyponatremia

This is the most easily correctable hyponatremia.Infusion of normal saline replenishes sodium and replaces intravascular volume inhibiting ADH release. Increased glomerular filtration rate enhances water excretion with production of dilute urine.

1litre of normal saline provides 154meq/L of sodium slowly raising the serum sodium by 1meq/L for every litre infused. Hypertonic saline(3% saline) is not indicated.

For gastrointestinal losses, sodium, potassium and even bicarbonate losses should be corrected.

Thiazide induced hyponatremia is often chronic and should be corrected slowly so as to avoid risk of osmotic demyelination syndrome(ODS) and potassium should also be supplemented.

Hyponatremia associated with mineralcorticoid deficiency is often chronic and responds to normal saline and fludricortisone.

Chronic hyponatremias are preferably managed by increased dietary salt intake[1,5,38].

Hypervolemic hyponatremia

This tends to be more difficult to correct, although severe hyponatremia tends to be less likely[5].

In congestive cardiac failure(CCF) or other oedematous states sodium chloride is generally avoided unless the patient is acutely symptomatic. Despite the reduced effective intravascular volume, fluid replacement would worsen the peripheral oedema, ascites and pulmonary oedema. Afterload reduction in congestive cardiac failure has the best outcomes in correcting the hyponatremia. Other therapies in CCF include angiotensin-converting enzyme inhibitors and beta-adrenergic blockers.

In nephrotic syndrome and cirrhosis, albumin infusion may have a temporary improvement of the hyponatremia but long term management involves solving the primary condition.

In hypervolemic hyponatremias, water restriction and loop diuretics are the mainstays of treatment, other treatments also include V1a receptor antagonists and Vaptans[38].

Normovolemic and other causes of hyponatremia

Adrenal insufficiency, hypothyroidism, psychogenic water intoxication, thiazide diuretics, vasopressin, hypokalemia, acquired immunodeficiency Syndrome(AIDS) and other specific causes of hyponatremia will respond to correction of the underlying problem.Although SIADH may respond to treatment of the condition leading to the syndrome, the hyponatremia is tackled directly as discussed below.

The Syndrome of Inappropriate ADH Secretion (SIADH)

Too fast too soon or too slow too late, controversies still exist on the rate of correction of hyponatremia that minimises the risk of neurological symptoms and the development of osmotic demyelination syndrome. Most authorities recommend a slow correction rate of 0.5-2mmol/L/hour not to exceed than 8-10mmol/L/day or 18mmol/L/48hours [14, 32]. Symptoms of hyponatremia respond to a sodium increase of as low as 5meq/L. The risk of ODS is said to be minimal with sodium increases of up to 12meq/L/day. Once the serum sodium has exceeded 125meq/L or symptoms have improved, aggressive correction is no longer indicated. Water restriction with or without enhancement of water excretion is usually sufficient for asymptomatic or mild hyponatremia. Hypertonic saline is indicated for severe or symptomatic hyponatremia.

SIADH is a diagnosis of exclusion. There are many causes including malignancies, intracranial diseases and drugs[52].

The Barter and Schwartz criteria for SIADH is as follows[53]:

-Decreased plasma osmolality (<275mosm/kg)

-Inappropriately concentrated urine (>100 mosm/kg)

-Euvolemic

-Elevated urine sodium (>20 mEq/L)

-Euthyroid, Eucortisolemic and no diuretic use.

Restriction of fluid intake

Restriction of fluid intake is the mainstay of treatment in both hypervolemic and euvolemic hyponatremia including SIADH. Fluid is restricted to less than the urine output, recommended total intake is 1-1.5L/day[54]. This measure is usually adequate for asymptomatic patients or hyponatremias of between 125-135meq/L. Effectiveness of the restriction can be predicted by the urine to serum electrolyte ratio[41]. The serum osmolality responds after several days.

Hypertonic saline(3% NaCl) and furosemide

Hypertonic saline with or without a loop diuretic(furosemide) is the treatment of choice for severe or symptomatic hyponatremia[5,6,7,8,31]. The loop diuretic will promote both salt and water loss hence the combination with hypertonic saline so as to achieve a net loss of water.

Ideally the amount of sodium lost in urine should be measured hourly and replaced. The loop diuretic should be given to achieve a urine output of 200-300ml/h. If the urine contains approximately 280 mosm/kg then 70 mosm/h should be lost with a urine output of 250ml/h. Replacing the 70 mosm/h using hypertonic saline which contains 1026 mosm/L would require only 68 ml/h. This causes a net water excretion of 250-68=182 ml/h with a rise in plasma sodium by 1meq/L/h. Practically replacing 25-30% of urine volume lost each hour with hypertonic saline will approximate the solute replacement required[5]. The hypertonic saline should be stopped once the plasma sodium is above 125meq/L. The maximum 24 and 48 hr plasma sodium increments discussed previously apply[14, 32].

The following formula can be used to estimate the change in plasma sodium when 1L of fluid is administered[11]:

$$\Delta \text{Plasma}[Na^+] = \frac{\text{fluid}[Na^+] - \text{plasma}[Na^+]}{\text{TBW} + 1}$$

The TBW is estimated as discussed previously. In current guidelines these formulas are not used, instead1ml/kg of hypertonic saline is expected to raise the serum sodium by 1meq/L[38].

Vasopressin antagonism

Vasopressin has 3 receptors namely V1a, V1b and V2. V2 mediates ADH while the others mediate vasoconstriction and adrenocorticotropic (ACTH) hormone release. Vasopressin receptor antagonists produce water diuresis without interfering with sodium excretion[7].

There are both oral and IV preparations available.
Nonselective (mixed V1A/V2): Conivaptan.
V1A selective (V1RA): Relcovaptan.
V1B selective (V3RA): Nelivaptan.
V2 selective (V2RA): Lixivaptan, Moxavaptan, Satavaptan, Tolvaptan.
Dual receptor activity reduces cardiac preload and total peripheral resistance, which are both of benefit in CCF[55].The use of V2 receptor antagonists is limited by increased thirst, orthostatic hypotension, high cost amongst other side effects[56]. They should also not be used in hypovolemic hyponatremia.

Salt and loop diuretics

Although limited data exists to support their efficacy, oral salt tablets have also been used alone or in combination with loop diuretics depending on the urine to serum electrolyte ratio[38]. High salt intake combined with furosemide has been used to impair renal tubular responsiveness to ADH[32]. Loop diuretics interferes with the countercurrent concentrating mechanisms by decreasing sodium chloride absorption at the thick ascending loop of Henle. The result is excretion of isotonic urine with considerable fluid loss. A dose of 9g of salt a day and 20mg of furosemide twice a day is recommended [11].

Other treatments

An antibiotic demeclocycline and an antidepressant lithium carbonate induce nephrogenic diabete insipidus and have both been used to treat SIADH. They are slow to work and lithium is associated with nephrotoxicity[57].

Urea at 30g/day has also been shown to increase solute excretion and enhance water excretion[58].

Extracorporeal procedures such as continuous veno-venous hemofiltration (CVVH) and slow low-efficiency daily dialysis (SLEDD) have also been used in exceptional circumstances especially in cardiology in the context of severe hypervolemic hyponatremia[59].

Although not a recommended treatment, hydrocortisone has also been shown to promote sodium retention in the kidneys. A dose of 1200mg/d has been shown to maintain sodium levels for two weeks and prevent excess sodium secretion [60].

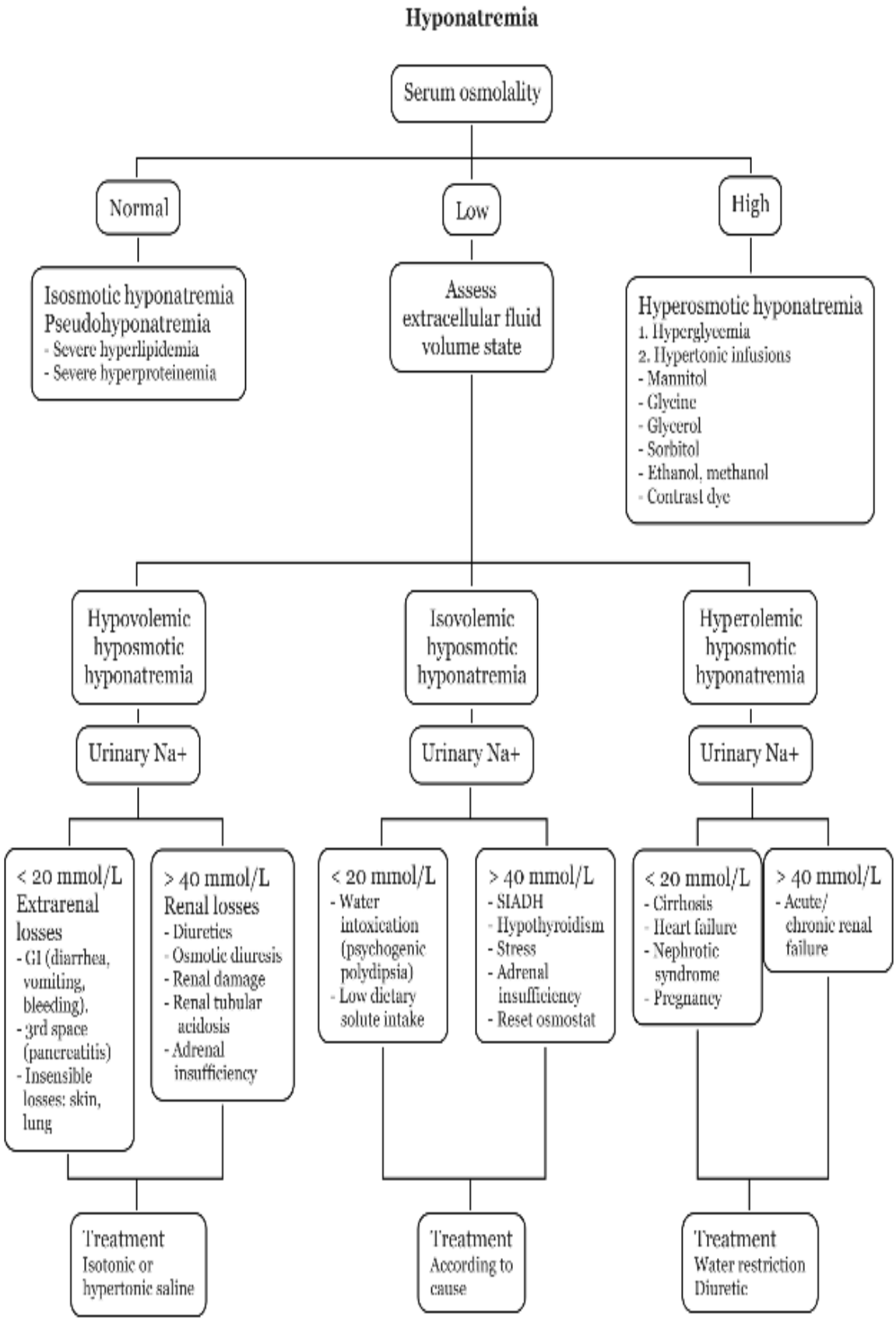

Figure 3: Treatment of Hyponatremias [3-5, 15]

2.6 The KNH ICU 2004 protocols on hyponatremia

SODIUM

Most abundant extra cellular cation and critical in determining the extra cellular osmolality. Requirements vary with age.

Neonates: 2-3 meq/kg/day

Adults: 1.5 meq/kg/day

Losses of Sodium

- SIADH production

- Diuretic abuse

- Renal salt wasting, Addison's disease

Sodium retention states

- heart failure, nephritic syndrome, chronic liver disease, glomerulonephritis

- mineralocortoid administration

Deficit correction

Dose (meq) = W x (140 – [Na+])

Kg (meq/L)

- Correction 0.6 – 1 mmol/L/Hr TILL Na+ is at 125 mmol/L

- Acute correction ½ dose over 8 hours then next over 1-3 days

- Rapid correction associated with central pentine myelinolysis

- Fluid restriction and use of diuretics may assist in correcting hyponatraemia

2.7 Table Salt

The table salt most commonly used at the KNH critical care units is Kensalt.

It is an iodated table salt fortified with potassium iodate as recommended by the health authorities for the prevention of goitre.

The ingredients are sodium chloride >97%M/M and potassiumiodate 50-84PPM [61].

A tea spoon of salt weighs approximately 6 g and contains 2400 mg of sodium or 104meq or mmol of sodium.

CHAPTER THREE: RESEARCH METHODOLOGY

3.0 Research Design

This was a prospective observational study. It consisted of40consenting adult patients with hyponatremia (plasma sodium <135meq/L) who had been prescribed enteral table salt. The study site was the Kenyatta National Hospital MainCritical Care Unit. Sodium levels were followed up with the routine morning blood gas and electrolyte analysis for up to 2 days. The outcome which was the change in plasma sodium levels was noted with progressive morning blood gas and electrolyte analysis until the hyponatremia was corrected or 2 days elapsedor the patient moved out of the unit. Also noted was any associated side effects of the table salt.

3.1 Variables

The dependent variables was the change inplasma sodium level with progressive morning blood gas and electrolyte analysis and the development of associated side effects namely; vomiting, diarrhoea, convulsions, abnormal posturing or movement and nystagmus.

3.2 Study Area

The study was conducted at the Kenyatta National Hospital Main Critical Care Unit with a total of 21adult beds. The Main CCU has an average of 50 new admissions per month. Patients admitted at the Main CCU consist of adults and children with various medical and surgical conditions. Kenyatta National Hospital is the largest referral facility and teaching hospital in Kenya with a bed capacity of 1800, 50 wards, 22 outpatient clinics, 24 theatres and an accident and emergency department.It has a total of 41 adult CCU beds consisting of a 21 bed Main CCU, 5 bed Cardiothoracic CCU, 5 bed Neurosurgery CCU, 5 bed Medical CCU and a 5 bed Resuscitation Room A which also functions as a holding area for pending CCU admissions. It also has a pediatric critical care unit, a neonatal critical care unitand a private wing critical care unit.

3.3 Target Population

Adults who had been prescribed table salt for hyponatremia and met the inclusion criteria at the Kenyatta National Hospital Main Critical Care Unit.

3.4 Exclusion and Inclusion Criteria

3.4.1 Inclusion Criteria

Adults with hyponatremia at the KNH Main CCU who had been prescribed enteral table salt and consented to participate in the study.

Adults with hyponatremia at the KNH Main CCU who had been prescribed enteral table salt and whose next gave consent to participate in the study.

3.4.2 Exclusion Criteria

Children with hyponatremia admitted at the KNH Main CCU.

Adults or next of kin who declined to give consent at the KNH Main CCU.

Patients who were receiving Hypertonic saline.

Patients who were receiving other medications for hypornatremia including vaptans, loop diuretics, demeclocycline, urea and steroids.

Patients who were not on enteral feeds.

Patients who were on fluid restriction <1.0 L/day.

Patients who were on dialysis.

3.5 Sample Size Determination and Sampling Procedure

3.5.1 Sample Size Determination

This was a cross-sectional study design and the sample size calculation was done based on single proportion estimation formula. Main CCU admissions were estimated at 50 patients per month with 30% prevalence of hyponatremia. This translated to an estimate of 15 eligible patients monthly hence 45 patients would be accessible during the 3 –month period of the study. Since this is a finite population the sample size was estimated using the formula with finite population correction as follows:

$$n' = \frac{NZ^2P(1-P)}{d^2(N-1) + Z^2P(1-P)}$$

Where

n' = sample size with finite population correction,

N = size of the target population = 45

Z = Z statistic for 95% level of confidence = 1.96

P = Estimated proportion of patients with corrected sodium levels after administration of table salt = 50% (No available current data).

d = margin of error = 5%

$$= \frac{45 \times 1.96^2 \times 0.5 \times 0.5}{0.05^2 (45-1) + 1.96^2 \times 0.5 \times 0.5}$$

n = 40

A minimum of 40 patients were sampled to estimate adequacy of enteral table salt in correcting hyponatremia within 5% level of precision.

3.52 Sampling Procedure

Convenient sampling procedure was used to select patients into the study. The patients with hyponatremia as diagnosed through routine investigations in the CCU were approached for recruitment into the study. Those that met the inclusion criteria were enrolled into the study consecutively until the desired sample size was achieved.

3.6 Research Instrument and Data Collection Procedure

3.6.1 Research Instrument

Research data consisting of primary medical conditions of the patient, initial level of hyponatremia, subsequent morning plasma sodium levels as per the blood gas and electrolyte analysis, total amount of fluids given, the total sodium content, plasma potassium levels, blood sugar level, initial level of serum urea, creatinine and albumin, hydration status, haemodynamic status and the associated side effects of the table salt were collected via a data collection tool by the researcher.

3.6.2 Data Collection Procedure

Written informed consent was obtained from the patient or next of kin once enteral table salt had been prescribed by the primary physician for hyponatremia as per the routine morning blood gas and electrolyte analysis.

The nutritionist and primary nurses of the patient were informed of the study.

Patients who met the inclusion criteria received table salt via the enteral route as prescribed by the primary physician.

Commercial table salt (kensalt) diluted in free water was given after feeds as is routine.

Successive plasma sodium was noted via the routine morning blood gas and electrolyte analysis.

Also noted was the total amount of fluids given, the total sodium content, plasma potassium levels, blood sugar levels, the initial level of serum urea, creatinine and albumin, hydration status, haemodynamic status and the associated side effects of the table salt.

3.7 Data Management and Analysis

Data was entered into and managed in Microsoft Excel 2013 data entry sheet pre-coded to reflect the design of the data collection tool. Data cleaning was done continuously during data collection and the final dataset was exported to SPSS version 21.0 statistical software for analysis. The study population was described using the socio-demographic and clinical characteristics by summarizing categorical data into percentages and continuous variables into means or medians. The sodium levels were presented as means with standard deviations and also categorized into normal sodium levels, hyponatremia or hypernatremia using appropriate laboratory cut-offs. Effectiveness of enteral table salt in correcting hyponatremia was calculated and presented as percentage of patients with normal sodium levels within 48 hours of administration. Side effects of using enteral table salt was documented and presented as the percentage number of patients with adverse effects associated with the use of salt. The findings of this study were presented in tables and graphs.

3.8 Laboratory Tests and Quality Control

3.8.1 Laboratory Tests

The laboratory test of primary interest is plasma sodium. Other laboratory tests of secondary interest due to their association with hyponatremia are plasma potassium, random blood sugar, serum urea, creatinine and albumin.

Plasma sodium, potassium and random blood sugar are tests that are included in the routine morning blood gas analysis. The samples are collected and processed as one by the CCU laboratory technician on night duty between 5am and 7amevery day. The process involves an aseptic technique of wearing clean gloves and swabbing the radial artery site with an alcohol swab. 1 millilitre of arterial blood is drawn into a 2 millilitre heparinised syringe with a gauge 25 needle. The samples are immediately taken to the KNH CCU laboratory and processed unseparated. Interpretation of results is based on the printed reference range included in the analysis report.

Serum urea, creatinine and albumin are tests that are routinely included under kidney and liver function tests for every CCU admission at least on a weekly basis and repeated whenever necessary. The samples are collected as one by the doctor on duty in the CCU and immediately handed over to the CCU support staff on duty to be taken to the KNH Renal Unit Laboratory for analysis by the laboratory technician on duty. The process of collection involves an aseptic technique of wearing gloves and swabbing the site of collection with an alcohol swab. The site may be any accessible vein or in case of a central venous catheter, the 2nd draw is what is collected and analysed. 3 to 5 millilitres of blood is drawn into a 5 millilitre plain syringe using a gauge 21 needle. The sample is immediately transferred to a plain (red top) vacutainer for transportation. Interpretation of results is based on the printed reference range included in the analysis report.

3.8.2 Quality Control

The machine used for the analysis of plasma sodium, potassium and random blood sugar is the Siemens RAPIDpoint 500 series which has an automated quality control mechanism that calibrates every six hours or after running several samples. An internal quality control is initiated every morning and an external quality control every month. The external quality control involves running samples provided by RIAS after which the results are verified by that company. The machine is serviced monthly by MEDTECH Company.

The machine used for the analysis of serum urea, creatinine and albumin is the BIOLIS 50i Chemistry Analyser. An internal quality control is conducted every morning and an external quality control every month. The external quality control involves running samples provided by RIAS after which the results are verified by that company. The machine is serviced monthly by LEUD Company.

3.9 Logistical and Ethical Considerations

Approval from KNH/UON Ethics and Research committee and a written study explanation to each patient/next of keen was provided and an informed consent obtained. The participants had the right to decline with the assurance of no penalty for refusal to participate. The same standard care was provided to both participants and non-participants as per the primary physician. Confidentiality reigned supreme with respect to information gathered from each participant and there was no additional cost or incentive for participating in the study.

3.10 Study Findings Dissemination

The findings of this study were disseminated through: presentation to members of the department of Anaesthesia of the University of Nairobi. Feedback was also given to the Critical Care team and a report sent to UON/KNH ERC.

CHAPTER FOUR: FINDINGS

4.0 Introduction

This study was conducted between 3rd October and 16th December 2017 at the Main KNH CCU. A total of 40 patients who satisfied the inclusion criteria were recruited successfully. There was 100% completion rate for the 40 patients; however a larger number had been recruited but did not complete the study as a result of being discharged from CCU and death resulting from the primary illness. The effectiveness of enteral table salt and associated side effects were evaluated.

4.1 Characteristics of the Participants

4.1.1 Demographic Characteristics

The patients ranged between 18 and 75 years with a mean age40.4 and a SD 16.2. The demographic characteristics are illustrated in the graphs below:

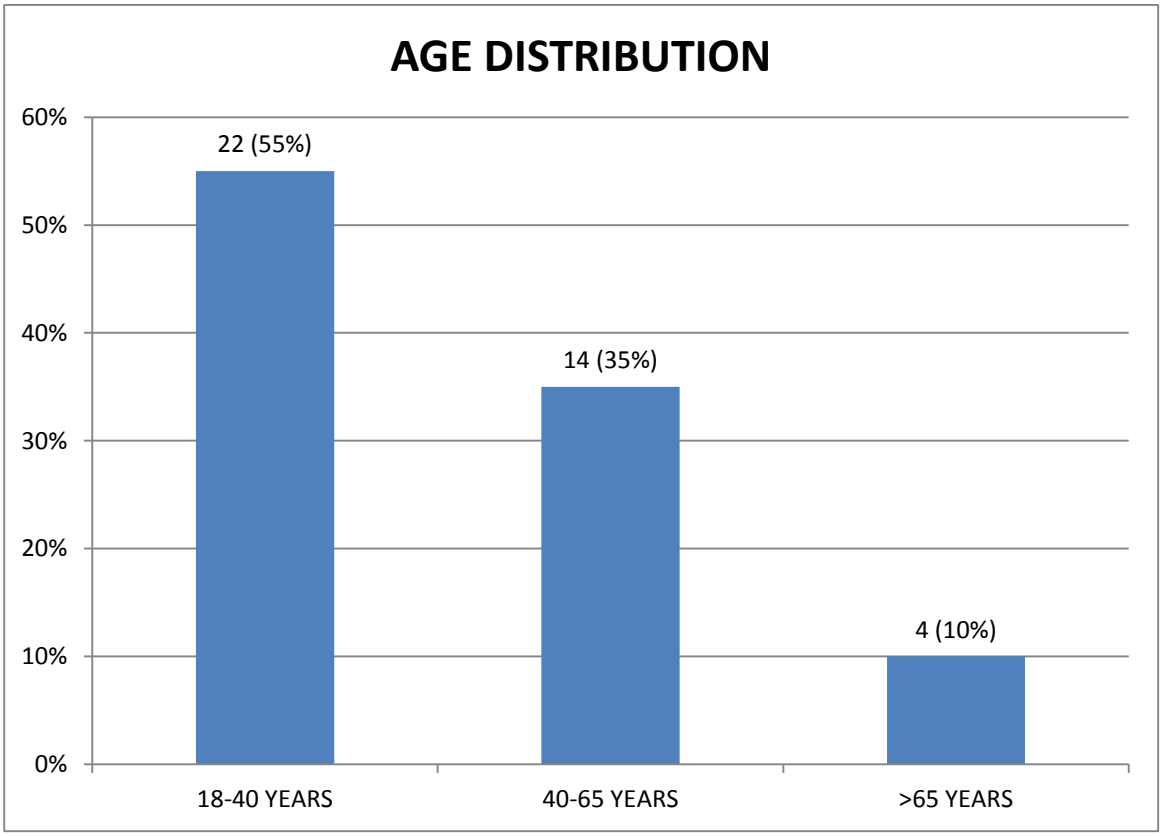

Figure 4:1 Age Distribution

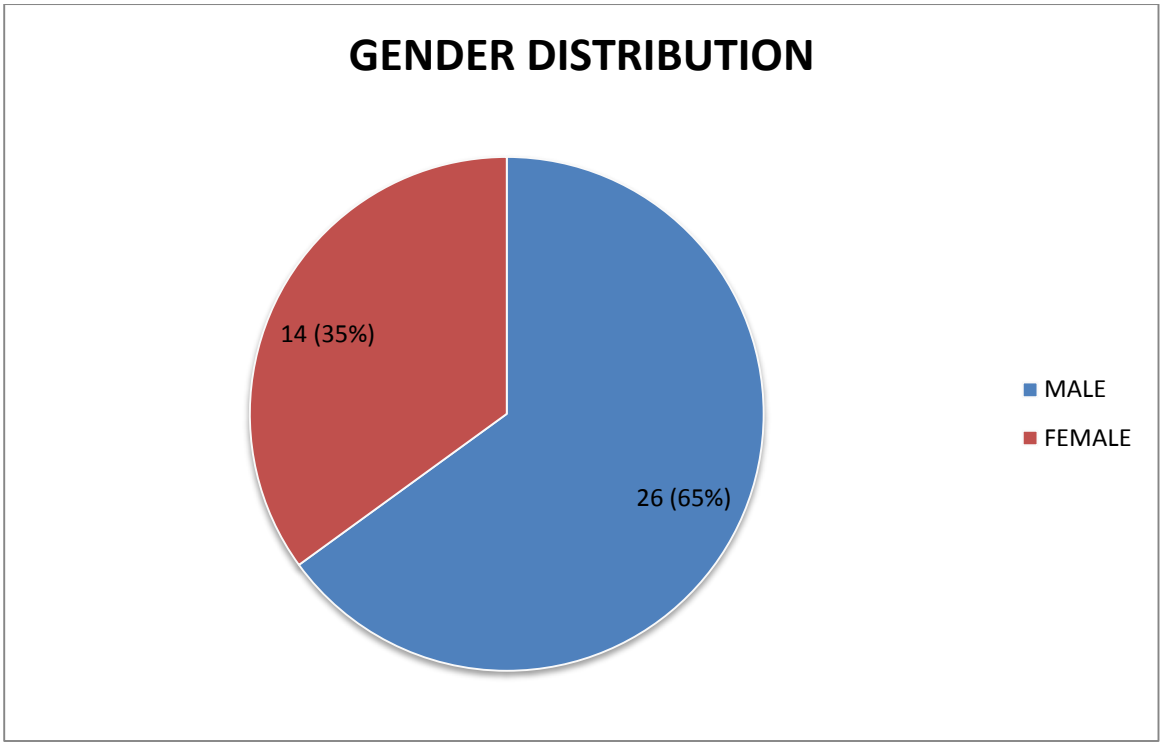

Figure 4.2: Gender Distribution

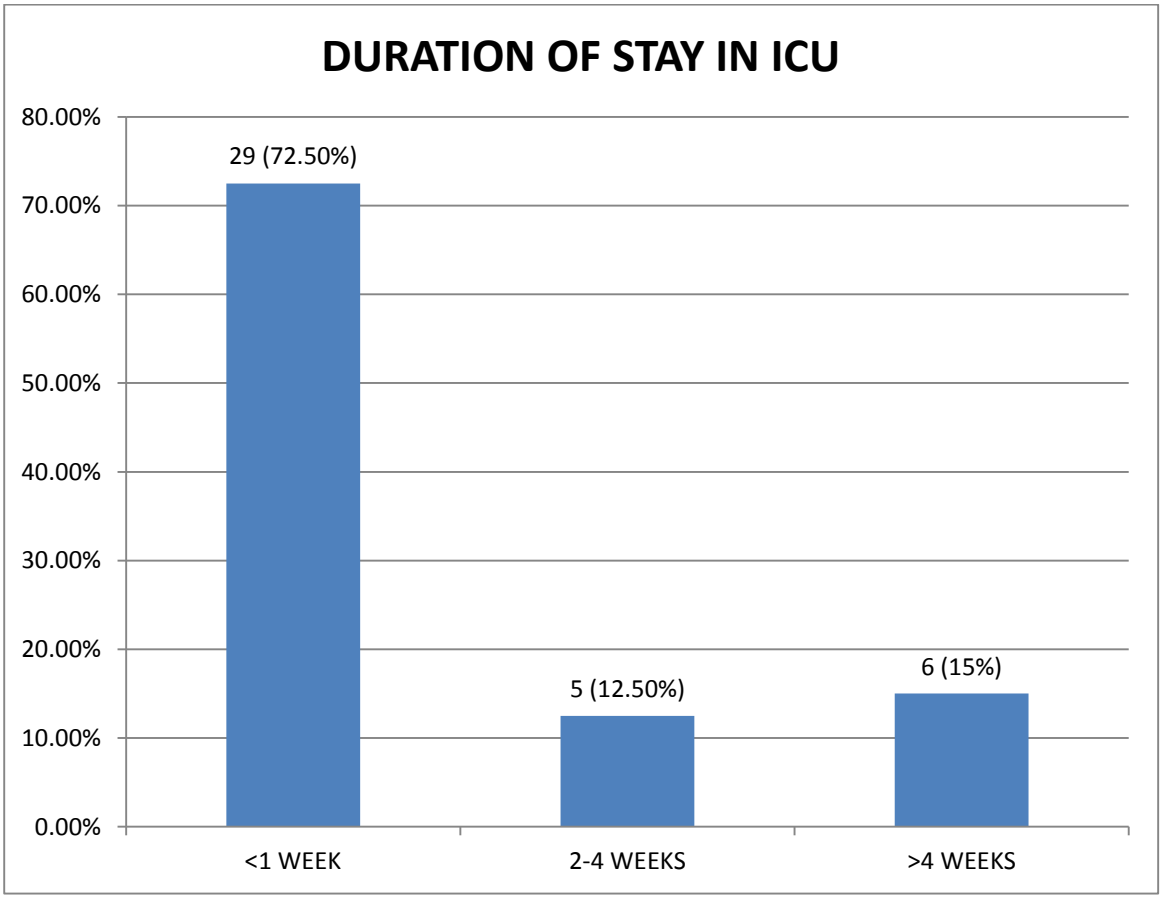

Figure 4.3: Duration of Stay in ICU

4.1.2 Clinical Characteristics

The clinical characteristics of the participants, at the point of recruitment, are illustrated in the table below:

Variable	Frequency (%)
Clinical co-morbidities	
Respiratory	7 (17.5)
Obstetric	4 (10.0)
Gastro intestinal	7 (17.5)
Neurologic	18 (45.0)
Musculoskeletal	6 (15.0)
Cardiovascular	3 (7.5)
Others	9 (22.5)
Fluid Status	
Oedematous	8 (20.0)
Non Oedematous	32 (80.0)
Morning Blood Sugar Levels	
Hyperglycemic	19 (47.5)
Normoglycemic	19 (47.5)
Hypoglycemic	2 (5.0)
Serum Urea Levels	
High	8 (20.0)
Normal	26 (65.0)
Low	6 (15.0)
Serum Creatinine Levels	
High	9 (22.5)
Normal	28 (70.0)
Low	3 (7.5)
Serum Albumin Levels	
High	3 (7.5)
Normal	2 (5.0)
Low	35 (87.5)
History of Cardiac Disease	
Yes	3 (7.5)
No	37 (92.5)
History of Renal Disease	
Yes	8 (20.0)
No	32 (80.0)
History of Hepatic Disease	
Yes	1 (2.5)
No	39 (97.5)
Received Mannitol in the Last 24 Hours	
Yes	2 (5.0)
No	38 (95.0)
Consumed Alcohol in the Last 24 Hours	
Yes	1 (2.5)
No	39 (97.5)

Table 4.1: Clinical Characteristics

4.2 Sodium Intake

The sodium intake consisted of the total intake of sodium from parenteral and intravenous routes. Parenteral sources included feeds, medicines and the table salt while intravenous sources included fluids and supplemental parenteral nutrition. The intake is illustrated in the table below:

Variable	**Day 0 All (n=40)**	Day 0 Corrected (n=29)	Day 0 Uncorrected (n=11)	**Day 1 All (n=40)**	Day 1 Corrected (n=29)	Day 1 Uncorrected (n=11)	**Day 2 (n=11)**	**Cumulative, All (n=40)**	**Increase**
Mean intake in mmol/L (SD)	**186.3 (98.4)**	174.9 (84.7)	220.1 (126.2)	**393.8 (129.6)**	397.8 (115.7)	356.5 (159.3)	**401.2 (108.2)**	**504.1 (469.3)**	**317.9 (199.4)**
Frequency (%) **OD** **BD** **TDS** **QID** **Mean 2.25 Tea Spoons Per Day**				**9 (22.5)** **15 (37.5)** **10 (25.0)** **6 (15.0)**	2 (6.9) 13 (44.8) 9 (31) 5 (17.3)	7 (63.6) 2 (18.2) 1 (9.1) 1 (9.1)	**4 (36.4)** **3 (27.3)** **4 (36.4)** **0**	**13 (25.5)** **18 (35.3)** **14 (27.5)** **6 (11.7)**	

Table 4.2: Sodium Intake. OD, Once a day; BD, Twice a day; TDS, Three times a day; QID, Four times a day.

Note that day 0 is the day the patient was recruited, before table salt supplementation was started.n40 refers to all the 40 patients, n29 refers to the 29 patients with corrected sodium levels within 24 hours of table salt supplementation and n11 refers to the 11 patients who received table salt for up to 48 hours. The 11 patients received a lower sodium intake compared to the other 29 patients on day 1 resulting in a change of sodium intake of 136.4mmo/L as compared to 222.9mmol/L. Cumulative intake includes day 2 intake for n11.

4.3 Blood Sodium and Potassium Levels

The blood sodium levels are illustrated in the table below:

Sodium	**Day 0 All (n=40)**	Day 0 Corrected (n=29)	Day 0 Uncorrected (n=11)	**Day 1 All (n=40)**	**Day 1 Corrected (n=29)**	Day 1 Uncorrected (n=11)	**Day 2 (n=11)**	**Overall, All (n=40)**
Mean mmol/L (SD)	131.6 (2.2)	132 (2.1)	130 (1.9)	137.0 (5.1)	139.3 (3.4)	131.1 (3.8)	136.0 (6.0)	138.4 (4.5)
Category,n (%)								
Normal				26 (65.0)	26 (89.7)	0	6 (54.5)	32 (80.0)
High				3 (7.5)	3 (10.3)	0	1 (9.1)	4 (10.0)
Low				11 (27.5)	0	11 (100)	4 (36.4)	4 (10.0)

Table 4.3: Blood Sodium Levels.n40, All 40 patients; n29 Patients with corrected sodium levels within 24 hours of table salt administration; n11, Patients who required 48 hours of table salt administration.

The 4 patients with hypernatremia, 3 had primarily neurologic pathology while the 4th had upper airway obstruction secondary to cancer of the oesophagus. Their daily sodium intake ranged from 273 to 503mmol/L (including 1 to 4tsp of salt). Their change in blood sodium levels ranged from 11.2 to 18.3mmol/L. Their daily fluid balance ranged from -1400 to 2250mls. 3 had normal blood potassium levels while the 4th was hypokalemic.

The 4 patients with persistent hyponatremia, 2 had primarily respiratory pathology (the first one also had gastrointestinal pathology) and 2 had primarily obstetric pathology. 3 had hypervolemia while the 4th had normovolemia. Their daily sodium intake ranged from 191 to 624mmol/L (including 1 to 4 tsp of salt). Their change in blood sodium levels ranged from -4.0 to 5.2mmol/L. Their daily fluid balance ranged from 50 to 3100mls. 2 patients had normal potassium levels while the other 2 were hypokalemic. 2 patients had normal albumin levels

while the other 2 had hypoalbuminemia. 2 had concurrent renal disease; the 3rd had concurrent cardiac disease while the 4th had episodes of diarrhoea.

The blood potassium levels are illustrated in the table below:

Potassium	**Day 0 All (n=40)**	Day 0 Corrected (n=29)	Day 0 Uncorrected (n=11)	**Day 1 All (n=40)**	**Day 1 Corrected (n=29)**	Day 1 Uncorrected (n=11)	**Day 2 (n=11)**	**Overall, All (n=40)**
Mean mmol/L (SD)	3.8 (0.9)	3.8 (0.9)	4.0 (1.0)	3.9 (0.8)	4.0 (0.8)	3.6 (0.6)	3.9 (0.8)	4.0 (0.8)
Category,n (%)								
Normal	20 (50)	15 (51.7)	5 (45.5)	24 (60.0)	18 (62.1)	6 (54.5)	6 (54.5)	24 (60.0)
High	3 (7.5)	2 (6.9)	1 (9)	3 (7.5)	3 (10.3)	0	0	3 (7.5)
Low	17 (42.5)	12 (41.4)	5 (45.5)	13 (32.5)	8 (27.6	5 (45.5)	5 (45.5)	13 (32.5)

Table 4.4: Blood Potassium Levels. n40, All 40 patients; n29 Patients with corrected sodium levels within 24 hours of table salt administration; n11, Patients who required 48 hours of table salt administration.

4.4 Effectiveness of Enteral Table Salt in Hyponatremia

The mean change in sodium levels is illustrated in the table below:

Sodium levels (mmol/L)	**Day 0 All (n=40)**	Day 0 Corrected (n=29)	Day 0 Uncorrected (n=11)	**Day 1 All (n=40)**	**Day 1 Corrected (n=29)**	Day 1 Uncorrected (n=11)	**Day 2 (n=11)**	**Overall All (n=40)**
Mean (SD)	131.6 (2.2)	132 (2.1)	130 (1.9)	137.0 (5.1)	139.3 (3.4)	131.1 (3.8)	136.0 (6.0)	138.4 (4.5)
Category, n (%)								
Normal				26 (65.0)	26 (89.7)	0	6 (54.5)	32 (80.0)
High				3 (7.5)	3 (10.3)	0	1 (9.1)	4 (10.0)
Low				11 (27.5)	0	11 (100)	4 (36.4)	4 (10.0)
Mean Change (SD)				5.5 (4.8)	7.3 (4.1)	0.65 (2.85)	4.9 (4.9)	**6.8 (4.5)**
Change per 104 mmol/L sodium intake								
Mean (SD)				1.8 (9.6)	2.7 (10.9)	-0.47 (3.94)	0.6 (8.2)	**1.7 (12.5)**
Median (IQR)				2.1 (0.9-3.3)	2.5 (1.6-4.0)	0.86 (-2.54 -1.48)	1.8 (-1.8-6.9)	2.7 (1.6-4.5)
Min-Max				-42.4-32.8	-42.4-32.8	-11.17 -2.65	-19.0-11.4	-49.5–32.8

Table 4.5: Change in Sodium Levels

4.4.1 Differences in Change of Sodium Levels between Demographic Characteristics

There was no significant difference in change of sodium levels between the different age groups and sex.

The difference in change of sodium levels as per the demographic characteristics is illustrated in the table below:

Variable	Frequency (%)	Mean Change per 104 mmol/L Sodium Intake (SD)	P Value
Age groups 18-40 40-65 >65	 22 (55.0) 14 (35.0) 4 (10.0)	 1.1 (9.9) 6.1 (9.3) -10.7 (25.9)	0.053
Sex Male Female	 26 (65.0) 14 (35.0)	 2.7 (11.6) -0.3 (14.3)	0.465

Table 4.6: Differences in Change of Sodium Levels between Demographic Characteristics

4.4.2 Difference in Change of Sodium Levels between Clinical Characteristics

There was a significant increase in sodium levels in the patients with high and low albumin as compared to those with normal albumin levels(P-value 0.014), there was also a significant increase in sodium levels in patients with no cardiac disease as compared to those with cardiac disease (P-value 0.024), however, the numbers of the two categories found to have statistical significance are skewed and therefore not representative. There was no significant difference in change of sodium levels between other clinical characteristics.

The difference in change of sodium levels as per the clinical characteristics is illustrated in the table below:

Variable	Frequency (%)	Mean Change per 104 mmol/L Sodium Intake (SD)	P value
Respiratory Yes No	 7 (17.5) 33 (82.5)	 -6.1 (19.4) 3.3 (10.2)	0.072
Obstetric Yes No	 4 (10.0) 36 (90)	 4.4 (2.3) 1.3 (13.1)	0.644
Gastrointestinal Yes No	 7 (17.5) 33 (82.5)	 2.0 (3.8) 1.6 (13.7)	0.931

Neurologic Yes No	18 (45.0) 22 (55)	3.1 (13.8) 0.5 (11.5)	0.523
Muscoloskeloton Yes No	6 (15) 34 (85)	2.7 (1.7) 1.5 (13.6)	0.829
Cardiovascular Yes No	3 (7.5) 37 (2.5)	3.8 (2.4) 1.5 (13.0)	0.766
Others Yes No	9 (22.5) 31 77.5)	-3.0 (17.6) 3.0 (10.6)	0.207
Dosing Frequency OD BD TDS QID	13 (25.5) 18 (35.3) 14 (27.5) 6 (11.7)	1.1 (21.4) 0.8 (13.0) 2.6 (1.2) 2.8 (1.3)	0.981
Fluid Status Oedematous Non Oedematous	8 (20.0) 32 (80.0)	-3.0 (18.8) 2.8 (10.4)	0.242
Fluid Balance Above 500mls 500mls or below	Day 1=29(72.5) Day 2=6(54.5) Day 1=11(27.5) Day 2=5(45.5)	Day 1= 2 Day 2= -0.4 Day 1=2.3 Day 2= 4.2	Day 1 0.862 Day 2 0.429
Blood Sugar Hyperglycemic Normoglycemic Hypoglycemic	19 (47.5) 19 (47.5) 2 (5)	1.5 (13.0) 1.6 (13.0) 3.9 (1.0)	0.968
Urea High Normal Low	8 (20.0) 26 (65.0) 6 (15)	3.6 (2.3) 2.4 (11.0) -4.2 (23.6)	0.465
Creatinine High Normal Low	9 (22.5) 28 (70.0) 3 (7.5)	-1.2 (15.6) 2.5 (12.3) 1.9 (1.1)	0.751
Albumin High Normal Low	3 (7.5) 2 (5.0) 35 (87.5)	3.1 (2.8) -22.8 (37.9) 2.9 (10.0)	0.014
Cardiac Disease Yes No	3 (7.5) 37 (92.5)	-13.8 (31.0) 2.9 (9.7)	0.024
Renal Disease Yes No	8 (20.0) 32 (80.0)	3.9 (1.9) 1.1 (13.9)	0.578

Hepatic Disease Yes No	 1 (2.5) 39 (97.5)	 -4.3 (0) 1.8 (12.6)	0.636
Received Mannitol Yes No	 2 (5.0) 38 (95.0)	 3.6 (1.4) 1.6 (12.8)	0.823
Consumed Alcohol Yes No	 1 (2.5) 39 (97.5)	 3.3 (0) 1.6 (12.7)	0.898

Table 4.7 : Difference in Change of Sodium Levels between Clinical Characteristics

4.5 Association between Persistent Hyponatremia and Hypokalemia

The overall (n=40) mean potassium level was 4.0mmol/L (SD 0.8) from an initial 3.8 (SD 0.9). The mean change in potassium level was 0.2mmol/L (SD 0.7).

24 patients (60%) had normal potassium levels, 3 patients (7.5%) had high potassium levels and 13 patients (32.5%) had low potassium levels.

9 patients (22.5%) developed or worsened hypokalemia during the study.

4 patients (10%) had persistent hyponatremia while 10 patients (25%) had hypokalemia during the study.

Of the 4 patients who had persistent hyponatremia, 2 of them were also hypokalemic. However there was no association between persistent hyponatremia and hypokalemia (P value 0.109).

4.6 Asssociated Side Effects of Enteral Table Salt

1 patient (2.5%) developed diarrhoea while 39 patients (97.5%) did not develop diarrhoea during the study. This particular patient had gastrointestinal and respiratory pathology. His sodium intake was 206mmol/L on day 0, 288mmol/L (including 1tsp of salt) on day 1 and 568mmol/L (including 4tsp of salt) on day 2. His overall change in sodium was 1mmo/L.

2 patients (5%) had deteriorating consciousness while 38 patients (95%) did not have deteriorating consciousness. Of the 2 patients, the first one had neurologic and musculoskeletal pathology. His sodium change was 4.25mmol/L. His sodium intake was 373mmol/L on day 0, 530mmol/L (including 3tsp of salt) on day 1 and 481mmol/L (including 3tsp of salt) on day 2. He also had a history of renal disease and was on mannitol infusion. The second patient had obstetric pathology. Her sodium change was 7.3mmol/L. Her sodium intake was 185mmol/L on day 0 and 306mmol/L (including 2tsp of salt) on day 1.

No patient experienced any of the other associated side effects namely; Nausea/Vomiting, Convulsions, Abnormal posturing/Movement and Nystagmus.

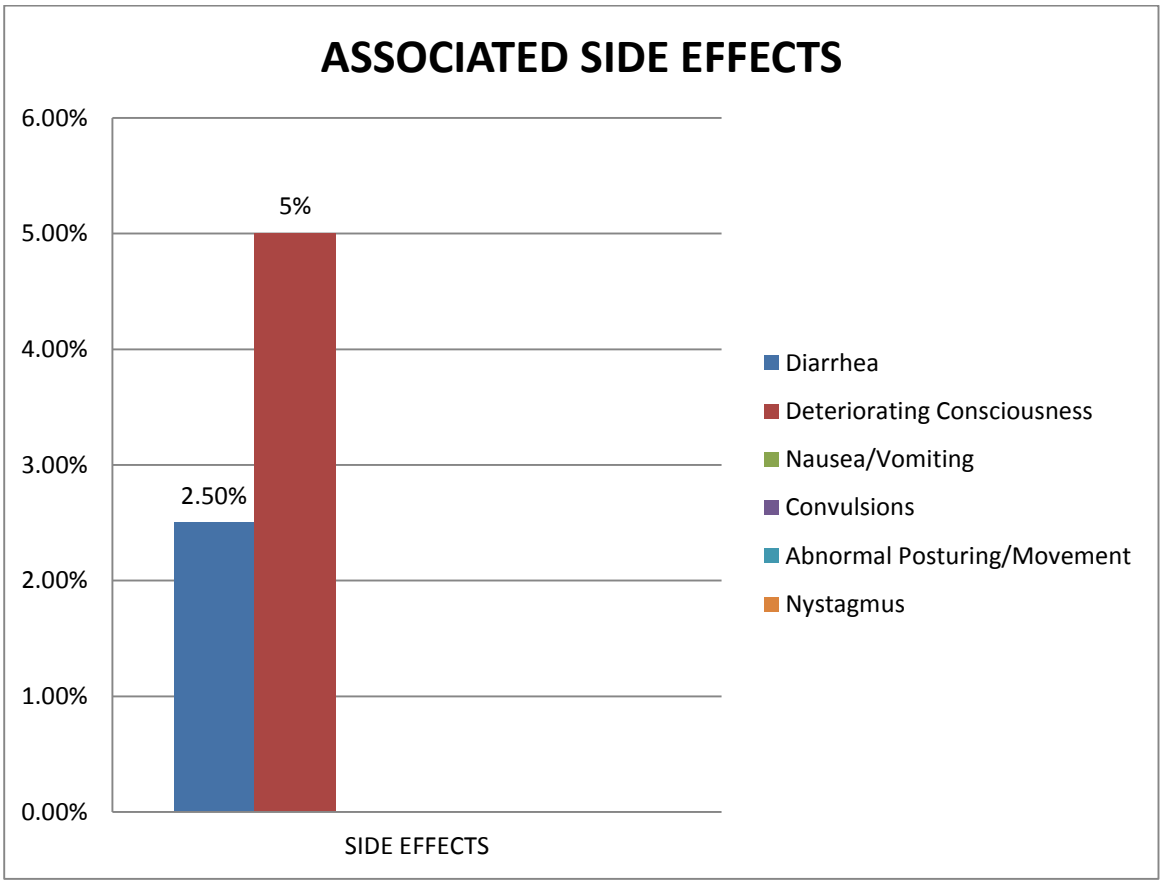

Figure 4.4: Associated Side Effects

CHAPTER FIVE: DISCUSSION, CONCLUSION, RECOMMENDATIONS AND LIMITATIONS

5.0 DISCUSSION

5.0.1 Introduction

Hyponatremia is the most common electrolyte abnormality in hospitalised patients. It is estimated to occur in 2-4% of hospitalised patients and in 15-30% of critically ill patients [2]. Mortality for patients with acute hyponatremia is quoted as high as 50% while that of chronic hyponatremia at 10-20% [4].

Management of hyponatremia is determined bythe severity of hyponatremia, acuteness of onset, presence or absence of symptoms, volume status and the etiology of the hyponatremia [5,6,7,8]. Severe (serum sodium below 125meq/L) or symptomatic hyponatremia is rapidly corrected with hypertonic saline (3% saline) while mild to moderate, asymptomatic or chronic hyponatremia is managed by total body water correction and treatment of underlying causes amongst other newer medications.

The principles of management of hyponatremia might not be applicable in many CCU cases creating the dilemma of what to do in situations where fluid cannot be restricted (patients on endogastric feeds, total parenteral nutrition or high fluid state requirement) or the underlying condition is not responding to treatment fast enough. This together with the inconsistent supply of hypertonic saline (with its feared complications mainly osmotic demyelination syndrome[9, 10]) and the unavailability of the newer drugs and slow sodium tablets has resulted in the use of enteral table salt in correcting most cases of hyponatremia at our KNH CCU set up.

Little, if any, data has been published about the use and effectiveness of enteral salt, as the sole agent, in correcting hyponatremia especially in the critical care set up. In the management of syndrome of inappropriate ADH secretion (SIADH), Binu et al [11] and Rose BD [12] describe the use of oral salt and furosemide but not in a critical care setup, neither do they discuss the effectiveness. Another case report by Karen et al [13] also describes the use of oral sodium in hyponatremia but in an outpatient set up and does not discuss its effectiveness. No local data concerning hyponatremia in the critical care set up is available.

5.0.2 Characteristics of the Participants

55% of the recruits were between the ages of 18 and 40 years. Men consisted of 65%. 45% had Neurologic pathology. Hence the majority of recruits consisted of young men with intracranial pathologies most commonly traumatic brain injury. This is attributed to the fact that most of the patients admitted at the KNH Main CCU were surgical cases. CNS pathology has been associated with SIADH and cerebral salt wasting syndrome (CSW) [19,21-25]. The exact mechanism of ADH release in SIADH remains unclear but stimulation of the neurohypophysis by the CNS pathology or possibility of ectopic ADH release from neuroendocrine tumours has been speculated. The mechanism of CSW syndrome is speculated to be as a result of central amplification of natriuretic peptides, especially brain natriuretic peptide, and decreased sympathetic outflow to the kidney resulting in urinary sodium wasting and volume depletion with resultant stimulation of ADH secretion[62-64].

5.0.3 Effectiveness of Enteral Table Salt in Hyponatremia

The mean change in serum sodium was 5.5mmol/L (SD 4.8) in 24 hours and an overall of 6.8mmol/L (SD 4.5) within 48 hours. In a small retrospective study by Ana Marie et al [65], furosemide was used to treat hyponatremia in conjunction with oral salt in euvolemic patients with SIADH. The serum sodium was noted to rise between 3 and 7mmol/L within 12-16 hours of therapy whose values are in keeping with this study. However, furosemide was the main subject of that study and smaller quantities of oral salt (4-5g) were used compared to this study's mean salt intake of 13.5g/day. In one of the largest observational studies, a report of the hyponatremia registry by Greenberg A et al [66], the median increase in serum sodium within 24 hours with common monotherapies in hyponatremia is quoted as follows; No treatment 1.0mmol/L (0.0-4.0), Fluid Restriction 2.0mmol/L (0.0-4.0), Isotonic Saline 3.0mmol/L (0.0-5.0), Hypertonic Saline 5.0mmol/L (1.0-9.0) and Tolvaptan 4.0mmol/L (2.0-9.0), whose range is consistent with the sodium increase in this study.

32 patients (80%) had normal sodium levels after 1 or 2 days of table salt administration while 4 patients (10%) had hypernatremia and 4 patients (10%) persisted with hyponatremia despite 2 days of table salt administration.

The 80% (32 patients) with normal sodium levels, 65% (29 patients) were corrected within 24 hours while the remaining 15% (3 patients) required 48 hours of table salt administration. On day 1, the 11 patients who had to receive table salt for up to 48 hours had a lower sodium intake compared to the other 29 patients whose sodium levels were corrected within 24 hours which could explain their extended requirement of the salt; however there was no other correlation in primary pathology, fluid balance and potassium levels between these two groups.

There was no significant difference in the change in sodium levels between the different demographic and clinical characteristics with the exception of cardiac disease and albumin levels; however it is worth noting that the numbers were too small to be of significant power.
There was no significant difference in change of sodium levels in patients with oedema (hypervolemic) versus those without. There were no clinically hypovolemic patients. The management of both hypervolemic and normovolemic hyponatremias involves fluid restriction[54], however in this set up table salt was given instead and there was no difference in response between the two groups.

There was no significant difference in change of sodium levels between patients with a fluid balance above 500mls per day and those with a fluid balance below 500mls. Hyponatremia is often an excess of water as opposed to a deficiency in sodium[5]; however fluid restriction was not practiced in this set as all patients received more than 1.5 litres of fluids per day.

There was no significant difference in change of sodium levels between patients who had high versus normal versus low serum urea and creatinine levels. High urea and creatinine levels are indicative of renal failure; inability to excrete fluid and resultant hypervolemic hyponatremia[16-21], however there was no difference in response between these two groups.
There was no significant difference in change of sodium levels between patients who had renal and hepatic disease versus those who did not. Renal and hepatic diseases are also associated with fluid retention and resultant hypervolemic hyponatremia[16-21], however there was also no difference in response between these two groups.

The difference in change in sodium levels was significantly higher in patients who had high and low serum albumin levels versus those who had normal serum albumin levels (P-value 0.014). Low albumin levels are associated with decreased plasma oncotic pressure, fluid retention and resultant hypervolemic hyponatremia and the vice versa applies to high albumin levels [16-21].

The difference in change in sodium levels was also significantly higher in patients without cardiac disease versus those with cardiac disease (P-value 0.024). Cardiac disease is associated with fluid overload and resultant hypervolemic hyponatremia[16-21]. However, the numbers of the two categories found to have statistical significance are skewed and therefore not representative.

It is worth noting that only 10% of the recruits persisted with hyponatremia or otherwise had treatment failure within the 48 hours of table salt administration. This translates to 90% effectiveness in correcting hyponatremia within 48 hours.

5.0.4 Association between Hyponatremia and Serum Potassium

4 patients (10%) had persistent hyponatremia while 10 patients (25%) had hypokalemia during the study. Of the 4 patients who had persistent hyponatremia, 2 of them were also hypokalemic. There was no association between persistent hyponatremia and hypokalemia (P value 0.109).
The overall (n=40) mean potassium level was 4.0mmol/L (SD 0.8) from an initial 3.8mmol/L (SD 0.9). The mean change in potassium level was 0.2mmol/L (SD 0.7). In the study by Ana Marie et al [65], the mean serum potassium was noted to drop from 4.4mmol/L (SD 0.6) to 4.1mmol/L (SD 0.4). This could be attributed to furosemide which inhibits the Na-K-Cl cotransporter in the thick ascending limb of the loop of Henle resulting in the loss of sodium, chloride and potassium in urine.

5.0.5 Associated Side Effects of Enteral Table Salt

1 patient (2.5%) developed diarrhoea while 39 patients (97.5%) did not develop diarrhoea during the study.
2 patients (5%) had deteriorating consciousness while 38 patients (95%) did not have deteriorating consciousness.
Both the diarrhoea and deteriorating consciousness cannot be solely associated with the table salt. The patient with diarrhoea already had gastrointestinal pathology; he had not received

supernormal quantities of sodium and had minimal change in blood sodium levels. Of the two patients with deteriorated levels of consciousness, one had polytrauma including head injury while the other had eclampsia and none had a significantly high change in sodium levels.

No patient experienced any of the other associated side effects namely; Nausea/Vomiting, Convulsions, Abnormal posturing/Movement and Nystagmus.

It is worth noting that the above mentioned symptoms may not be easily detectable in unconscious/semi conscious patients.

5.1 CONCLUSION

We, therefore, conclude from our findings that enteral table salt is 90% effective in correcting hyponatremia in the critical care set up. We also conclude that it is relatively safe.

A tea spoon of salt has been demonstrated to raise the plasma sodium by an average of 1.7mmol/L hence the dosing amount and frequency should be based on the deficit.

This study brings out a different angle in the balance between fluid and electrolytes; which is 'topping up the solute' where there is solvent excess as opposed to reducing the solvent to balance out the solute.

5.2 RECOMMENDATION

We recommend the use of enteral table salt in adult patients for correcting hyponatremia in the CCU set up where other modalities may not be applicable.

We also recommend a randomised control trial with a larger sample of patients and for a longer duration of follow up to prove the findings and to determine whether enteral table salt is equally effective between the different types of hyponatremias.

5.3 LIMITATIONS

The relatively small sample size used may have limited the power of the study or hindered the ability to detect differences in response between the different types of hyponatremias.

REFERENCES

1. Verbalis JG, Goldsmith SR, Greenberg A, Korzelius C, Schrier RW, Sterns RH, et al. Diagnosis, evaluation and treatment of hyponatremia: Expert panel recommendations. Am J Med. 2013;126(Suppl 10):S1–42.
2. Upadhyay A, Jaber BL, Madias NE. Incidence and prevalence of hyponatremia. Am J Med.2006;119(Suppl 1):S30–5.
3. Barash P et al, editors: Cliical anaesthesia (6th ed), Philadelphia, 2009, Lippincott Williams & Wilkins.
4. Mitchell P,Edward A, Jean-Louis, Patrick M. Textbook of critical care (6th ed), Philadelphia: Elsevier- Heath Sciences Division; 2011.
5. Frederic S, Darryl Y, Jannie R. Current diagnosis and treatment: critical care (3rd ed), New York, N.Y.: McGraw-hill Education LLC..
6. Adrogué HJ, Madias NE. The challenge of hyponatremia. J Am Soc Nephrol. 2012;23:1140–8.
7. Verbalis JG, Goldsmith SR, Greenberg A, Schrier RW, Sterns RH. Hyponatremia treatment guidelines 2007: Expert panel recommendations. Am J Med. 2007;120:S1–21.
8. Sterns RH, Nigwekar SU, Hix JK. The treatment of hyponatremia. Semin Nephrol. 2009;29:282.
9. Arieff A I, Guisado R. Effects on the central nervous system of hypernatraemic and hyponatraemic states.Kidney Int 197610104–106.106
10. Karp B, Laureno R. Pontine and extrapontine myelinolysis: a neurologic disorder following rapid correction of hyponatraemia. Medicine 199372359–373.373
11. Binu p, ambika G, Praveen V. Syndrome of inappropriate antidiuretic hormone secretion: Revisiting a classical endocrine disorder. Indian J Endocrinol Metab. 2011 Sep; 15(Suppl3): S208–S215.
12. Rose BD. New approach to disturbances in the plasma sodium concentration. *Am J Med* 1986;81:1033-40.
13. Karen E, Michael S, A Ross. Salt and water: a simple approach to hyponatremia. CMAJ. 2004 Feb 3; 170(3): 365–369.
14. Adrogué HJ, Madias NE. Hyponatremia. N Engl J Med 2000; 342: 1581–6
15. Mackey, D. C., Butterworth, J. F., Mikhail, M. S., Morgan, G. E., & Wasnick, J. D. (2013). Morgan and Mikhail's clinical anaesthesiology (5th ed.). New York, N.Y.: McGraw-hill Education LLC..
16. Halperin M, Goldstein M. *Fluid, electrolyte and acid-base physiology: a problem based approach*. 3rd ed. Philadelphia: WB Saunders Company; 1998.
17. Preston R. Acid-base, fluids and electrolytes made ridiculously simple. Miami: Medmaster; 1997.
18. Kumar S, Beri T. Sodium. Lancet 1998352220–228.228
19. Chung HM, Kluge R, Schrier R. Clinical assessment of extracellular fluid volume in hyponatremia. *Am J Med* 1987;83:905-8
20. Oren R M. Hyponatremia in congestive heart failure. Am J Cardiol 200595(95A)2B–7B.7B

21. Anderson R J, Chung H M, Kluge R. *et al* Hyponatraemia: a prospective analysis of its epidemiology and the role of vasopressin. Ann Intern Med 1985102164–168.168
22. Kahn T. Reset osmostat and salt and water retention in the course of severe hyponatremia. *Medicine (Baltimore)* 2003;82:170-6.
23. Adrogue HJ, Madias NE, Hyponatremia. *N Engl J Med* 2000;342:1581-86.
24. Sterns RH, Cappuccio JD, Silver SM, Cohen EP. Neurologic sequelae after treatment of severe hyponatremia: A multicenter perspective. *J Am Soc Nephrol* 1994;4:1522-30.
25. Sterns RH, Thomas DJ, Herndon RM. Brain dehydration and neurologic deterioration after correction of hyponatremia. *Kidney Int* 1989;35:69-75.
26. Goldman MB, Luchins DJ, Robertson GL. Mechanisms of altered water metabolism in psychotic patients with polydipsia and hyponatremia. N Engl J Med 1988;318:397–403
27. Jose CJ, Perez-Cruet J. Incidence and morbidity of self-induced water intoxication in state mental hospital patients. Am J Psychiatry 1979;136:221–2
28. Hariprasad MK, Eisinger RP, Nadler IM, Padmanabhan CS, Nidus BD. Hyponatremia in psychogenic polydipsia. Arch Intern Med. 1980;140:1639–42.
29. Fox BD. Crash diet potomania. Lancet. 2002;359:942.
30. Laureno R, Karp BI. Myelinolysis after correction of hyponatremia.Ann Intern Med 1997;126:57-62.
31. Arieff A, Llach F, Massry S G. Neurological manifestations and morbidity of hyponatraemia: correlation with brain water and electrolytes. Medicine 197655121–129.129
32. Ellis SJ. Severe hyponatraemia: complications and treatment.QJM 1995;88:905-909.
33. Reynolds R, Secki J R. Hyponatraemia for the clinical endocrinologist. Clin Endocrinol (Oxf)200563366–374.374.
34. Weisberg LS. Pseudohyponatremia. A reappraisal. *Am J Med* 1989;89:315-8.
35. Maas AHJ, Sigaard-Andersen O, Weisberg HF, Zijlstra WG. Ion-selective electrodes for sodium and potassium: a new problem of what is measured and what should be reported. *Clin Chem* 1985;31:482-5.
36. Katz MA. Hyperglycemia-induced hyponatremia: calculation of expected serum sodium depression. *N Engl J Med* 1973;289:843-4.
37. Hillier TA, Abbott RD, Barrett EJ. Hyponatremia: evaluating the correction factor for hyperglycemia. *Am J Med* 1999;106:399-403.
38. Manisha S, rakesh S. Hyponatremia: a practical approach. Indian J Endocrinol Metab 2014 Nov-Dec; 18(6): 760–771.
39. Rose BD. Hypoosmolal states — hyponatremia. In: Rose BD, Post TW, editors. *Clinical physiology of acid-base and electrolyte disorders*. 5th ed. New York: MacGraw Hill; 2001. p. 696-745.
40. Milionis HJ, Elisaf MS. Hyponatraemia in a patient with hepatic cirrhosis. *Nephrol Dial Transplant*1999;14:787-9.
41. Furst H, Hallows KR, Post J, Chen S, Kotzker W, Goldfarb S, et al. The urine/plasma electrolyte ratio: A predictive guide to water restriction. Am J Med Sci. 2000;319:240–4

42. Decaux G, Schlesser M, Coffernils M, Prospert F, Namias B, Brimioulle S, et al. Uric acid, anion gap and urea concentration in the diagnostic approach to hyponatremia. Clin Nephrol. 1994;42:102–8.
43. Beck LH. Hypouricemia in the syndrome of inappropriate secretion of antidiuretic hormone. *N Engl J Med* 1979;301:528-30
44. Maesaka JK. An expanded view of SIADH, hyponatremia and hypouricemia. *Clin Nephrol* 1996;46:79-83.
45. Decaux G, Musch W, Penninckx R, Soupart A. Low plasma bicarbonate level in hyponatremia related to adrenocorticotropin deficiency. J Clin Endocrinol Metab. 2003;88:5255–7.
46. Graber M, Corish D. The electrolytes in hyponatremia. *Am J Kidney Dis* 1991; 18:527-45.
47. Decaux G, Crenier L, Namias B, Gervy C, Soupart A. Normal acid-base equilibrium in acute hyponatremia and mixed alkalosis in chronic hyponatremia induced by arginine vasopressin or 1-deamino-8-D-arginine vasopressin in rats. *J Lab Clin Med* 1994;123:892-8.
48. Davison JM, Shiells EA, Phillips PR, Lindheimer MD. Influence of humoral and volume factors on altered osmoregulation of normal human pregnancy. *Am J Physiol* 1990;258(4 Pt 2):F900-7.
49. Linas SL, Berl T, Robertson GL, Aisenbrey GA, Schrier RW, Anderson RJ. Role of vasopressin in the impaired water excretion of glucocorticoid deficiency. *Kidney Int* 1980;18:58-67.
50. Hanna FW, Scanlon MF. Hyponatraemia, hypothyroidism and role of arginine-vasopressin. *Lancet*1997;350:755-6.
51. Robert w, Shweta B. Diagnosis and management of hyponatremia in acute illness. Curr Opin Crit Care. 2008 Dec; 14(6): 627-634
52. Bartter FC, Schwartz WB. The syndrome of inappropriate secretion of antidiuretic hormone. Am J Med 1967;42:790–806
53. Schwartz W.B., Bennett W., Curelop S., Bartter F.C. (1957)Syndrome of renal sodium loss and hyponatremia probably resulting from inappropriate secretion of antidiuretic hormone.Am J Med 23: 529–542
54. . Gross P. Treatment of hyponatremia. Intern Med 2008;47:885–91
55. Udelson J E, Smith W B, Hendrix G H. *et al* Acute haemodynamic effects of conivaptan, a dual V1a and V2 vasopressin receptor antagonist in patients with advanced heart failure. Circulation 20011042417–2423.2423
56. Zeltser D., Rosansky S., van Rensburg H., Verbalis J.G., Smith N. (2007) Assessment of the efficacy and safety of intravenous conivaptan in euvolemic and hypervolemic hyponatremia. Am J Nephrol 27: 447–457
57. Forrest J.N., Cox M., Hong C., Morrison G., Bia M., Singer I. (1978) Superiority of demeclocycline over lithium in the treatment of chronic syndrome of inappropriate secretion of antidiuretic hormone. N Engl J Med 298: 173–177
58. Decaux G, Brimioulle S, Genette F, Mockel J. Treatment of the syndrome of inappropriate secretion of antidiuretic hormone by urea.Am J Med. 1980;69:99–106.

59. Salahudeen A.K., Kumar V., Madan N., Xiao L., Lahoti A., Samuels J., et al. (2009) Sustained low efficiency dialysis in the continuous mode (C-SLED): dialysis efficacy, clinical outcomes, and survival predictors in critically I11 cancer patients. Clin J Am Soc Nephrol 4: 1338–1346.
60. Katayama Y, Haraoka J, Hirabayashi H, et al. A randomized controlled trial of hydrocortisone against hyponatremia in patients with aneurysmal subarachnoid hemorrhage. Stroke 2007;38:2373–5.
61. "QUALITY AWARDS". *Kensalt Limited*. N.p., 2016. Web. 9 June 2016.
62. Casulari LA, Costa KN, Albuquerque RC, Naves LA, Suzuki K, Domingues L. Differential diagnosis and treatment of hyponatremia following pituitary surgery. J Neurosurg Sci. 2004;48:11–18.
63. Palmer BF. Hyponatraemia in a neurosurgical patient: syndrome of inappropriate antidiuretic hormone secretion versus cerebral salt wasting. Nephrol Dial Transplant. 2000;15:262–268.
64. Berendes E, Walter M, Cullen P, et al. Secretion of brain natriuretic peptide in patients with aneurysmal subarachnoid haemorrhage. Lancet. 1997;349:245–249.
65. *Endocrine Abstracts* (2015) **37** EP672 | DOI: 10.1530/endoabs.37.EP672
66. Greenberg A, Verbalis JG, Amin AN, et al. Current treatment practice and outcomes. Report of the hyponatremia registry. *Kidney International*. 2015;88(1):167-177. doi:10.1038/ki.2015.4.

APPENDICES

Appendix 1: Questionnaire

Data collection Tool

1. Date_____
2. Study number_____
3. Age in years_____
4. Sex_____
5. Clinical diagnosis_____
6. Day in ICU Stay_____
7. Vitals-Blood Presssure_____

   -Heart Rate_____

8. Physical exam- Oedema; Present_____Absent_____

- Skin Turgor; Normal_____Reduced_____

9. Sodium levels in mmol/L(Based on morning Blood Gas Analysis)
   Day 0_____
   Day 1_____
   Day 2_____
10. Potasium levels in mmol/L(Based on morning Blood Gas Analysis)
    Day 0_____
    Day 1_____
    Day 2_____
11. Sodium intake

	Day 0	Day 1	Day 2
From table salt			
From feeds			
From IV fluids			
From other sources			
Total			

12. Number of times Table salt was given/day_____
13. Blood sugar levels g/dl(Based on Morning Blood Gas Analysis)_____
14. Levels of -Urea_____
    -Creatinine_____
    -Albumin_____
    (Based on the most recent (<1week) routine laboratory work ups)

15. Fluid Balance

	Day 0	Day 1	Day 2
Input			
Output			
Balance			

16. Is the patient known to have a Cardiac_____Renal_____or Hepatic Disease_____

If Yes Specify Type_____

17. Has the patient recently received

Mannitol_____, Methanol/Ethanol_____ or Radiocontrast_____

18. Did the patient receive hypertonic saline during the study

Yes_____ No_____

19. Has the patient experienced any of the following symptomsduring the study;

Vomiting_____ Diarrhea_____

Deteriorating consciousness_____ Convulsions_____

Abnormal posturing or movement_____ Nystagmus_____

Appendix 2: Consent Form

CONSENT INFORMATION DOCUMENT

Title

The effectiveness of enteral table salt in hyponatremia at the Kenyatta National Hospital.

Investigator

Dr. Mohammed Yahya Rashid

Supervisors:

Dr. Antony Gatheru and Dr. George Njogu

Introduction

Hyponatremia(a reduction of the mineral sodium in blood) is the most common mineral abnormality in critical care patients. It is associated with higher mortality both as a result of the hyponatremia itself and in contribution to the primary ailment.

Objectives of Study

This study aims to determine the effectiveness of enteral (ingested) table salt that is routinely used in correcting a reduction of the mineral sodium in blood in our critical care set up. It also aims to identify any associated side effects and to aid in developing a protocol on its use.

Procedure

If you agree to participate in the study, I will do an initial physical examination, capture medical details from your hospital file and follow up your blood sodium levels with the routine morning blood gas and mineral analysis.

Benefits

You will not incur any cost as a result of participating in this study. The findings from the study may benefit future patients with a reduction of the mineral sodium in blood.

Risks

Being observational, this study shall not alter or influence your management.

Voluntarism

Please also note that your participation is voluntary and you have a right to decline or withdraw from the study. Your withdrawal of participation will not affect your treatment or management in any way whatsoever.

Confidentiality

The information obtained from you will be treated with confidentiality and will be handled by me.

CONSENT CERTIFICATE

I certify that the study has been fully explained to me and I am willing to participate in it.

Participant's/ next of kin's signature/ thumbprint……

Date……..….

I confirm that I have clearly explained to the participant/ next of kin the nature of the study and the contents of this consent form in detail and he/she has decided to participate/authorize the participation voluntarily without any coercion or undue pressure.

Investigator's Signature…….Date.…….

Witness Signature.....Date.....

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Appendix 2 (b): Fomu ya idhini

MAELEZO YA FOMU YA IDHINI

Kichwa

Ufanisi wa meza chumvi kwa kurekebisha upungufu wa sodiamu mwilini katika hospitali ya kitaifa ya Kenyatta.

Mpelelezi

Dkt. Mohammed Yahya Rashid

Wasimamizi

Dkt. Antony Gatheru na Dkt. George Njogu.

Utangulizi

Upungufu wa sodiamu mwilini ndio hutokea zaidi kuliko upungufu wa vipengele vengine katika wagonjwa mahututi. Upungufu huu unahusishwa na vifo zaidi kwa sababu ya upungufu wa hio sodiamu na pia katika kuchangia kwa ugonjwa msingi.

Madhumuni ya Utafiti

Utafiti huu utasaidia kujua ufanisi wa meza chumvi inayotumiwa mara kwa mara kurekebisha upungufu wa sodiamu mwilini kwa wagonjwa wetu mahututi. Utafiti huu pia utasaidi katika kutambua madhara yanayohusishwa na utabibu huu na pia kusaidia kutengeza utifaki wa jinsi ya kutumia meza chumvi.

Utaratibu

Ukikubali kushiriki katika utafiti huu, nitakuchunguza mwili, nitapekua faili yako ya hospitali na kufuatiliza sodiamu yako inayopimwa kila asubuhi.

Faida

Hautalipa gharama yoyote ya kushiriki katika huu utafiti. Matokeo ya huu utafiti yatafaidisha wagonjwa wengine wa upungufu wa sodiamu mwilini.

Madhara

Utafiti huu hautaingilia kati matibabu unayopewa au utakayopewa na daktari wako.

Uhuru wa Kushiriki au Kutoshiriki

Ushiriki ni wakujitolea, sio lazima kushiriki katika huu utafiti, na pia unaweza kubadili nia yako wakati wowote kuhusu kuendelea kushiriki, bila ya kuathiri huduma zako za kiafya.

Usiri

Haki zako zitalindwa, habari utakayotoa au ile itakayopatikana kukuhusu itakuwa siri wakati wote na utatumika kwa huu utafiti pekee yake.

FOMU YA IDHINI

Nimekubali kwamba nimeelezwa kikamilifu kuhusu utafiti huu na nimekubali kushiriki.

Sahihi/ alama ya kidole ya mgonjwa/ mhusika wake.....

Tarehe.....

Ninathibitsha ya kwamba nimetoa maelezo sahihi kwa mgonjwa/mhusika wake kuhusu huu utafiti na yale yote yaliyomo kwa ustadi, naye mgonjwa/mhusika wake ametoa uamuzi wa kushiriki bila ya kushurutishwa.

Sahihi ya mchunguzi……Tarehe……

Sahihi ya shahidi……...Tarehe……

Ukiwa na maswali yeyote kuhusu utafiti huu, wasiliana na:

1. Dr. Mohammed Yahya Rashid
   Simu ya mkono: 0733 398057
   Barua pepe: dryahyarashid@gmail.com

2. Dr. Antony Garheru
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   College of Health Sciences
   Sanduku la posta 19676-00202
   Nairobi
   Simu: +254202726300-9 Ext 44355
   Barua pepe: uonknh_erc@uonbi.ac.ke

Appendix 3: Ethical Approval

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/267

13th September , 2017

Dr. Mohammed Yahya Rashid
Reg. No.H58/75446/2014
Dept. of Anaesthesia
School of Medicine
College of Health Sciences
University of Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 13 SEP 2017 KNH/UoN-ERC P.O. Box 20723-00202 NAIROBI

Dear Dr. Rashid

REVISED RESEARCH PROPOSAL – THE EFFECTIVENESS OF ENTERAL TABLE SALT IN HYPONATREMIA AT THE KENYATTA NATIONAL HOSPITAL CRITICAL CARE UNIT (P271/05/2017)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above proposal. The approval period is from 13th September, 2017 – 12th September 2018.

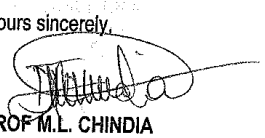
This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website**http://www.erc.uonbi.ac.ke**

Protect to discover

Yours sincerely,



PROF M.L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chair, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine,UoN
The Chair, Dept. of Anaesthesia, UoN
Supervisors: Dr. Anthony Gatheru, Dr. George Njogu

Appendix 4: Study Registration Certificate

KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   DR. MOHAMMED YAHYA RASHID
2. Email address: dryahyarashid@gmail.com Tel No. 0733398057
3. Contact person (if different from PI) N/A
4. Email address: N/A Tel No. N/A
5. Study Title
   THE EFFECTIVENESS OF ENTERAL TABLE SALT IN HYPONATREMIA AT THE KENYATTA NATIONAL HOSPITAL CRITICAL CARE UNIT
6. Department where the study will be conducted ANAESTHESIA AND CRITICAL CARE
   (Please attach copy of Abstract)
7. Endorsed by Research Coordinator of the Department where the study will be conducted.
   Name: ..... Signature ..... Date .....
8. Endorsed by KNH Head of Department where study will be conducted.
   Name: AL HEZZA O. REAY Signature ..... Date 26-9-2017
9. KNH UoN Ethics Research Committee approved study number P271/05/2017
   (Please attach copy of ERC approval)
10. I DR. MOHAMMED YAHYA RASHID commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Research and Programs.
    Signature ..... Date 25TH SEPTEMBER 2017
11. Study Registration number (Dept/Number/Year) ANES/Thesis/162/2017
    (To be completed by Research and Programs Department)
12. Research and Program Stamp .....

All studies conducted at Kenyatta National Hospital **must** be registered with the Department of Research and Programs and investigators **must commit** to share results with the hospital.

Version 2: August, 2014

Appendix 5: Turnitin Original Report

THE EFFECTIVENESS OF ENTERAL TABLE SALT IN HYPONATREMIA

ORIGINALITY REPORT

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