THE EFFECT OF INTRAOPERATIVE CO-ADMINISTRATION OF RINGERS LACTATE COMBINED WITH 0.9% NORMAL SALINE ON SERUM ELECTROLYTES AND LACTATE IN PATIENTS UNDERGOING ELECTIVE CRANIOTOMY

DR ANDREW KIMATHI MURIITHI

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

2018

STUDENT'S DECLARATION

I declare that this dissertation is my original work and has not been submitted for a degree award in this or any other university. All resources contained herein have been duly acknowledged.

Dr. Andrew Kimathi Muriithi, MBChB (Moi)

Post graduate student in Anaesthesia

University of Nairobi

Email: amuriithi@gmail.com

Tel: +254721450900

Registration number: H58/69675/2013

Signature: ……. Date: ……..

SUPERVISOR'S APPROVAL

This dissertation has been submitted with our approval as university supervisors:

Dr. Lee Ngugi Kigera

MBChB, M.Med Anaesthesia(UoN)

Diploma (WFSA),GCSRT-(Clinical trials)Harvard Medical School

Lecturer Department of Medical physiology-Kenyatta University

Consultant Anaesthesiologist, Pain specialist

Signature..... Date.....

Dr. Thomas Chokwe

MBChB, M.Med Anaesthesia (UoN)

Diploma in Solid Organ Transplantation Anaesthesia, Chulalongkorn University

Lecturer and Chairperson, Department of Anaesthesia-University of Nairobi

Consultant Anaesthesiologist, Transplant anaesthesia

Signature..... Date.....

Dr. George Njogu,

MBChB, MMed Anaesthesia (UoN),Neuroanaesthesia (UCT)

Department of Anaesthesia,Kenyatta National Hospital.

Signature..... Date.....

DEDICATION

I would like to dedicate this dissertation to my colleagues in the anaesthesia residency program who encouraged me through the writing of this dissertation.

ACKNOWLEDGEMENTS

I would like to acknowledge my supervisors Dr Lee Kigera, Dr George Njogu and Dr Thomas Chokwe for guiding me through this research process. In addition, I express my gratitude to my family and colleagues who have given me both emotional support and helped with data collection.

I would like to thank Mr Martin Njenga, my research assistant and Mr Francis Njiiri my statistician for the man hours put to develop this dissertation.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

ASA	American Society of Anaesthesiologists
BBB	Blood Brain Barrier
BE	Base Excess
BG	Blood Glucose
BGA	Blood Gas Analysis
BMI	Basal Metabolic Index
BUN	Blood Urea Nitrogen
Ca^{2+}	Calcium ion
CCU	Critical care unit
Cl^-	Chloride ion
ECG	Electrocardiogram
HCO_3^-	Bicarbonate ion
HCT	Hematocrit
ICP	Intracranial pressure
K^+	Potassium
Kg	Kilogram
KNH	Kenyatta National Hospital
mmHg	Millimetres of mercury

mmol/l	millimoles per litre
mOsm/kg	milliosmoles per kilogram
Na^+	Sodium
PCO_2^-	Partial Pressure of Carbon dioxide
PO_2^-	Partial Pressure of Oxygen
TJ	Tight Junction
UoN	University of Nairobi

OPERATIONAL DEFINITIONS

Craniotomy: This is surgical removal of a part of the skull

Colloids: This is a fluid that contains both water and electrolytes, and that has large molecules that do not diffuse across a semi permeable membrane.

Crystalloid: A substance whose particles are smaller than those of a colloid, form a true solution, and are therefore capable of passing through a semi permeable membrane.

Arterial blood gas analysis: Is a test which measures the amounts of oxygen and carbon dioxide in the blood, as well as the acidity (pH) of the blood.

Electrolytes: Are the ionized or ionizable constituents of a living cell, blood, or other organic matter.

Osmotherapy: Is dehydration by means of intravenous injections of hypertonic solutions of sodium chloride, dextrose, urea, mannitol, or other osmotically active substances, or by oral administration of glycerine, isosorbide, glycine, and others; used in the treatment of cerebral oedema and increased intracranial pressure.

ABSTRACT

Background

Intravenous fluids are used in virtually all surgical specialties for fluid maintenance. The most common fluids used are 0.9% Normal Saline and Ringers Lactate. In the neurosurgical patients, the osmotic force exerted by the electrolytes sodium and chloride have a key role in the movement of fluid across the brain capillaries. Normal Saline used as monotherapy has been shown to cause metabolic acidosis and arrhythmias when infused in large amounts, thus co-administration with ringers lactate ameliorates these potential side effects.

Objectives

The objective of this study was to describe the effect of co administered ringers lactate and 0.9% normal saline on serum sodium, potassium, chloride and lactate levels in neurosurgical patients undergoing elective craniotomy.

Study Design and Methods

This was a descriptive cross sectional study carried out in Kenyatta National Hospital, neurosurgical theatres. Data was collected from the anaesthesia chart on type and amount of intravenous fluid used, acid base balance from the blood gas analysis strip done hourly were recorded on the data collection sheet. The sample size was 71 patients scheduled for elective craniotomy meeting the inclusion criteria. All the data collected in the study was sorted, coded and entered in a computer using SPSS Version 21. T- tests were used to compare mean changes in serum sodium, potassium, chloride and lactate to the crystalloid infused and Chi-square tests were used to compare proportions.

Findings: There was a marginal reduction in serum sodium with infusion of combined crystalloids, within a normal safety margin. Serum potassium and lactate steadily increased

every hour with infusion of crystalloids with no correlation to blood loss. Serum chloride marginally increased from the 2nd to 3rd hour and stabilized at the 4th hour. No correlation was seen to with blood loss.

Conclusion: Both N/S and R/L are safe crystalloids to infuse in combination therapy in elective craniotomy patients.

1.0 CHAPTER ONE: INTRODUCTION

Intravenous fluids are used routinely in surgery to maintain intravascular volume and replace blood loss.[1] A common fluid choice typically used in neurosurgery is normal saline 0.9% as a monotherapy to achieve these goals.[1,2,3]Normal saline 0.9% and ringers lactate however have been noted to have side effects such as hyperchloremic metabolic acidosis[4] and arrhythmias [16], making the choice of maintenance fluid used important.

Other fluid regimens have also been studied as possible fluid choices to be used intraoperatively in neurosurgical practice and mitigate against some of the above listed side effects. These fluids have serum osmolality close to that of the human body as well as an electrolyte mix that is physiologically acceptable, such as normal saline 0.9% with addition of sodium bicarbonate, ringers lactate and plasmalyte. [1,4] In Kenyatta National Hospital, 30 elective craniotomy cases and 35 emergency craniotomies are performed on average every month, with both Normal Saline 0.9% and ringers lactate used as maintenance fluids.

The purpose of this study was to document hourly changes in serum electrolytes and serum lactate levels when administering standard fluid practices in existence comprising of normal saline 0.9% and ringers lactate in elective craniotomies at the Kenyatta National Hospital neurosurgery theatre.

2.0 CHAPTER TWO: LITERATURE REVIEW

2.1The blood brain barrier and its effects on fluid physiology

Fluid redistribution in the brain through the capillaries presents unique physiologic variations occasioned by the Blood Brain Barrier (BBB). The BBB inhibits the free paracellular diffusion of water-soluble molecules by an elaborate network of complex tight junctions (TJs) that interconnects the endothelial cells. In addition, the absence of fenestrae and an extremely low pinocytotic activity inhibit transcellular passage of molecules across the barrier.[5]

The capillary membrane in the cerebral capillaries is relatively impermeable to most of the low molecular weight solutes present in blood .[5]Serum electrolytes and their shifts thus play a key role to this regard, particularly the ions Na^+ and Cl^-.[2,3,5] These solutes are effective at exerting an osmotic force across the cerebral capillary membrane. The oncotic pressure is extremely small in comparison to the huge osmotic pressure exerted by the effective small solutes in the cerebral capillaries. [3,5]

Starling's forces describe the factors determining the movement of fluid across the capillary endothelium.[6]Movement into the interstitial space is driven by the hydrostatic pressure gradient. This flow is counteracted by the colloid osmotic gradient. These forces are governed by the following formula: [5]

Net filtration= (Pc – Pif) – (¶p - ¶if)

Pc = Capillary hydrostatic pressure (35 mmHg)

Pif = Interstitial hydrostatic pressure (usually zero)

¶p = Oncotic pressure due to plasma proteins (28 mmHg)

¶if = Oncotic pressure due to interstitial proteins (3 mmHg)

Hence net flow:

Arterial end: 10 mmHg out of capillary

Venous end: 10 mmHg into capillary

Based on the above formula, a one milliOsmole /kg increase in osmotic gradient between blood and brain interstitial fluid will exert a force of 17 to 20 mmHg. At an osmolality of 287 mOsm/kg then the total osmotic pressure is about 5400mmHg as can be calculated with the *van't Hoff equation*. In comparison, the plasma oncotic pressure of 25 mmHg is tiny. [5]

This therefore implies that small changes in plasma tonicity can have a marked effect on the total fluid volume of the intracranial compartment.[3,5,6] It is not just the intracellular volume of the brain cells but also the volume of the brain extracellular fluid that are decreased by an increase in plasma osmolality. In other tissues of the body, an increase in plasma osmolality would increase interstitial fluid volume but decrease intracellular fluid volume in that tissue.[3,5,6]

2.2 Introduction to intravenous fluids, their uses and side effects

Intravenous fluids are divided into two broad categories, namely, crystalloids and colloids.[1,7]The role of intravenous fluids is to maintain intravascular volume, and are used for both resuscitative fluid therapy as well as maintenance fluids at a time when intravascular fluid volume is depleted due to preoperative dehydration, intraoperative blood loss, or redistribution of fluid into different physiological spaces.[1,2,3]

The most commonly used crystalloid solutions for the maintenance of intravascular volume in surgical practice are 0.9% normal saline and ringers lactate.[7,8] Normal saline 0.9%

contains 154mmol/l of Na^+ and Cl^- ions, and has an osmolality of 308, with a pH of 5. Ringers Lactate, has an electrolyte composition of Na^+ 130mmol/l, Cl^- 109mmol/l, K^+ 4mmol/l, Ca^{2+} 3mmol/l, lactate 28mmol/l, osmolality of 275 and a pH of 6.5. [7]

Ringers lactate has an electrolyte content closer to the body's internal milieu, and is thus a good adjunct fluid to be used in this study for mixed crystalloid solution.[3,7] It is now used widely as a good adjunct to Normal Saline as both a fluid of hourly maintenance in the operating room, as well as for fluid resuscitation. [1,7,9,10]Ringers lactate however, is not devoid of its side effects, and can cause a metabolic alkalosis secondary to metabolism of lactate which produces bicarbonate when used as a monotherapy[2.7].

Normal saline has been used as a standard of care in intravenous fluid management over the years in neurosurgery. [1,4,5] Monotherapy infusions of this fluid however has been shown to cause a hyperchloremic metabolic acidosis when infused in large amounts.[2,11,12] Dextrose-containing solutions such as 5% Dextrose should be avoided in patients with neurologic injuries as they may cause cerebral oedema.[4]

A Cochrane review was conducted by Bertrand et al [7], comparing buffered and non-buffered perioperative administration of fluids in adults, and in particular, 1 study compared administration of Normal saline and ringers lactate and their effects on serum sodium, potassium, chloride and lactate. The study by Waters et al [27] noted that patient who received a monotherapy of normal saline had a higher incidence of hyperchloremic metabolic acidosis, and received more blood products compared to the arm that received ringers lactate as a monotherapy.

A prospective, randomized controlled study compared the changes in acid-base balance and serum electrolytes with the use of intravenous balanced and non-balanced crystalloid

solutions intraoperatively during elective neurosurgery The intravenous fluids used were 0.9% normal saline and Sterofundin®, which contains Na^{+} 140mmol/l, K^{-} 4mmol/l, Cl^{-} 127mmol/l, Ca^{2+}2.5mmol/l and Mg^{2+} 1mmol/l, with a total of 30 study participants in 2 equally randomised groups. This study concluded that a balanced solution (Sterofundin ® ISO) provided significantly better control over acid-base balance, sodium and chloride levels when used as Intraoperative fluid maintenance and replacement during elective neurosurgery cases.[5]

Another randomized control study was conducted using normal saline serum (0.9%) co-administered with Ringer's lactate added on one arm, and the other arm had half-normal saline study group, 80 ml of sodium bicarbonate per litre was added and injected to compensate the fluid retention and loss. There was no significant difference in the two groups and the changes observed in these three markers were balanced between the two groups. Analysis of variance with repeated testing also showed no significant differences between the two groups (P = 0.99). Changes in these three markers were balanced between two groups. The mean level of each of these markers in the measured time periods was consistent in the two groups.[422]

2.3 The role of osmotherapy in neurosurgery and its interactions with intravenous fluids

Osmotherapy has been used as a strategy to reduce brain bulk, and has been documented from as early as 1919, through the works of Weed and McKibben, where they used concentrated salt solutions to achieve reduction of brain bulk on experimental animals. [13]

20% Mannitol and 3% hypertonic saline have been used in respect to osmotherapy to reduce intracranial pressure.[14]Mannitol has been traditionally used to achieve this goal at a dose of 0.25g-2g/kg.[4,14] It is widely available in our setup at the Kenyatta National Hospital and is used extensively in neurosurgery practice for this purpose.

Hypertonic saline has also been shown to have good results in overall reduction of intracranial pressure and increase in systemic perfusion with 30% saline given as a single bolus in two traumatic mannitol resistant patients. [14,15] Hypertonic Saline administered at concentrations of 3-23.4% has been shown to reduce the ICP after brain trauma. [14,15,21,22]

The initial target of serum osmolality is often set at 300–320 mOsmol/kg. Acute renal failure might develop when serum osmolality exceeds 320 mOsmol/kg during mannitol infusion. Therefore, measurement of serum osmolality during hyperosmolar agent infusion is of clinical importance to determine clinical efficacy, adjust dosage and avoid side effects. [14]

The formula used to calculate serum osmolality is:[14]

$2*([Na^+]+[K^+])+BG+BUN$

BG=Blood serum glucose in mmol/l

BUN=Blood Urea Nitrogen

2.4 Side effects noted in the use of osmotherapy when combined with crystalloids

Use of Mannitol has been reported to cause intraoperative hyperkalemia in some patients after co-admininstration with RL.[16] There were two reported cases of hyperkalemia intraoperatively in patients who have had no prior kidney injury, or rhabdomyolysis preoperatively.[16] Other randomized trials conducted have shown a decrease in serum sodium and bicarbonate ion levels, however the maintenance crystalloid fluid was not specified. [4,20]

2.5 Blood gas analysis and neurosurgery

The use of blood gas analysis is standard in neurosurgery practice intraoperatively,[4,20,24,25] The parameters monitored in standard neurosurgery anaesthesia are the serum electrolytes, the partial pressure of oxygen and carbon dioxide, the arterial pH and serum lactate.[4,20,24,25]

Serum lactate has been studied in neurosurgery practice due to advances in neurosurgery prolonging operation durations. [24]Serum lactate is used as a surrogate to check tissue perfusion globally within the body, and increases may point toward anaerobic respiration as an alternative source of energy production with lactic acidosis ensuing.

Serum lactate however is not devoid of potential confounders. Garavaglia et al, In Toronto, Canada [24] looked into the Basal Metabolic Index (B.M.I), as a risk factor for increased serum lactate levels in patients undergoing craniotomy. They hypothesized that prolonged craniotomy time would lead to increase of serum lactate, and conducted a prospective observational study of 18 patients that looked into the other expected risk factors for lactatemia such as the hemoglobin, hypotension intraoperatively and mannitol administration. Their study showed an early increase in serum lactate levels correlating to the B.M.I, however not related to the length of surgery.

Based on the studies quoted above, its has been noted that crystalloid combination therapies that have electrolyes and pH values closer to those of normal body physiology are associated with less side effects. [2,3,4] The evidence put forward by the case reports which pointed out to potential interactions of the crystalloid fluids, as seen by Kiichi et al also further supports the need for a larger structured study to tease out a potentially safer regime and clearly point out any similarities pointing towards potential derangements that are unsafe for our patient population.[16]

In Kenyatta National Hospital, both normal saline 0.9% and ringers lactate are routinely used as maintenance intravenous fluids in both elective and emergency craniotomies.

2.6 Study Justification

Crystalloid fluids are used in virtually all forms of surgery as intravenous fluid therapy for replacement of blood loss and for hourly maintenance of fluid balance in the body while patients undergo surgery.

The choice of intravenous fluid used is thus key in neurosurgical patients to maintain a normal serum osmolality, with key emphasis to the levels of sodium, the major ion governing osmolality and movement of water within the brain.

There is no local data on the effect that of intravenous fluids have on serum electrolytes in craniotomy patients, thus documentation of the serum electrolytes and serum lactate is thus a key factor to be looked into as this is a practice done within our hospital setting at the Kenyatta National Hospital Neurosurgery theatres.

Serum osmolality has been shown to have a big role in the movement of water from the brain across the blood brain barrier. Crystalloid fluids are however not devoid of their side effects, such as hyperchloremic metabolic acidosis when massive amounts of 0.9% normal saline are infused, which is a crystalloid used in common practice in neurosurgery for maintenance fluid. In neurosurgery, the operations tend to be lengthy, and the blood loss may be significant requiring large amounts of these fluids to be used. The co-administration of Ringers Lactate helps mitigate against this risk, however changes in both the osmolality of the blood and change in the sodium ion is yet to be documented. There has been no life threatening side effects recorded on the mixed fluid regimens when electrolytes were measured. [4,16]

This information will thus be beneficial in adding onto the body of knowledge in the field of neuro-anaesthesia in the world over.

2.7 Research Question

What are the serum electrolyte and acid-base changes intraoperatively that were associated with administration of normal saline 0.9% and ringers lactate in neurosurgical patients?

2.8 Objectives

2.8.1 Broad Objective

To characterize serum electrolyte changes in neurosurgical patients receiving ringers lactate and 0.9% normal saline combination during elective craniotomy.

2.8.2 Specific Objectives

1. To describe the effect of combined ringers lactate and 0.9% normal saline on the intraoperative level of serum sodium in patients undergoing elective craniotomy.
2. To describe the effect of combined ringers lactate and 0.9% normal saline on the intraoperative level of serum potassium in patients undergoing elective craniotomy.
3. To describe the effect of combined ringers lactate and 0.9% normal saline on the intraoperative level of serum chloride in patients undergoing elective craniotomy.
4. To describe the effect of combined ringers lactate and 0.9% normal saline on the Intraoperative level of serum lactate in patients undergoing elective craniotomy.

3.0 CHAPTER THREE: METHODS

3.1 Study Design:

This was a descriptive cross-sectional study. The exposure variable and the outcome was measured at the same point in time.

3.2 Study Area:

The study took place at Kenyatta National Hospital's Main theatre block, in particular, the Neurosurgery theatre suite allocated to the department of neurosurgery for elective craniotomies to be performed.

3.3 Study Population:

Adult patients undergoing elective craniotomy surgery who met the inclusion criteria.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

1. Patients who were scheduled for elective craniotomy surgery
2. Patients above the age of 18 years and below 70 years.
3. ASA I to ASA III patients
4. Patients or their guardians in cases where participants were confused gave written informed consent to participate in the study

3.4.2 Exclusion Criteria

1. Patients with renal failure or undergoing renal replacement therapy
2. Patients with diabetes insipidus or syndrome of inappropriate anti diuretic hormone syndrome being actively managed preoperatively.
3. Patients undergoing surgery of the pituitary gland.
4. Repeat craniotomies

3.5 Sample size

The desired sample size was calculated using the formula as;

$$n = \frac{(u+v)^2\sigma^2}{(\mu-\mu_0)^2}$$

Where:

n= sample selected

u = One-sided percentage point of the normal distribution corresponding the power at 80% therefore 0.84.

v = Percentage point of the normal distribution corresponding to 95% confidence level therefore 1.96

σ = Standard deviation of 9.0 mmol/L of the average patients with normal baseline sodium levels (135-144 mmol/L)

$(\mu-\mu_0)$ =Required absolute error or precision. The difference between mean, μ and the hypothesized value, μ_0. This will be given by 3.0 mmol/L

The standard deviation of 9.0 mmol/l of sodium is obtained from the medically agreed average ranges of patients with normal baseline sodium levels. The absolute error term or precision has been set by the researcher. The required size of the precision of +/- 3.0 mmol/L was selected so that the sample size become 70.56 thus 71 patients.

3.6 Recruitment

All patients scheduled for elective craniotomy and fulfilling the inclusion criteria were included in this study. Preoperative lab indices on the baseline serum electrolytes, were copied from the file to the data collection sheet as well as the intraoperative intravenous fluid amounts administered, electrolyte measurements taken every hour from the blood gas analysis strips.

3.7 Sampling procedure

The principal investigator reviewed the patients in the ward on the evening before the intended surgery. Study participants were identified based on the inclusion and exclusion criteria outlined above and a detailed explanation about the study was done to obtained an informed consent.

Patients listed for surgery were assessed for eligibility and enrolled. Those not meeting the eligibility criteria, and those who refused to participate in the study were excluded. Convenience sampling was used to identify patients who will be included in the study. This is because data collection was done over a short period of time as well as the simplicity of sampling.

Every patient in the elective craniotomy theatre list was selected. The investigator recruited patients into the study consecutively until the required sample size is attained.

3.8 Data collection, management and analysis

The patients initials, hospital number, age, weight, preoperative lab values, total amount of fluids administered intraoperatively, mannitol amount given, urine output, blood gases and other descriptive characteristics were recorded in the data collection sheet copied from the data recorded by the anaesthesia provider in the anaesthesia chart in the operating room. The data collection sheet was entered into an excel spread sheet and exported to SPSS version

21.The aim of the analysis was to compare changes in serum electrolyte and lactate levels in neurosurgical patients undergoing elective craniotomy.

To ensure that the data recorded in theatre was correct, a copy of the blood gas analysis strip was also be made by the principal investigator as a record for cross referencing.

The key outcome measures (sodium, potassium, chloride and lactate) were continuous variables therefore mean differences and standard deviations were used and their confidence intervals and p-values were used to compare electrolyte changes intraoperatively. T tests were used to compare means and chi square tests to compare proportions. The values from these outcome measures answered objective 1 to 4 of this study. Data was presented using bar graphs and tables where appropriate.

3.9 Collection of blood gases by the anaesthesia provider and quality control

The blood gas analysis was conducted intraoperatively by the anaesthesia provider every hour during the provision of anaesthesia for craniotomy patients.

Once the patient was anaesthetized, the anesthesia provider used an aseptic technique by wearing gloves and cleaning the site for blood to be drawn using cotton wool and spirit. A baseline sample of 1cc of blood was drawn from the radial artery of the patient using a heparinised 2cc syringe and a gauge 25 needle. The sample was then taken to the critical care unit laboratory.

The machine used for blood gas analysis at the critical care unit is a Siemens RAPIDpoint 500 series, which had a maintenance free cartridge based system which incorporated automatic quality control for assured maintenance of quality of results. The automatic quality control reports were attached as an appendix

3.10 Ethical Considerations

Approval to carry out the study was sought and obtained from the KNH/UoN Ethics and Research Committee.

Written informed consent was obtained from each participant/relative/guardian

The study respected the right of the patients to decline participation

There was no additional cost or incentive for participating in the study

There was no penalty for refusal to participate in this study.

The information obtained from each participant was treated with utmost confidentiality

Patient privacy was also be upheld by coding the forms used to mask their identity.

Participants were allowed to withdraw at any point in the study

CHAPTER FOUR: FINDINGS

4.1 Characteristics of the study population

The study population comprised of 72 participants with 38 being female and 34 being male. The mean age of the study population was 42 years, and the mean BMI of the study population was 26.73, which lies in the overweight category of BMI stratification.

Table 1: Gender Distribution

		N	%
Gender	Male	34	47.2
	Female	38	52.8

Table 2: Age, weight, height and BMI computation of the population

	MEAN
Age	**42**
Weight (kg)	**67**
Height (cm)	**165**
B.M.I	**26.73**

Table 3: ASA class distribution of the total patient population

ASA CLASS	n
1	6
2	48
3	18

The incidence of patients in ASA class I to class III who had normal sodium levels was 60%, with 25% of the patients noted to have hyponatremia and 13.8% having hypernatremia.

The incidence of patients in ASA class I to class III who had normal potassium levels was 81.9%. It was noted that 2.7% of the patient population had hyperkalemia and they were exclusively in ASA class III, while those with hypokalemia were 15.4%

The incidence of patients with normal chloride levels in ASA class I to III was 86%, with 8% of the patient population having hypochloremia, and 6% with hyperchloremia.

The incidence of patients with normal serum lactate levels within ASA class I to III was 73.6%, with 26.3% of the patients noted to have hyperlactatemia. It was noted that 52% of those with hyperlactatemia were in ASA class III.

There was no noted statistically significant change in all the means of the measured parameters on the blood gas analysis strip per hour, as shown in the table below.

Table 4: Hourly average of all measured variables from the blood gas analysis strip

Time	PH	pCO2	pO2	HCO3	Na	K^-	CL	Lactate	HCT	Glucose	Urine
1ST HR	7.4	4.7	20.6	22.0	138.7	3.7	100.0	1.3	39.3	6.1	223
2ND HR	7.4	4.5	18.3	24.1	138.1	3.9	100.8	1.5	38.3	7.0	287
3RD HR	7.4	4.4	19.2	23.1	136.5	4.2	102.2	1.9	38.7	6.8	332
4TH HR	7.4	4.4	20.9	25.0	137.1	4.3	101.7	2.1	37.8	7.2	508
p-value	0.999	0.989	0.765	0.788	0.897	0.582	0.886	0.124	0.788	0.711	0.241

The distribution of hourly intravenous fluids infused intraoperatively is shown below.

Figure 1: Distribution of patients receiving normal saline per hour

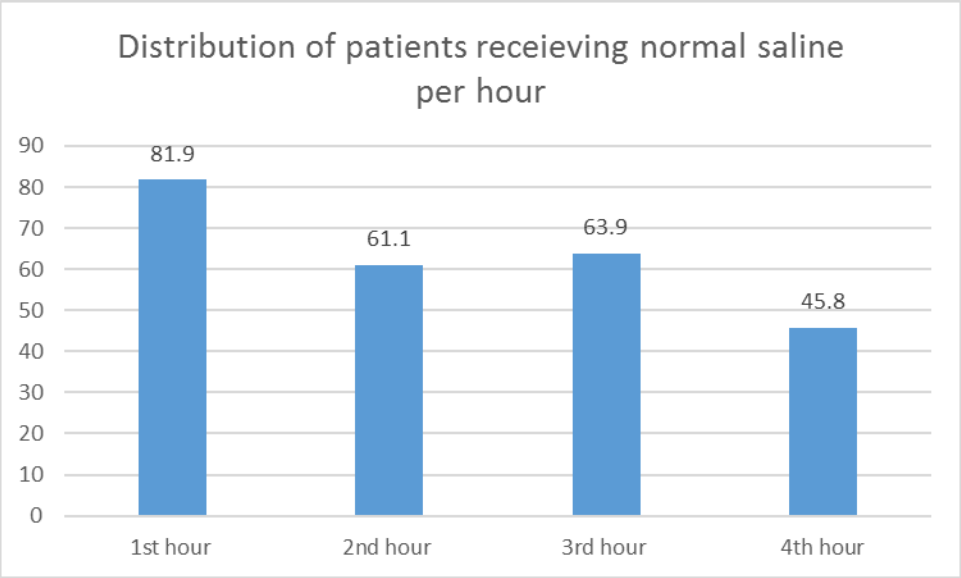
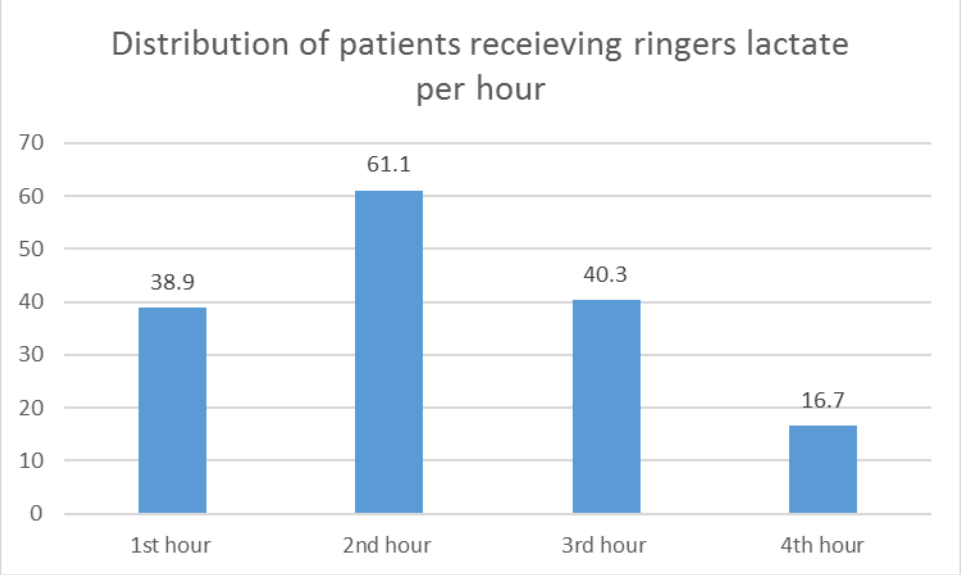


Figure 2: Distribution of patients receiving ringers lactate per hour



Graphs showing hourly trends of sodium, potassium, chloride and lactate

Figure 3: Serum sodium hourly trend

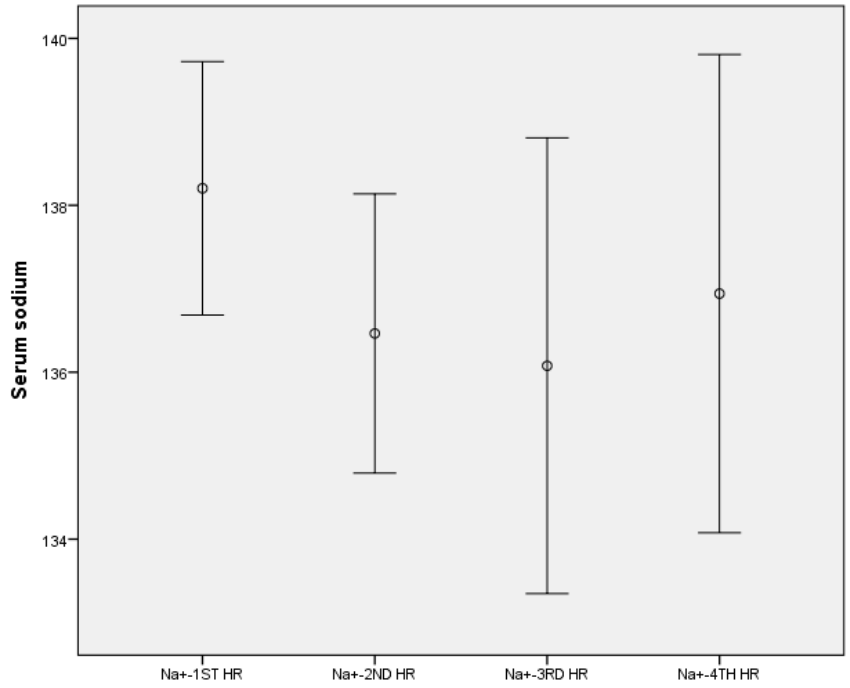


Figure 4: Serum potassium hourly trends

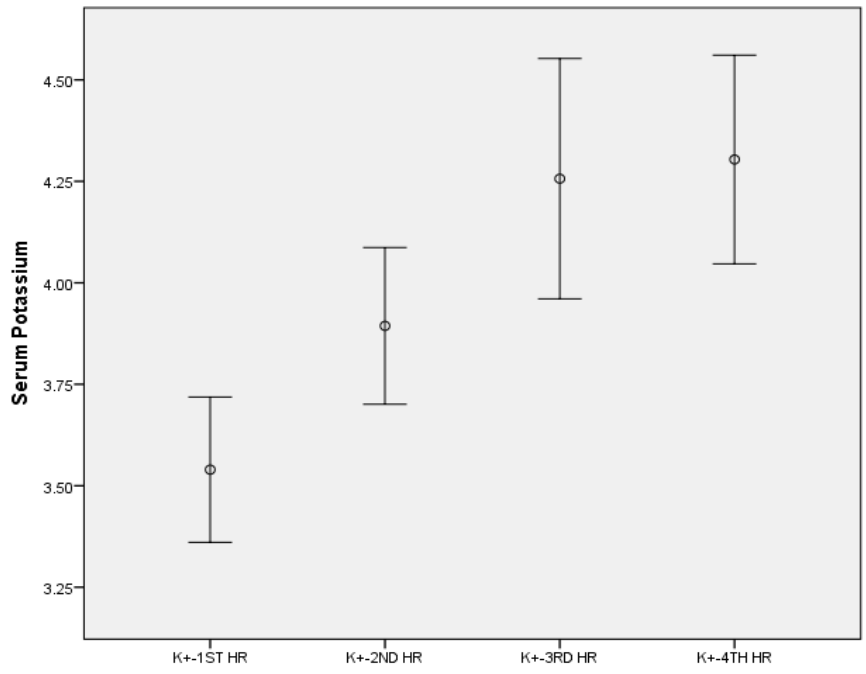


Figure 5: Serum chloride hourly trends

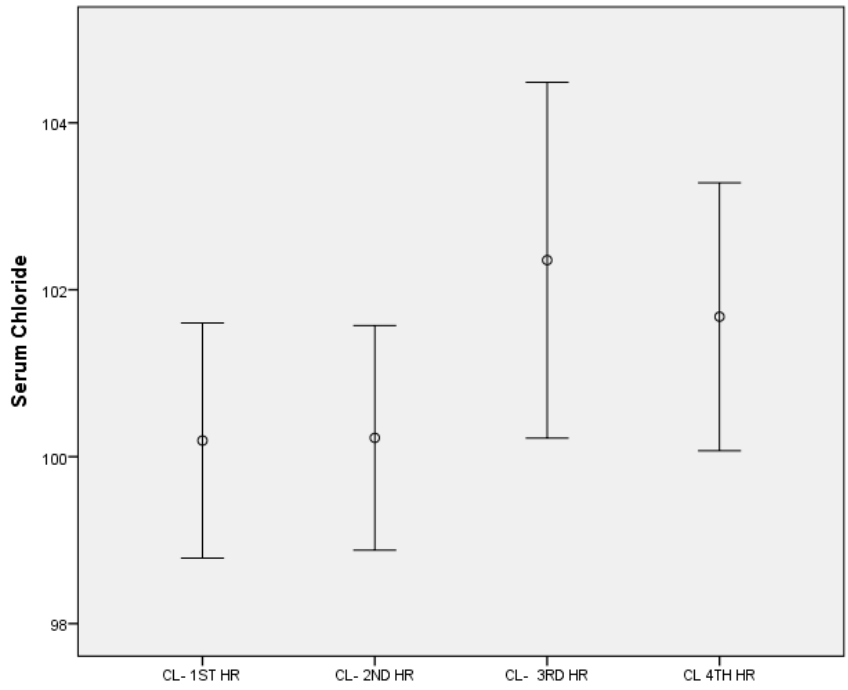


Figure 6: Serum Lactate hourly trends

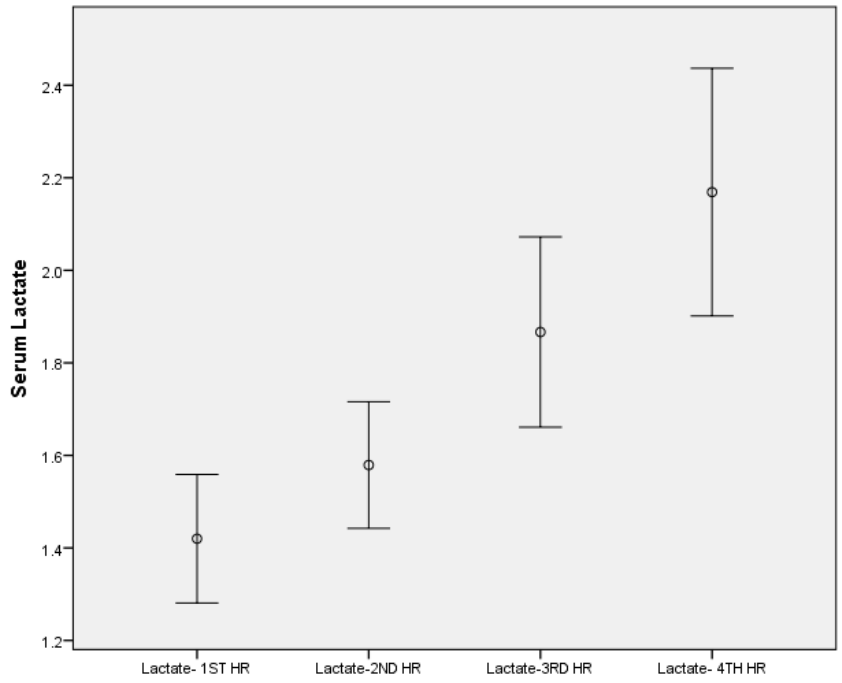


Table 5: Correlation of blood loss to changes in serum sodium, potassium, chloride and lactate

		BLOOD LOSS			
		Valid N	Mean	Standard Deviation	p-value
Chloride	Hypochloremia	4	475	119	0.864
	Normal	62	456	211	
	Hyperchloremia	6	412	236	
Lactate	Hypolactatemia	0	.	.	0.089
	Normal	53	429	217	
	Hyperlactatemia	19	523	162	
Sodium	Hyponatremia	18	482	234	0.145
	Normal	44	469	202	
	Hypernatremia	10	335	149	
Potassium	Hypokalemia	7	386	157	0.435
	Normal	59	447	213	
	Hyperkalemia	2	600	141	

There was no significant change in serum sodium, potassium, chloride and lactate when correlated to mean blood loss

CHAPTER FIVE: DISCUSSION, CONCLUSION, LIMITATIONS AND RECOMMENDATIONS

DISCUSSION

The mean age of the study population was noted to be 42 years of age, with 52% of the population noted to be female. The mean BMI of the study population was noted to be overweight, with a BMI of 26.73, with 75% distributed between ASA I and II.

The incidence of patients with normal sodium levels within ASA class I to ASA class III was 61%, with 25% of the patients noted to have hyponatremia and 14% with hypernatremia. The patients who were noted to have hyponatremia had a higher blood loss, with a mean of 482mls compared to those with normal sodium, who had a blood loss of 469mls while those with hypernatremia had a mean blood loss of 335mls. Our study noted no clinically significant drop in serum sodium when combined infusions of 0.9% normal saline and ringers lactate were infused, with a marginal drop seen between the 1st and 3rd hour, stabilising at the 4th hour. It is important to note that despite the drop in serum sodium, the clinical values of the average patient population still remained within the normal reference range. This was in keeping with Bertrand et al's[7] Cochrane review who noted that combined infusions of ringers lactate and normal saline had no significant decrease in serum sodium when used in combination.

The incidence of patients with normal potassium levels in the study population from ASA class I to ASA class III was noted to be 81.9%, with hyperkalemia seen predominantly in ASA III patients at 2.7%. The patients who were in the hyperkalemia group had a mean blood loss of 600mls, compared to those who had a normal potassium value with a mean blood loss of 447mls. The effect of this blood loss on the potassium ion was however not clinically

significant. Waters et al [28] compared infusions of both ringers lactate and normal saline in combination intraoperatively, with no reported cases of clinically significant hyperkalemia or potassium rise. Bertrand et al[7] in their review of blood loss as an independent factor to cause a rise in serum potassium also found no clinical significance in their patient cohort linking blood loss to hyperkalemia.

The incidence of patients with normal chloride levels in ASA class I to III was 86%, with 8% of the patient population having hypochloraemia, and 6% with hyperchloremia. In the sub group that was noted to have hyperchloremia, the mean blood loss was 412mls, compared to a mean blood loss of 456mls in the cohort with normal chloride levels, while the cohort who had hypochloremia had a mean blood loss of 475mls. There was no clinically significant rise in serum chloride with co-administration of normal saline and ringers lactate noted in our study. This was in keeping with literature by Bertrand et al[7] and Stephen's[2] review of saline based solutions, that both demonstrated combined crystalloids did not cause clinically significant rises in serum chloride. There was no significant correlation noted in the rise of serum chloride with blood loss in keeping with Bertrand et al's[7] meta-analysis.

Concerning serum lactate, the incidence of patients with normal serum lactate levels was 73.6%, compared to 26.3% of the patients who had hyperlactatemia. It was noted that 52% of those with hyperlactatemia were in ASA class III. The mean blood loss in patients who had hyperlactatemia was 523mls, compared to those with normal lactate values at 429mls. The mean blood loss was however noted not to be statistically significant to affect the serum lactate. The study noted a significant increase of serum lactate from the 1st to the 4th hour with normal saline and ringers lactate co-administration. This was in keeping with Kulla et al's randomised control trial of buffered vs non buffered solutions in the Cochrane review by

Bertrand[7], which noted that combined crystalloids infusions had no significant increase in serum lactate.

5.1 CONCLUSION

1. There was no clinically significant drop in serum sodium levels intraoperatively. Combinations of normal Saline and ringers lactate are safe to use as combined infusions in elective craniotomies and have no adverse effects on the sodium ion.

2. There is no clinically significant rise noted in serum potassium.

3. Serum chloride analysis noted no clinically significant rise.

4. Serum lactate has no noted clinically significantly rise with combination crystalloid therapies of normal saline and ringers lactate.

5.2 LIMITATIONS

1. This was an observational study, thus the choice of crystalloids infused and the volume infused were solely at the discretion of the anaesthesia provider
2. The durations of the surgery conducted were different, and as such the volume of crystalloids infused may be confounded.
3. The commencement time of the surgery and starving periods were not controlled, and as such fluid deficits may play a role in the amount required to be infused at the start of the craniotomy.

5.3 RECOMMENDATIONS

1. A randomized control trial where the type and volume of crystalloid infused can be controlled.
2. The use of mixed crystalloid regimes should continue as there were no noted adverse results when the electrolytes were compared.

REFERENCES

1. Katharina Floss, Mark Borthwick. Intravenous fluid therapy-background and principles. Hospital Pharmacist 2008;55:271
2. Stephens RC, Mythen MG. Saline-based fluids can cause a significant acidosis that may be clinically relevant. Crit Care Med. 2000;28:3375-3377.
3. Williams EL, Hildebrand KL, McCormick SA, Bedel MJ. The effect of intravenous lactated Ringer's solution versus 0.9% sodium chloride solution on serum osmolality in human volunteers. Anesth Analg. 1999;88:999-1003. Abstract
4. Mohammadali Attari, Shahryar Sane, Akbar Bordar. Comparison of the effects of two different formulas of fluids in craniotomy patients. Adv Biomed Res 2014, 3:257
5. Kerry Brandis. Fluid Physiology. Available from http://www.anaesthesiamcq.com/FluidBook/fl4_5.php (Accessed 10th February 2016)
6. Engelhardt B, Sorokin L, The blood-brain and the blood-cerebrospinal fluid barriers: function and dysfunction. Semin Immunopathol. 2009 Nov; 31(4):497-511.
7. Bertrand G, Neil S, Mike J. A balanced view of balanced solutions. Critical Care 2010; 14:325
8. Frederick A. Coller, Vernon Dick. Maintenance of Normal Water Exchange with Intravenous fluids. JAMA 1936;107(19):1522-1527
9. Krishna K, Dileep N. A meta-analysis of randomized control trials of intravenous fluid therapy on major elective open abdominal surgery: getting the balance right. Proceedings of the Nutritional Society 2010;69(4):488-489
10. Martin GS, Lewis CA. Fluid management in shock. Semin Respir Crit Care Med. 2004;25:683-694.

11. Wilcox CS. Regulation of renal blood flow by plasma chloride. J Clin Invest. 1983;71:726-735. Abstract
12. Wilkes NJ, Woolf R, Mutch M. The effects of balanced versus saline-based hetastarch and crystalloid solutions on acid-base and electrolyte status and gastric mucosal perfusion in elderly surgical patients. Anesth Analg. 2001;93:811-816. Abstract
13. Weed LH, McKibben PS: Experimental alteration of brain bulk. Am J Physiol 48:531–555, 1919
14. Malik ZA, Mir SA, Naqash A, Sofi KP, Wani AA. A prospective, randomized, double blind study to compare the effects of equiosmolar solutions of 3% hypertonic saline and 20% mannitol on reduction of brain-bulk during elective craniotomy for supratentorial brain tumor resection. Anesth Essays Res 2014;8:388-92.
15. Qureshi AI, Suarez JI, Bhardwaj A, Mirski M, Schnitzer MS, Hanley DF, et al. Use of hypertonic (3%) saline/acetate infusion in the treatment of cerebral edema: Effect on intracranial pressure and lateral displacement of the brain. Crit Care Med. 1998;26:440–6.
16. Kiichi Hirota, Tomoko Hara, Satoshi Hosoi, Yukiko Sasaki, Yasufumi Hara, and Takehiko Adachi. Two cases of hyperkalemia after administration of hypertonic mannitol during craniotomy. J Anesth 2005 19:75–77
17. Monroe A. Observations on the structure and function of the nervous system, Edinburgh: Creech & Johnson; 1783.
18. Kelly G. An account of the appearances observed in the dissection of two of three individuals presumed to have perished in the storm of the 3rd, and whose bodies were discovered in the vicinity of the Leith on the morning of the 4th of November 1821, with some reflections on the pathology of the brain, Trans Med Chir Sci Edinb 1824;1:84-169

19. Steiner, LA; Andrews, PJ (2006). "Monitoring the injured brain: ICP and CBF". British Journal of Anaesthesia97 (1): 26–38

20. Pirjo h. Manninen, Arthur M. Lam, Adrian Gleb, Stephen Brown. The effect of high dose mannitol on serum and urine electrolytes and osmolality in neurosurgical patients. Can J Anaesth 1987;34:442-6.

21. Worthley LI, Cooper DJ, Jones N. Treatment of resistant intracranial hypertension with hypertonic saline: Report of two cases. J Neurosurg. 1988;68:478–81.

22. Qian Li, Ming Xu. Correlation of measured and calculated serum osmolality during mannitol or hypertonic saline infusion in patients after craniotomy: a study protocol and statistical analysis plan for a randomized control trial. BMJ Open 2014;4 e004921.

23. Suarez JI, Qureshi AI, Bhardwaj A, Williams MA, Schnitzer MS, Mirski M, et al. Treatment of refractory intracranial hypertension with 23.4% saline. Crit Care Med. 1998;26:1118–22.

24. M. Garvaglia, T.H. Mak, M.D. Cusimano, A. Rigamoti. Body Mass Index as a risk factor for increased serum lactate during craniotomy. Minerva Anestesiologica 2013;10:1132-39.

25. *Kenneth M Sutin; Marino, Paul L. (2007). The ICU book. Hagerstwon, MD: Lippincott Williams & Wilkins. ISBN 0-7817-4802-X*

26. Burdett E, Dushianthan A, Bennett-Guerrero E, Cro S, Gan TJ, Grocott MPW, James MFM, Mythen MG, O'Malley CMN, Roche AM, Rowan K. Perioperative buffered versus non-buffered fluid administration for surgery in adults. *Cochrane Databaseof Systematic Reviews* 2012, Issue 12. Art. No.: CD004089. DOI: 10.1002/14651858.CD004089.pub2

27. Kirkwood B, Sterne J. Essential medical statistics. Malden MA: Blackwell Science. Inc; 2005.
28. Waters JH1, Gottlieb A, Schoenwald P, Popovich MJ, Sprung J, Nelson DR Normal saline versus lactated Ringer's solution for intraoperative fluid management in patients undergoing abdominal aortic aneurysm repair: an outcome study. Anesth Analg. 2001 Oct;93(4):817-22.

APPENDICES

Appendix I: Data Collection Tool

NAME: AGE: SEX: WARD:

I.P. NUMBER: DATE: WEIGHT:

DIAGNOSIS: PATIENT LENGTH (cm):

PROPOSED OPERATION:

PREOPERATIVE A.S.A STATUS:

PRE OPERATIVE LABS:

HAEMATOLOGY	HB	WBC	PLATELETS	HCT	
BIOCHEMISTRY	UREA	CREATININE	SODIUM	POTASSIUM	CHLORIDE

PARAMETER	INDUCTION	1ST HOUR	2ND HOUR	3RD HOUR	4TH HOUR	5TH HOUR	6TH HOUR
Ph							
pCO2							
pO2							
HCO3-							
Na+							

k+							
Cl-							
Lactate							
HCT%							
Glucose							
I.V FLUID AMOUNT &TYPE							
URINE OUTPUT (ML)							
MANNITOL (ML)							

Nb. Ideal wt men: 50kg+2.3kg for every inch over 5ft women: 45.5kg+2.3kg for every inch over 5ft

Appendix II : Consent Forms

THE EFFECT OF INTRAOPERATIVE CO-ADMINISTRATION OF RINGERS LACTATE COMBINED WITH 0.9% NORMAL SALINE ON SERUM ELECTROLYTES IN PATIENTS UNDERGOING CRANIOTOMY

Informed Consent form:

This Informed Consent form is for surgical patients undergoing elective craniotomy at Kenyatta National Hospital neurosurgical theatre. This consent will be administered to the patient. We are requesting these patients to participate in this research project whose title is "the effect of Intraoperative co-administration of ringers lactate combined with 0.9% normal saline on serum electrolytes in patients undergoing elective craniotomy" between November and January 2016.

Principal investigator: Dr. Andrew Kimathi Muriithi

Institution: School of Medicine, Department of anesthesia- University of Nairobi

Supervisors: Dr.Ngugi, Dr.Chokwe, Dr.Njogu

This informed consent has three parts:

1. Information sheet (to share information about the research with you)
2. Certificate of Consent (for signatures if you agree to take part)
3. Statement by the researcher

You will be given a copy of the full Informed Consent Form.

A. English

Part I: Information sheet

Introduction

My name is Dr Andrew Kimathi Muriithi, a post graduate student under the Department of Anesthesia at the University of Nairobi, School of Medicine. I am carrying out a study on the effect of Intraoperative co-administration of ringers lactate combined with 0.9% normal saline on serum electrolytes in patients undergoing elective craniotomy at Kenyatta National Hospital. This will be determined by taking 1ml of arterial blood from an arterial line that will be fixed intraoperatively every hour until completion of surgery. The blood sample taken will be subjected to arterial blood gas sampling and finding will be recorded on a data sheet. The information collected will help in the creation of a fluid protocol for patients undergoing elective craniotomy at the Kenyatta National Hospital.

I am inviting you to participate in my study and you are free to either agree immediately after receiving this information or later after thinking about it. You will be given the opportunity to ask questions before you decide and you may talk to anyone you are comfortable with about the research before making a decision. After receiving this information concerning the study, please seek for clarification from either myself or my assistant if there are words or details which you do not understand.

All the information which you provide regarding yourself and your condition will be kept confidential and no one but the researchers will see it. The information about you will be identified by a number and only the researchers can relate the number to the patient. The information will not be shared with anyone else unless authorized by the Kenyatta National Hospital/University of Nairobi – Ethics and Research Committee (KNH/UoN-ERC).

Your involvement in this research will be through blood samples taken intraoperatively and you will not expose yourself to any risks if you consent to participate. Participation in this study is out of your own free will, you will not be denied medical care in case you refuse to participate in the study .You may stop participating at any time with no consequences whatsoever. All the information that you give us will be used for this research only.

This proposal has been reviewed and approved by the KNH/UoN-ERC which is a committee whose work is to make sure research participants are protected from harm. The contact information is given below if you wish to contact any of them for whatever reason;

- **Secretary, KNH/UoN-ERC**

  P.O. Box 20723 KNH, Nairobi 00202

  Tel 726300-9

  Email: uonknh_erc@uonbi.ac.ke

- University of Nairobi research supervisors

  1. **Dr Chowke T.M.**

     Chairman, Department of Anaesthesia,

     University of Nairobi.

     Mobile phone 0722 528 237

  2. **Dr. Lee Ngugi**

     Lecturer, Department of Physiology,

     Kenyatta University.

Mobile phone 0722 757 875

3. **Dr. George Njogu.**

   Consultant Anaesthesiologist,

   Kenyatta National Hospital.

   Mobile phone 0722 712 207

- Principal researcher:

  Dr. Andrew Kimathi Muriithi

  Department of Anesthesia, School of Medicine,

  University of Nairobi.

  P.O. Box 13857, Nairobi 00400

  Mobile phone 0721 450 900

Part 2: Consent by patient **Serial Number.....**

I…….....from…….....

do agree to be part of the study the risks and benefits of which have been fully explained as by Dr Andrew Kimathi Muriithi. My participation is voluntary and will not be expecting any financial benefits.

Full name…….

Sign …….

Date ……

Investigator's signature ……..

Witness signature.....

Thumb Print Of Patient

Part 3: Statement by the researcher

I have accurately read out the information sheet to the participant, and to the best of my ability made sure that the participant understands the following:

- Refusal to participate or withdrawal from the study will not in any way compromise the quality of care and treatment given to the patient.
- All information given will be treated with confidentiality.
- The results of this study might be published to enhance knowledge and to help formulate an intravenous fluid protocol for patients undergoing craniotomy at the Kenyatta National Hospital

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Informed Consent Form has been provided to the participant.

Name of researcher taking consent…….

Signature of researcher taking the consent…… ……

Date……

B. Swahili

Fomu ya idhini

Kuamua athari ya kupeana 0.9% normal saline pamoja na ringers lactate kwa wangojwa wanaopasuliwa ubongo na athari ya haya madawa kwa serum electroliti katika hospital kuu ya Kenyatta

Sehemu ya kwanza – Maelezo ya Daktari mtafiti.

Utangulizi

Mimi ni Dkt Andrew Kimathi Muriithi, kutoka shule ya Elimu ya Afya Idara ya Anesthesia Chuo Kikuu cha Nairobi (University of Nairobi). Mimi nafanya utafiti ili kuamua athari ya kupeana 0.9% normal saline pamoja na ringers lactate kwa wangojwa wanaopasuliwa ubongo na kuangalia athari ya haya madawa kwa serum electroliti katika hospital kuu ya Kenyatta. Hii itakuwa kuamua na ukusanyaji wa takwimu kwa njia ya kuchukua damu kipitia mishipa na kupeleka damu hii kwa maabara kuchunguza serum elektrliti na kujaza haya matokeo katika fomu maalumu hadi upasuaji itakapokamilika.

Taarifa zilizokusanywa zitasaidia madaktari kuchunguza madhara ya maji inayopeanwa kupitia mishipa kwa wagonjwa wanaofanyiwa upasuaji wa ubongo ili tuweze kuandika itifaki ya maji maalum inayopaswa kupeanwa.

Nakukaribisha kushiriki katika utafiti wangu na wewe uko huru kukubaliana mara moja baada ya kupokea taarifa hii au baadaye baada ya kufikiria kuhusu jambo hili. Utapewa nafasi ya kuuliza maswali kabla ya kuamua na unaweza kuzungumza na mtu yeyote uliye starehe naye kuhusu utafiti kabla ya kufanya uamuzi. Baada ya kupokea habari hii juu ya

utafiti, unaweza tafuta ufafanuzi kutoka aidha mtafiti mwenyewe au msaidizi wangu kama kuna maneno au maelezo ambayo haujayaelewa.

Taarifa zote ambazo wewe utatoa kuhusu hali yako itakuwa siri na hakuna mtu ila watafiti wataiona. Habari kukuhusu itakuwa inatambuliwa na nambari tambulishi na watafitipekeyao ndio wataweza jua vile yanahusiana nambari na mgonjwa. Taarifa hayatashirikiwa na yeyote isipokua aliyepewa idhini na Hospitali ya Taifa ya Kenyatta / Chuo Kikuu cha Nairobi - Maadili na Kamati ya Utafiti (KNH / UoN-ERC).

Ushiriki wako katika utafiti huu utakuwa kupitia binafsi na kwa simu, na hautapata madhara kwa kukubali kushiriki. Hakutakuwa na gharama za ziada zilizotumika kwa ajili ya kushiriki katika utafiti. Kushiriki katika utafiti huu ni kwa hiari yako mwenyewe, na hautakanushwa huduma ya matibabu kwasababu ya kukataa kushiriki katika utafiti. Unaweza kuacha kushiriki wakati wowote na hautapata madhara yeyote. Taarifa zote utanipa itatumika kwa utafiti huu peke yake.

Unaweza kuuliza maswali yeyote kuhusu utafiti huu na ukiridhika tafadhali ijaze fomu ya idhini iliyopo hapa chini. Unaweza pia kuuliza swali lolote baadaye kwa kupiga simu kwa mtafiti mkuu ama mkuu wa idara ya anesthesia katika chuo kikuu cha Nairobi ama waalimu wasimamizi wa utafiti ukitumia nambari za simu zifuatazo;

- Katibu wa utafiti, Hospitali kuu ya Kenyatta na Chuo kikuu cha Nairobi.
  Sanduku la Posta 20723 KNH, Nairobi 00202.
  Nambari ya simu 726300-9.

- Waalimu wakuu wa Anesthesia, Chuo kikuu cha Nairobi:

  1. Dkt. Chokwe T.M.

Mwalimu Mkuu Anaesthesia,

Chuo kikuu cha Nairobi

Nambari ya simu 0722 528 237

2. Dkt. Lee Ngugi

   Msimamizi wa utafiti,

   Chuo kikuu cha Kenyatta

   Nambari ya simu 0722 757 875

3. Dkt. George Njogu.

   Msimamizi wa utafiti,

   Chuo kikuu cha Nairobi

   Nambari ya simu 0722 712 207

- Mtafiti Mkuu: Dkt. Andrew Kimathi Muriithi,
  Idara ya Anesthesia, Shule ya Afya – Chuo kikuu cha Nairobi,
  Sanduku la Posta 59022 Nairobi 00200.
  Nambari ya simu: 0721 450 900

Sehemu ya pili: Idhini ya mgonjwa

Namba Tambulishi……

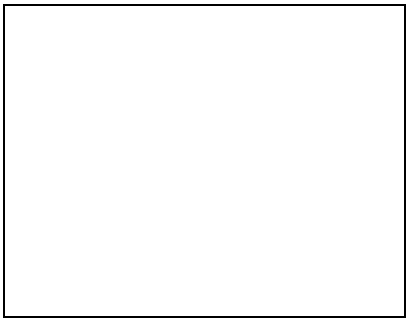
Mimi .....……kutoka .....nimekubali kushiriki katika utafiti huu unaofanywa na Dkt. Andrew Kimathi Muriithi kutokana na hali ambayo nimeelezwa na sio kwa malipo ama shurutisho lolote.

Jina la mshiriki……..

Sahihi…….

Tarehe……....

Sahihi ya Mtafiti……



Alama Ya Kidole Cha Gumba

Sehemu ya tatu – Dhibitisho la mtafiti

Hii nikuidhinisha ya kwamba nimemueleza mshiriki kwenye utafiti kuhusu utafiti huu na pia nimempa nafasi ya kuuliza maswali. Nimemueleza yafuatayo;

- Kwamba kushiriki ni kwa hiari yake mwenyewe bila malipo.
- Kushiriki hakutasababisha madhara ama kuhatarisha maisha kamwe.
- Anaweza kujiondoa kutoka kwa utafiti huu wakati wowote bila kuhatarisha matibabu anayoyapata katika hospital kuu ya Kenyatta.
- Habari ambazo atapeana hazita tangazwa hadharani bila ruhusa kutoka kwake (mshiriki) na pia kutoka kwa mdhamini mkuu wa utafiti wa hospital kuu ya Kenyatta na chuo kikuu cha matibabu.

Jina la Mtafiti ……

Sahihi…….....

Tarehe…….....

Appendix III: Table 1. Variations in Colloids and Crystalloids Formulations

TYPES OF INTRAVENOUS FLUIDS

Solution	**pH**	**Na^+**	**Cl^-**	**K^+**	**Ca^{++}**	**Lactate**	**Glucose**	**Osmolality**	**Other**
0.9% normal saline	5.0	154	154	0	0	0	0	308	0
Ringers Lactate	6.5	130	109	4	3	28	0	275	0
5% dextrose in water (D_5W)	4.0	0	0	0	0	0	50 g/L	252	0
0.45% normal saline with dextrose ($D_5$1/2 NS)	4.5	77	77	0	0	0	50 g/L	406	0
Albumin (5%)	6.4-7.4	130-160	130-160	< 1	0	0	0	309	50 g/L albumin
Albumin (25%)	6.4-7.4	130-160	130-160	< 1	0	0	0	312	250 g/L albumin
Hetastarch 6%	5.5	154	154	0	0	0	0	310	60 g/L starch
Pentastarch 10%	5.0	154	154	0	0	0	0	326	100 g/L starch
Dextran-40 (10% solution)	3.5-7.0	154	154	0	0	0	0	311	100 g/L dextran
Dextran-70 (6% solution)	3.0-7.0	154	154	0	0	0	0	310	60 g/L dextran
Haemaccel 3.5%	7.4	145	145	5	6.25	0	0	293	35 g/L gelatin
Gelofusine	7.4	154	125	0	0	0	0	308	40 g/L gelatin

All electrolyte ions are expressed in mmol/l.

Appendix iv :B.G.A Quality control report for the Siemens RAPIDPoint 500

Report duration 22.03.2017 to 28.03.2017

VARIABLE	**pH**	**pCO2(kPa)**	**PO2(kPa)**	**Na+ (mmol/l)**	**K+(mmol/l)**	**cl- (mmol/l)**	**Lactate(mmol/l)**
Target	7.35-7.45	4.5-6kPa	10.6-13.3kPa	135-145	3.5-5.5	96-106	0.5-1
Mean	7.37	5	11.2	140	4.5	100	0.7
S.D	0.005	0.19	0.14	0.3	0.01	0.01	0.005
Minimum	7.31	4.4	9	138	3.5	95	0.5
Maximum	7.34	6	13	141	3.9	102	0.6