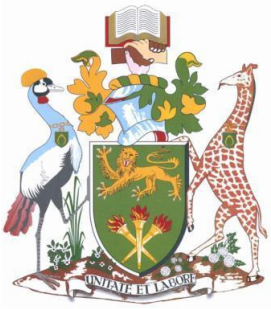

EFFECT OF PERI-OPERATIVE INTRAVENOUS FLUIDS ON RECOVERY OF INTESTINAL FUNCTION AFTER CAESAREAN DELIVERY UNDER SPINAL ANAESTHESIA AT KENYATTA NATIONAL HOSPITAL

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A dissertation Submitted In Part Fulfillment of the Requirements For The Degree Of Master Of Medicine (Anaesthesia) of The University Of Nairobi.

February, 2018

STUDENT'S DECLARATION

This dissertation is my original work and has not been presented for a degree or any other purposes in any institution.

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DEDICATION

To my beloved mother who motivated me to pursue a career in medicine.

To my mentors Dr. T, Muithya and Dr.S.Wakaba who instilled in me the passion to pursue anaesthesia.

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I sincerely thank the following:

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LIST OF ABBREVIATIONS

ASA - American Society of Anaesthesiologist's physical status classification

BMI - Body Mass Index

IQR - Inter-Quartile Range

LOS - Length of Hospital Stay

POI - Post Operative Ileus

POD - Post-Operative Day

RCTs - Randomised Controlled Trials

SA - Spinal Anaesthesia

SMD - Standard Mean Difference

TOD - Total Opiate Dose

WMD - Weighted Mean Difference

OPERATIONAL DEFINITIONS

Ileus (POI) refers to failure of the gut to function normally after intra-or extra-peritoneal surgery. Postoperative ileus affects patients after undergoing bowel resection surgery and is a significant cause of morbidity (1).

Post-operative ileus presents with anorexia, abdominal distension/discomfort, pain, nausea and vomiting and delayed passage of flatus/stool (1).

Although ileus has many causes, the postoperative state is the most common for its development. The small intestines resume activity several hours after surgery, the stomach in 1 to 2 days, and the large gut 72 to 120 hours after surgery. If postoperative ileus persists longer than 5 days, it is considered pathologic and is sometimes called paralytic ileus (1).

Several criteria can help to determine if ileus has resolved. These include Time to first Flatus, the duration to normal bowel sounds, the period to tolerance of first solid food, Time to Defecation, and Post-operative antiemetic requirement. These signs indicate that the patient has coordinated motility from the gastro-esophageal junction to the rectum. Proof of this is ability to tolerate oral intake and passage of stool (2).

ABSTRACT

Background: Ileus refers to the delay of regular bowel movement following intra-abdominal surgery and lasts 2 to 3 days. It is a major problem after operation that delays recovery. Several studies on adults have investigated the effect of "Liberal" versus "Restrictive" peri-operative fluid regimes on ileus after abdominal surgery in the non-obstetric population. Restrictive fluid regimen (<2700 mls) intra-operatively was found to be associated with enhanced intestinal recovery although data remains scanty in cesarean delivery.

During caesarean delivery under spinal anaesthesia different regimes of intravenous fluids are used peri-operatively. Literature review revealed no studies conducted on their effect on intestinal recovery as well as no data on the incidence of post-operative ileus in the obstetric population. A study was necessary to determine the incidence ileus after surgery, the optimal peri-operative fluid regime for recovery of intestinal function after caesarean delivery (determined by time to tolerance first oral feed, time to flatus and time to defecation) and assist in developing a protocol for peri-operative intravenous fluids administration during caesarean delivery.

Objective: The aim of this study was establish the effect of perioperative intravenous fluid volume on recovery of intestinal function after caesarean delivery under spinal anaesthesia. We also sought to find out the incidence of ileus postoperatively.

Materials and Methods: This research was conducted as a prospective observational study after getting ethical approval from Kenyatta National Hospital – University of Nairobi Ethics and Research committee. 150 patients who delivered through caesarean section under spinal anaesthesia at KNH between March 2016 and May 2016 were recruited using consecutive sampling technique and followed up from admission into theatre up to 3 days post operatively in the postnatal wards. Intravenous fluids administered preoperatively, intra-operatively and post-operatively were documented and their effect on intestinal recovery post-operatively was evaluated. The outcomes of interest for recovery of intestinal function were time to first normal bowel sounds, time to tolerance of the first solid food, time to first flatus and time to defecation.

Collected data was analysed using SPSS version 21. Descriptive statistics was used to determine prevalence of ileus after surgery. Regression analysis was undertaken to establish how various independent variables influence development of ileus postoperatively. A paired t-test, Pearson

correlation test and analysis of variance (ANOVA) was run to determine association between perioperative intravenous fluids and development of postoperative ileus.

Results: Results from 150 patients were collected and analysed. Majority of patients (50%) were between 24 and 32 years, had BMI range of 26 to 32 and average parity was 3 to 5. Prevalence of ileus after caesarian delivery was 5.6%. The results of Pearson correlation test and ANOVA showed that preoperative intravenous fluids (normal saline 501 – 1000 ml) significantly influenced duration to first flatus (P=0.011), time to normal bowel rounds (P=0.029) and time to first oral feed(P=0.045).

Conclusion: Prevalence of postoperative ileus in the obstetric population was established to be similar to that in abdominal surgery patients in studies conducted elsewhere. There is a significant association between pre-operative intravenous fluid administration and recovery of intestinal function postoperatively. We also noted that 501-1000mls of normal saline pre-operatively led to enhanced recovery of intestinal function compared to other fluid volumes. Intra-operative fluids were found to have no significant effect on gut recovery after operation. This study had the limitation of being an observational study. A larger randomized controlled study should be carried out to better understand the effect of immediate post-operative fluid volumes on recovery of intestinal functions.

1.0 CHAPTER ONE: INTRODUCTION

Caesarean delivery involves extraction of a baby through incision in the abdomen and uterus. Gastrointestinal manipulation during the procedure predisposes the patient to post-operative ileus.

Post-operative ileus is defined by at least two of the following 5 signs on or after third day after surgery:

- Nausea and vomiting
- Delayed tolerance of oral diet
- No gas or stool passed during the preceding 24hrs
- Abdominal swelling
- Evidence of ileus on abdominal X-Ray (5,6)

Physiologic ileus resolves within 2-3 days (small intestines and stomach resume function within hours and 1-2 days respectively whereas large gut regains activity within 3-5 days) after sigmoid motility returns to normal. Morbidity due to ileus is characterized by discomfort and pain, atelectasis/hypostatic pneumonia, abdominal distension, nausea and vomiting (4, 5, 6, 7)

Both Spinal and general anesthesia may be used for caesarian delivery. They both have different risks intra-operatively and post-operatively. General anesthesia is associated with increased intra-operative blood loss due to halogenated volatile agents, thromboembolic complications, pulmonary infection, impaired gastrointestinal motility and prolonged length of hospital stay compared to spinal anesthesia (8, 9).

1.1 Literature Review

The post-operative state is the most common cause of ileus (4). Pathogenesis of ileus involves the autonomic and central nervous systems as well as local and regional substances which lead to ileus (10).

1.1.1 Pathophysiology of Ileus

Post-operative ileus develops in phases. First phase involves the sympathetic nervous system, while the second phase involves hormonal and inflammatory mechanisms. The final phase involves para-sympathetic nervous system stimulation and plays a critical role in the resolution of ileus (4).

Neurological phase: This is the phase of the enteric nervous system (ENS) and the sympathetic nerves. Glial cell dysfunction of the ENS could lead to interruption of the intestinal mucosal barrier. Alpha-2 adrenergic receptors in the inflamed muscularis mucosae are then stimulated worsening ileus by increasing synthesis of messenger RNA of the inducible nitric oxide synthetase (i-NOS mRNA) with the release of nitrogen monoxide (NO) which leads to ileus (4).

Hormonal and Inflammatory phase: As the neurological phase declines, there is increased inflammation of intestinal mucosa that involves monocytes, macrophages and mast cells that produce pro-inflammatory molecules and auto-regulate themselves. Intestinal manipulation leads to inflammation by activating dendritic cells which produce interleukin-12 (IL-12). IL-12 activates T1 helper lymphocytes (T1H) which migrate to regions that have not been manipulated causing inflammation by production of alpha interferon (IFN alpha) through recruitment of microphages. This is called the "field effect". During this second phase, intestinal mucosal barrier permeability is raised which increases inflammation (4).

Phase of Ileus resolution and vagal activation: Increased vagal tone reduces manipulation induced intestinal inflammation. The mediators include nicotinic alpha 7 acetylcholine receptors (alpha 7 and ACHR) and 5- hydroxytryptamine 4 receptors (5-HT4R). Stimulation of 5-HT4R increases acetylcholine release from myenteric cholinergic neurons. This activates alpha-7 – nAChR on monocytes and macrophages hence reducing the inflammatory response. Vagal system mediates the phase of resolution (4).

Other causes of ileus post-operatively include:

- Drugs (general anaesthesia, opioids, anticholinergics, amitryptyline).
- Trauma (fractured ribs, fractured spine).
- Pneumonia/peritonitis/Sepsis.
- Endocrine and metabolic disorders (Diabetes mellitus, Addison's disease, myxoedema coma and low potassium levels).
- Biliary and renal colic.
- Cardiopulmonary insufficiency (e.g. myocardial infarction).
- Head injury and trauma to spinal cord.
- Retroperitoneal pathologies (e.g. hematomas) (11).

Perioperative fasting causes intravascular hypovolemia which, compounded with intraoperative hemodynamic instability and post-operative fluid deficit, can cause delayed intestinal recovery due to a compromised splanchnic circulation (8).

European Society of Anaesthesiology guidelines recommend that adults should be take clear fluids and solid food up to 2 hours and 6 hours before surgery respectively (12). Contrary to these guidelines, patients in our hospital are maintained nil per oral for long periods before surgery thus effecting perioperative fluid status.

The common indications for intravenous fluid administration in elective surgery are:-

- Correction of preoperative fluids deficits for maintenance of CVP.
- Control of intra-operative and post-operative hemodynamics.
- Avoidance of blood transfusion and post-operative renal failure.
- Substitution for non-enteral nutrition post operatively.
- Prevention of hypotension during regional anesthesia/analgesia (10).

Effective interventions targeting the different phases of ileus that have been studied include Alvimopan (an opioid receptor antagonist) and Lidocaine which act on neurological stage of ileus by antagonizing the effects of opioids and reducing pain respectively (13, 14). Prokinetic agents such as intravenous magnesium sulfate (40mg/kg bolus to 10mg/kg infusion during operating period) and metoclopramide decrease the interval of return of transit (15, 16).

Mastication of gum mimics dietary intake hence stimulates vagal nerves, which has an anti-inflammatory effect. This leads to cephalo-caudal stimulation of digestion by increasing the activity of neural and humoral factors on multiple parts of the gastrointestinal tract. This as well increases serum concentration of peptide hormones (17, 18).

Reduction of intravenous flux (by early resumption of diet) and coffee intake post-operatively reduces the incidence of ileus (19, 20, 21).

1.1.2 Perioperative Fluid Management and Intestinal Recovery

Studies in surgery other than caesarean delivery have demonstrated that peri-operative fluid management influences intestinal recovery post-operatively. However, the effect of peri-operative fluid management on post-operative intestinal recovery remains imprecise (10).

A cohort study done to establish the causes of ileus after abdominal surgery demonstrated statistically significant correlation with volume of blood loss during operation, duration of surgery and total dose of opioids (22)

Goal directed fluid therapy (GDT) effect on recovery of internal function post-operatively has been investigated in randomized controlled trials. Goal directed therapy involves use of cardiac output, pulse rate, venous (CVP) and arterial (MAP) pressure to guide intravenous fluid therapy. Studies done involve patients of varying fitness undergoing colorectal surgery (as determined by cardiopulmonary exercise testing – CPET) (23), general surgery patients randomized to GDT (with standard fluid management) patients versus standard fluid management groups (vascular, upper gastrointestinal and hepatobiliary surgeries) (24) and general urologic and gynecologic patients randomized to GDT and standard fluid management control groups. (25)

Standard fluid management aims to optimize total blood volume by administering 10mls/kg of crystalloid fluid followed by 8ml/kg/hour in the duration of surgery.

The outcomes of interest included readiness of discharge, duration of hospital stay, complications after operation, and period to toleration of first solid feed and antiemetic requirements (23, 24, 25).

Goal directed therapy (with standard fluid management) compared to standard fluid management was shown to prolong time to readiness of discharge with increased length of hospital stay in fit patients but it was not significant in unfit patients (23). When GDT (without standard fluid therapy) was compared against standard fluid management, it was shown to reduce duration of hospital stay, time to tolerance of first oral feed, nausea and vomiting after surgery, antiemetic requirements and complications postoperatively (Wound sepsis, Pneumonia, Urinary Tract Infection, Pulmonary emboli and Arrhythmias) (24,25).

The outcome of interest and surgeries were different in each study hence the study population was not homogenous (23, 24, 25).

Stratified Meta-analyses of randomized controlled trials of various methods of fluid therapy that have been done involve comparisons of restricted (<1.75 liters/d), liberal (>2.75 liters/d) and fluid balance therapy (1.75-2.75 liters/d) (27); perioperative liberal fluid therapy (LVR) versus

goal directed therapy (GDT) or restricted fluid regime (34) and standard, restrictive and supplemental fluid regimes (28).

The outcomes of interest were post-operative complications (Wound dehiscence, anastomotic leak, wound sepsis, pneumonia, arrhythmias, and urinary tract infection), duration to first flatus, normal bowel movements, (27, 28) and total period of of hospital stay (26, 27, 28).

Analysis revealed statistically significant reduction in duration of time to first flatus, normal bowel movements, postoperative complications and total length of hospital stay for fluid restricted patients compared to liberal and goal directed fluid therapy patients (27, 28).

This benefit was also found in patients maintained in state of fluid balance compared to patients who were maintained on fluid restriction and liberal fluid therapy (26).

Restrictive versus liberal fluid therapy studies have been done with patients being randomized in surgeries varying from laparoscopic cholecystectomy (29) and elective colorectal surgery (30, 33, and 34) to gastric resection and pancreaticoduodenectomy (31, 32).

The outcomes of interest included post-operative pulmonary function, exercise capacity (30), duration to first flatus, first bowel motion (30, 31, 33), post-operative morbidity and complications (31, 32, 34).The duration of hospital stay was also included in the studies (29, 30, 31, 32, 34).

Pulmonary function and exercise capacity were shown to be better in the liberal group compared to restricted group (29).

Sodium and fluid restriction did not shorten duration to first flatus and bowel movements (30). Fluid restriction (without sodium restriction) shortened the period to first flatus and defecation (31). It also significantly reduced post-operative complications (vomiting, wound dehiscence, wound sepsis, peritonitis, pneumonia and atelectasis) and the length of hospital stay (31, 32, 34)

The study outcomes varied because of difference in sample sizes, extent of different surgeries and volumes of fluid and electrolytes administered in restrictive and liberal groups (29, 30, 31, 32, 33, 34).

Post-operative nausea and vomiting was evaluated as a primary outcome in laparoscopic cholecystectomy and gynecological surgery with patients randomized to restrictive and liberal fluid therapy groups. Restrictive fluid therapy significantly reduced the incidence of nausea and vomiting post operatively (35).

Other studies have been conducted with the objective of minimizing intraoperative variation of pulse pressure by randomizing gastrectomy and colectomy patients into restrictive Ringer's lactate group (R-RL), goal-directed Ringer's lactate group (GD-RL) and a colloid (hydroxyethyl starch) goal-directed group (GD-C) (36) vis-a-vis maximization of intraoperative stroke volume guided by Esophageal Doppler monitoring, with (colorectal surgery) patients being randomized into esophageal Doppler (guided maximal stroke volume Doppler group, D-group) and normal body weight with zero balance group (Zero balance, Z –group)(37).

The outcomes of interest were duration to passage of flatus, period of hospital stay and complications postoperatively (wound sepsis, wound dehiscence, anastomotic leak, pneumonia, arrhythmias)(36, 37)

Goal directed hydroxyethyl starch therapy was found to be superior to goal directed lactated Ringers therapy and restrictive lactated Ringer's therapy in shortening time to passage of flatus and length of hospital stay (36) while goal directed fluid therapy was found to add no benefit compared to zero balance therapy (and normal body weight) in reducing post-operative complications or duration of hospital stay (37)

Overall, restrictive management fluid regimes were found to have better abdominal surgery outcomes compared to liberal and goal directed fluid therapy regimes.

1.1.3 Caesarean Delivery and Ileus

Caesarean section is a common obstetric surgery which triggers postoperative changes in autonomic nervous system leading to decreased bowel movements. The ileus that ensues leads to pain after surgery, abdominal swelling, reduced tolerance to feeds and delayed recovery (38).

The indications of caesarean section include previous classical caesarean, placenta previa grade 4 and placenta abruption, breech presentation or transverse lie, genital herpes in the mother, severe pre-eclampsia, uterine malformations (bicornuate uterus), cervical dystocia, ovarian and cervical malignancies, fetal distress and maternal request (38).

The type of uterine incision during caesarean delivery is associated with different degrees of maternal morbidity (puerperal infection, delayed wound healing, blood transfusion, hysterectomy). A systematic meta-analysis revealed that maternal morbidity was significantly higher in classic incision and inverted "T" incision compared to low transverse caesarean delivery (39)

In pregnancy, the cardiovascular system undergoes physiological changes in order to ensure adequate oxygen and nutrient supply to the fetus. The plasma and red blood cell volume expands by 1500-1600mls which increases the stroke volume and the cardiac output. Placenta auto transfusion (300-500mls) increases blood volume. The increase helps in mitigating the blood loss of delivery but placental auto transfusion in addition to fluid loading and infusion can lead to a liberal intra-operative fluid administration state (40).

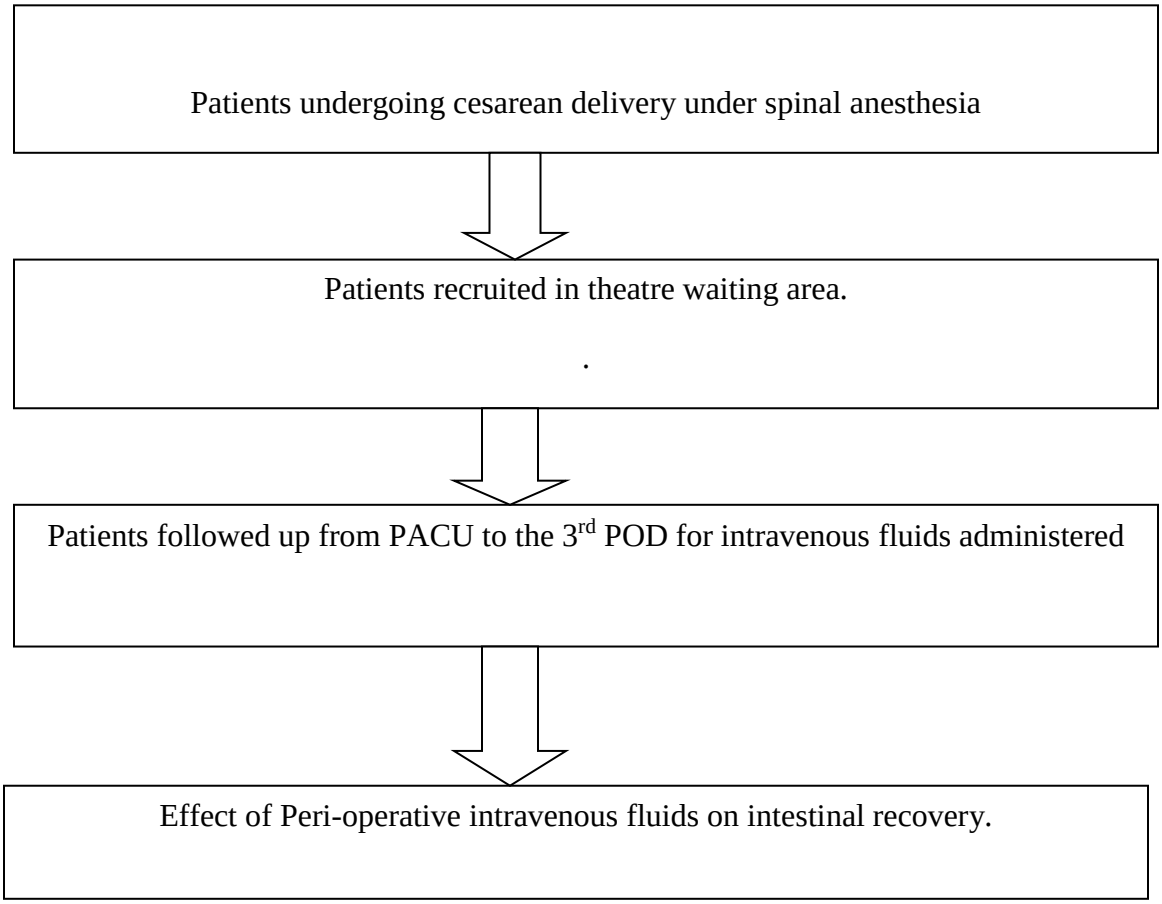
1.1.4 Intravenous Fluid Therapy and Caesarean Delivery

During caesarean deliveries, patients are predisposed to intraoperative hypotension due to neuro-axial sympatholytic effect, aorto-caval compression and preoperative fasting. Fluid coloading with colloids and crystalloids (10-20 mls/kg) is more effective than the use of crystalloids only. It has also been shown to be more superior to pre-loading. Vasopressor drugs (phenylephrine and ephedrine) are also used intra-operatively during hypotension and their use is reduced in co-loaded patients compared to pre-loaded patients (41).

The volume of fluid used intra-operatively in cesarean delivery may exceed the restrictive intra-operative fluid regime that has been studied in general surgery due to fluid loading and administration during episodes of hypotension (3). Intra-operative drugs and mode of anaesthesia are also contributing factors to post-operative morbidity. Spinal anesthesia (compared to general anesthesia) for cesarean delivery has been shown to reduce the need for analgesia after surgery, lowers incidence of nausea and vomiting postoperatively, promotes early mobilisation due to better analgesia and enhances faster tolerance to oral feeds (because fewer medications are used intra-operatively that predispose to ileus) (42). Opioids and general anesthetics reduce gastro intestinal motility. Prokinetics such as metoclopramide enhance gut motility reducing the extent of post-operative ileus (43).

In some obstetric conditions/emergencies, it is challenging to assess the effect of fluid status on intestinal recovery post-operatively. Pre-eclampsia is associated with organ dysfunction and electrolyte imbalance. Fluid restriction is essential to avoid fluid overload (44). Postpartum hemorrhage patients require high volume of fluids for resuscitation and blood transfusion while emergency caesarian delivery patients' volume status cannot easily be ascertained because they are referral patients (45). Therefore, it is difficult to ascertain the effect of perioperative fluid management on recovery of intestinal function after surgery in these patients.

CONCEPTUAL FRAMEWORK



2.0 CHAPTER TWO: STUDY JUSTIFICATION

The actual data on post-operative ileus incidence in Africa is not available (14).

Fasting for too long during labour before caesarean delivery at Kenyatta National Hospital leads to fluid deficits whose impact on post-operative ileus has not been established.

During caesarean delivery under spinal anaesthesia different regimes of intravenous fluids are used and their effect on intestinal recovery has not been established. Published data on the incidence of ileus after surgery in obstetric population is lacking and a protocol for peri-operative intravenous fluids use during caesarean delivery has not been established. No study is available locally that demonstrates the optimal obstetric peri-operative intravenous fluid management for enhanced recovery of gut function after surgery. This study was to determine the prevalence of post-operative ileus and assist in developing a protocol for peri-operative intravenous fluids administration during caesarean delivery.

Ileus is common after abdominal operations and is a cause prolonged hospital stay due to increased post-operative morbidity and hence high cost of healthcare. There has been no study that compares the economic impact of post-operative analgesic needs and anti-emetic requirements between standard post-operative care and peri-operative intravenous fluid administration.

Upon demonstration of the effects of peri-operative intravenous crystalloids in the local population, the study is expected to improve the standard peri-operative fluid management cost-effectively. Lack of local peri-operative intravenous fluid administration data at KNH necessitates a study that can support early feeding.

3.0 CHAPTER THREE: OBJECTIVES AND HYPOTHESIS

3.1 Study Question

Does peri-operative fluid therapy affect recovery of intestinal function after caesarean delivery under spinal anaesthesia?

3.2 Objectives

3.2.1 General Objective

To determine the effect of peri-operative intravenous fluids on recovery of intestinal function after caesarean delivery under spinal Anaesthesia in ASA II patients.

3.2.2 Specific Objectives

a) To determine time to first flatus.

b) To determine time to first bowel sounds.

c) To determine time to first defecation.

d) To determine the optimal peri-operative intravenous fluids regime for recovery of intestinal function after caesarean delivery.

e) To estimate the proportion of women with unresolved ileus beyond 3 days after Caesarean delivery.

3.3 Hypothesis

3.3.1 Null Hypothesis

Peri-operative intravenous fluids have no effect in recovery of intestinal function post cesarean delivery.

3.3.2 Alternative Hypothesis

Peri-operative intravenous fluids have a significant effect on recovery of intestinal function post caesarean delivery.

4.0 CHAPTER FOUR: RESEARCH METHODOLOGY

4.1 Study Design

This was a prospective observational study involving patients undergoing caesarean delivery under spinal anaesthesia at the Kenyatta National Hospital. Follow was up to 3 days post-operatively because this is the time majority of patients are discharged after caesarean delivery (as indicated in the KNH post-natal ward registry).Patients not discharged by the third day post operatively (and without complications) were followed up to the fifth day and analysed during data interpretation. Standard intra-operative and post-operative care was maintained in all patients.

All intravenous fluids administered to patients from theatre up to 3 days post-operatively including intraoperative estimated blood loss (EBL) were documented and the effect on recovery of intestinal function post-operatively analysed.

Patients participating in the study were assessed every hour (from post anaesthesia care unit) for 4 hours post caesarean section (then 4 hourly) until all of the following had occurred: Time to first flatus , duration to normal bowel sounds , period of time to first defecation and time taken to tolerance of first solid food. Post-operative antiemetics requirement was also assessed. The study provided evidence for the effects of peri-operative intravenous fluids to recovery of intestinal function post caesarean delivery under spinal anaesthesia.

4.2 Study Site

The research was carried out at the Kenyatta National Hospital.

KNH is a referral and teaching hospital whose clientele is from rural and urban populations.

The bed capacity of the hospital is 1800 with 50 wards, 20 outpatient clinics, 24 operating theatres and a casualty department.

There are 2 maternity theatres whose working personnel include 2 obstetricians, 2 anaesthetists and 9 nurses. Post-operatively, patients are admitted into post natal wards with a capacity of 128 beds.

Approximately fifteen [15] to twenty [25] Caesarean deliveries are performed under spinal anaesthesia daily at the hospital.

4.3 Study Population

The study population comprised of ASA II women slated for Caesarean delivery under spinal anaesthesia at KNH during the period from March 2018 to May 2018.

4.4 Eligibility Criteria

4.4.1 Inclusion Criteria

a. ASA II patients slated to undergo spinal anesthesia for caesarean delivery.
b. Patients who consented for the study.
c. Patients undergoing caesarean delivery via a lower uterine segment transverse incision.

4.4.2 Exclusion Criteria.

a. Patients who did not consent for the study
b. Patients who underwent general anesthesia
c. Patients who were converted from spinal to general anesthesia
d. Patients with electrolyte disturbances.
e. History of abdominal surgery other than caesarean delivery.
f. Intra- and post-operative complications (post-partum hemorrhage, intestinal obstruction, sepsis).
g. Patients with poorly controlled diabetes mellitus or cardiac disease.
h. Patients with severe pre-eclampsia slated to undergo caesarean delivery under spinal anesthesia.

4.5 Sample Size Estimation

The main outcome of this study was the proportion of women who had sustained post-operative ileus beyond 2 days post caesarean delivery under spinal anaesthesia.

Using the Cochran W. G. sample size formula;

$n = \frac{(z_{\alpha/2})^2 p(1-p)}{(e)^2}$ Where

$z_{\alpha/2}$ is critical value of a standard normal distribution at (1-α) % level of confidence=1.96

p is estimated proportion of women with unresolved ileus beyond 3 days = 11% (37).

e is the estimated level of precision

At 95% level of confidence and 5% error margin, and assuming p=11%, we recruited 150 patients.

4.6 Sampling Technique

The sampling was done using consecutive convenience sampling method of all the women undergoing caesarean delivery in labour ward and meeting the inclusion criteria at Kenyatta National Hospital.

The Sampling frame for this study was the list of all women undergoing caesarean delivery under spinal anaesthesia during the study period.

4.7 Recruitment to the Study

The study participants for caesarean section were recruited from theatre patients' receiving area. The study participants received an explanation about the study after which a written informed consent was be obtained voluntarily.

4.8 Description of Study Protocols

The first trained research assistant explained to the caesarean delivery mothers in theatre receiving area about the purpose of the study, obtained consent and recruited them. Weighing of patients was done during recruitment. The research assistant documented the time surgery began, intra-operative estimated blood loss, intravenous fluids/blood and blood products administered intra-operatively. This minimized errors and bias.

The principal investigator examined and followed up the patients for outcomes (within 2 hours after surgery) hourly beginning from Post anaesthesia care unit for 4 hours then 4 hourly after surgery during the patient's wakeful time. The patients were followed up until discharge and management interventions were done in case of complications. Rescue analgesics post-operatively were administered as required. The investigator also documented the post-operative intravenous fluids administered to patients post-operatively.

All participants received standard analgesics and an antiemetic for prophylaxis against post-operative nausea and vomiting.

KNH protocol for spinal anaesthesia and the intraoperative multimodal analgesia plan was administered to all patients (Appendix III).

The anaesthesia provider was not directly involved in the study. The First trained research assistant recorded any intraoperative complications, analgesics and anti-emetics administered for each patient intra-operatively.

The principal investigator filled the research questionnaire at the postnatal ward and monitored/followed up for Time to first flatus, duration of time to normal bowel sounds, time period to defecation, the duration to tolerance of first solid food and post-operative antiemetic requirements. Any patient who complicated during monitoring/follow up had appropriate intervention administered and was to be excluded from the study.

4.9 Expected Complications and Management.

Post-operative nausea and vomiting was managed by standard administration of antiemetic prophylaxis and in case of vomiting in the postnatal ward. Rescue analgesics were administered as required.

4.10 Data Collection and Management

Pre-testing of study instrument was carried out to structure and modify the research instrument by clarifying grammar and language used so as to avoid bias and misinterpretations of the questions. The questionnaire was also pre-tested for consistency, timing, accuracy and reliability. The study questionnaire was filled by first trained research assistant who was in theatre and the principal investigator at the postnatal ward. At the end of the day, questionnaires were checked for completeness and missing entries corrected.

All data were entered into a password-protected Microsoft® excel database. All data collection instruments were kept into a secure lockable cabinet only accessible to the principal investigator, the data collector, data clerk and statistician. All data collection tools were devoid of identifiable indicators.

The exposure variable was peri-operative intravenous fluids (crystalloids). All patients were given standard peri-operative care. The outcomes of interest were Time to first flatus, period of time to normal bowel sounds, total time to defecation, duration of time to tolerance of first solid food and post-operative antiemetic requirements. Other variables including multimodal analgesic agents used intra-operatively, intraoperative complications and duration of surgery were analysed.

The internal consistency reliability of the research findings were determined using average inter-items correlation. Formative validity was applied to outcomes assessment in order to assess how well the study tools were able to provide information to help improve post-operative care

protocol whereas sampling validity (content validity) ensured that the study tools covered broad range of areas within the concept under study.

4.11 Data Storage, Privacy/Security and Archival

Data collected was kept locked and confidential at all times.

Electronic forms of data were protected with confidential passwords at all times.

Data was locked and only accessible to the investigator and data manager.

Data was preserved until analysis, presentation and archival were done.

4.12 Data Analysis and Presentation

Data collected in the study was sorted, coded and entered in a computer using SPSS version 21.

The data was cross-checked against the data files for any inconsistencies and entry errors. The entry of data and cleaning was carried out throughout the study process.

Measures of central tendency and dispersion (median, mean, interquartile ranges and standard deviation) were utilised in summarizing continuous variables. Categorical variables were summarized by the use of counts, proportions and percentages.

For bivariate comparisons involving continuous variables, t-test (if means) was used. For bivariate comparisons involving 2 categorical variables Chi-squared tests and Fishers /Mann Whitney U test if the sample size is small and distribution not parametric were to be used.

For multivariate comparisons, odds ratio with 95% CI has been used to determine whether peri-operative intravenous fluid management is an independent factor associated with ileus while adjusting for confounders. Kaplan Meier survival analysis has been used to compare Time to first flatus, duration of time to normal bowel sounds, amount of time to defecation, period of time to tolerance of first solid food and post-operative antiemetic requirements. P values of <0.05 were considered statistically significant. Study findings have been presented using figures, tables, pie-charts and bar-graphs. Conclusions and recommendations have been based on the results.

4.13 Study Findings Dissemination.

The findings of this study will be disseminated through; presentation to members of anaesthesia department of the University of Nairobi, manuscripts, presentation in clinical conferences,

publication in a peer-reviewed journal, feedback to the theatre team and a report to UON/KNH ERC.

4.14 Study Limitations and Bias Minimization

During the surgery, different anaesthesia providers might have used different analgesics and sedatives which might affect the study findings but these were taken into account during data analysis.

The timing of 2 hours from end of surgery was strictly adhered to for the beginning of assessment of the outcomes of interest.

Post-operative complications and rescue analgesia needs that may arise were taken into consideration during data analysis.

It was assumed that the patients were truthful in reporting passage of first flatus and stool. It was also assumed that post-operative intravenous fluid volumes infused were recorded accurately in the wards.

5.0 CHAPTER FIVE: ETHICAL CONSIDERATIONS

The patients meeting the study inclusion criteria were briefed with information concerning the research i.e. the research objectives, benefits and any adverse effects.

Participation in the research was completely voluntary

Each patient, even after giving consent to participate retained the right to opt out of the research any time without repercussions.

No monetary or other forms benefits were to be realized in acceptance to participate in the research as a respondent.

Each respondent was entitled to full information concerning the progress and findings of the research.

No extra cost was incurred by the participants.

Information obtained was kept confidential and was only utilised for purposes of the research.

A respondent who consented to participate confirmed such consent by appending her signature or thumb print on the Consent Form (Appendix II).

Any complications and/or rescue analgesia needs that arise were to be managed by the care givers at the post-natal wards.

Ethical approval was sought and obtained from the KNH/UON-Ethics and Research Committee before carrying out the study. Permission for the study was also sought and obtained KNH administration.

6.0 CHAPTER SIX: RESULTS

150 patients scheduled for caesarian delivery through spinal anaesthesia were recruited in the study. 2.7% (4 patients) had elective caesarian delivery while 97.3% (146 patients) underwent emergency caesarian delivery.

Data was collected from all study subjects and analyzed for effect of Perioperative intravenous fluid infusion on recovery of gastro-intestinal function after caesarian delivery under spinal anaesthesia.

Table 1: Demographic Parameters of Participants

	Mean	Standard Deviation	Median	Inter-Quartile Range
Age	28	5	28	24 - 32
BMI	29	5	29	26 - 32
Parity	4	2	3	3 - 5

As shown above (Table 1), the median age of this population was 28 years with an IQR of 24 – 32. The median BMI was 29 with an IQR of 26 – 32. This population had a median parity of 3 children with an IQR of 3 – 5.

Difficult foetal extraction in 1.3% of patients (2 patients) was encountered as the only intraoperative complication.

Table 2: Intra-operative complications

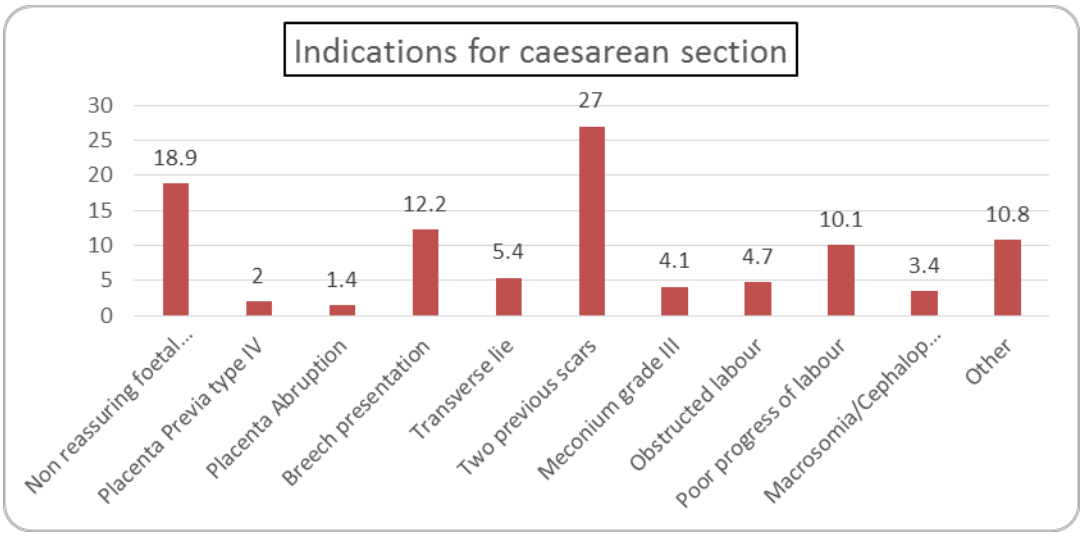
Intra-operative complications	N	%
Difficult foetal extraction	2	1.3
Extensive uterine incision	0	.0
Bladder injury	0	.0
Others(rectus-abdominis left tear)	1	.7

Commonest indications for surgery included two previous scars (27%) non-reassuring foetal status (18.9%), breech presentation (12.2%) and poor progress of labour (10.1%) (Table 3) and (Figure 1).

Table 3: Indications for surgery

		n	%
What is the type of surgery	Elective	4	2.7
	Emergency	146	97.3
What is the indication for caesarean section	Non reassuring foetal state	28	18.9
	Placenta Praevia type IV	3	2.0
	Placenta Abruption	2	1.4
	Maternal request	0	.0
	Breech presentation	18	12.2
	Transverse lie	8	5.4
	Two previous scars	40	27.0
	Meconium grade III	6	4.1
	Obstructed labour	7	4.7
	Poor progress of labour	15	10.1
	Macrosomia/Cephalopelvic disproportion	5	3.4
	Other	16	10.8

Figure 1: Indications for Surgery



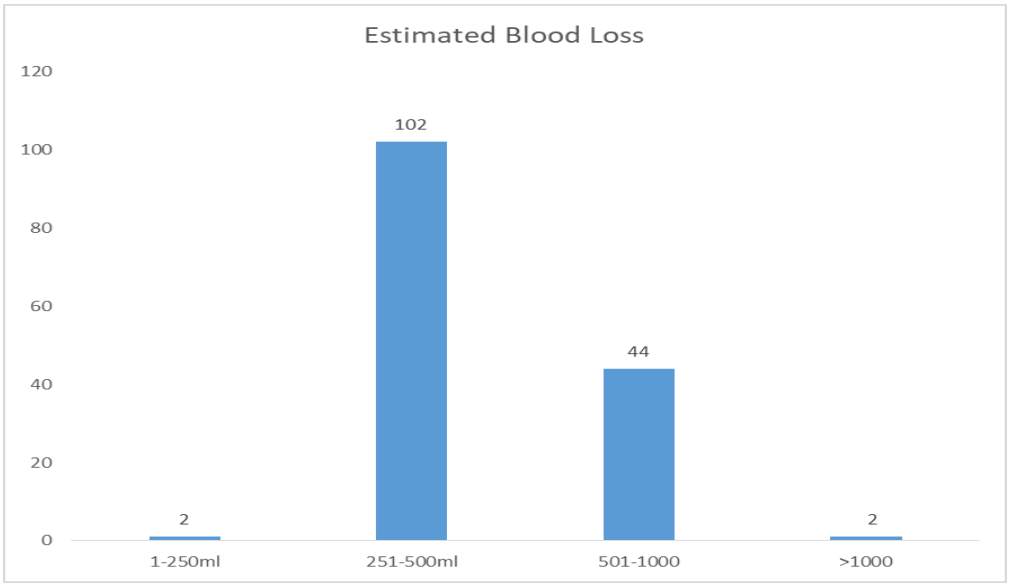
Average duration of surgery was 1.3 hours (range of 1.0 – 1.5 hours) with 68.9% of patients having EBL of 251 mls – 500 mls in comparison with 29.7% patients who had an EBL of 501 mls–1000 mls (Fig 2).

Table 4: Duration of Surgery and Estimated blood loss

	Mean	Standard Deviation	Median	Percentile 25	Percentile 75
What was the surgical Incision time	12:11	6:01	12:30	9:00	16:00
Duration of surgery (hrs)	1.3	.3	1.3	1.0	1.5
EBL?	524	161	500	450	550
Entry time to PACU?	12:28	5:56	13:10	8:50	16:15

Estimated Blood Loss	N	%
1-250ml	2	.7
251-500ml	102	68.9
501-1000	44	29.7
>1000	2	.7

Figure 2: EBL during Caesarean Delivery



Consultants performed most of the surgeries (69.3%) followed by Registrar part II (26.0%) and Registrar part I (4.7%) (Fig 3).

Table 5: Co-morbidities

		N	%
	Diabetes	3	2.0
Other comorbidities	Hypertension	14	9.3
	Others	5	3.3

Figure 3: Cadres that performed surgery

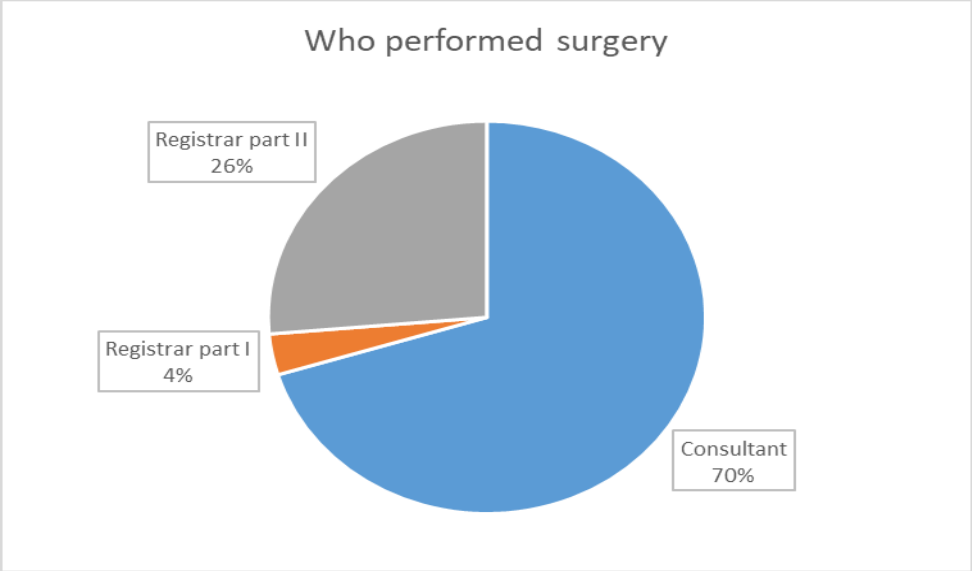


Table 6: Intraoperative analgesics

	N	Mean dose
i. Fentanyl	141	24
ii. Tramadol	62	100
iii. Paracetamol	83	15
iv. Diclofenac	104	133
v. Others	27	60

Intraoperatively, analgesics administered included Diclofenac (69.3%), Paracetamol (55.3%) and Tramadol (41.3%) of patients (Table 6).

The volume of intravenous fluids administered preoperatively, intraoperatively and postoperatively varied. Preoperatively, 66% of patients (99 patients) received restrictive fluid

regime of normal saline (mean = 909 mls), 32% (49 patients) received ringers lactate (mean = 536 mls) and 1.3% (2 patients) were given colloids (mean = 500 mls) and whole blood (mean = 450 mls). During surgery, 67.3% of patients (101 patients) were administered normal saline (mean 1089 mls), 9.3% (14 patients) ringers lactate (mean 723 mls), 17.3% (26 patients) normal saline and ringers lactate (mean 841 mls), 3.3% (5 patients) colloids (mean = 600 mls) and 2.6% (4 patients) blood 9mean = 463 mls) (Table 7).

Table 7: Intravenous fluids administered preoperatively and intra-operatively

	Preoperatively		intra-operatively	
	n	Mean	n	Mean
i. Crystalloids a Normal saline 0.9%	99	909	101	1089
i. Crystalloids b Ringers lactate mls	49	536	14	723
i. Crystalloids c N/saline + R/lactate			26	841
ii. Colloids mls	1	500	5	600
iii. Blood mls	1	450	4	463
iv. Blood products mls	0	.	0	.

Table 8: Fluids administered postoperatively

	Day 1		Day 2		Day 3	
	n	Mean	n	Mean	n	Mean
Colloids Post-operative	5	900	3	833	3	667
Normal saline 0.9% Post-operative	93	1219	0	.	0	.
Ringer's lactate Post-operative	28	760	0	.	0	.
N/saline + R/lactate	28	672				
Blood transfusion Post-operative	0	.	1	500	0	.
Other blood products Post-operative	0	.	0	.	0	.

In the first postoperative day, 93 patients (62%) received restrictive fluid regime of normal saline (mean = 1219 mls), 18.7% ringers lactate (mean = 760 mls), 18.7% ringers lactate and normal saline and 3.3% colloids (mean = 900 mls). Crystalloids were not administered in the second and third postoperative days but 2% of patients received colloids on both days (mean = 833 mls and 667 mls respectively). Blood was transfused in the second postoperative day to 1 patient (0.6%) (Mean = 500 mls) (Table 9).

Majority of patients received between 500 – 1000 mls of normal saline and <500 mls of ringers lactate perioperatively (Fig 4). The only post-surgical complication experienced in 96% of patients was surgical site pain.

		pre-operatively		Intra-operatively		post-operatively	
	Amount	**n**	**%**	**n**	**%**	**n**	**%**
Normal Saline	<500ml	41	41.4	20	17.9	12	10.8
	500-1000ml	39	39.4	59	52.7	58	52.3
	>1000ml	19	19.2	33	29.5	41	36.9
Ringer Lactate	<500ml	45	92.9	16	61.5	28	62.5
	500-1000ml	4	7.1	8	30.8	13	29.2
	>1000ml	0	0	2	7.6	3	8.3
Normal Saline+ Ringer Lactate	<500ml			7	26.9	9	32.1
	500-1000ml			18	69.2	16	57.1
	>1000ml			1	3.8	3	10.7

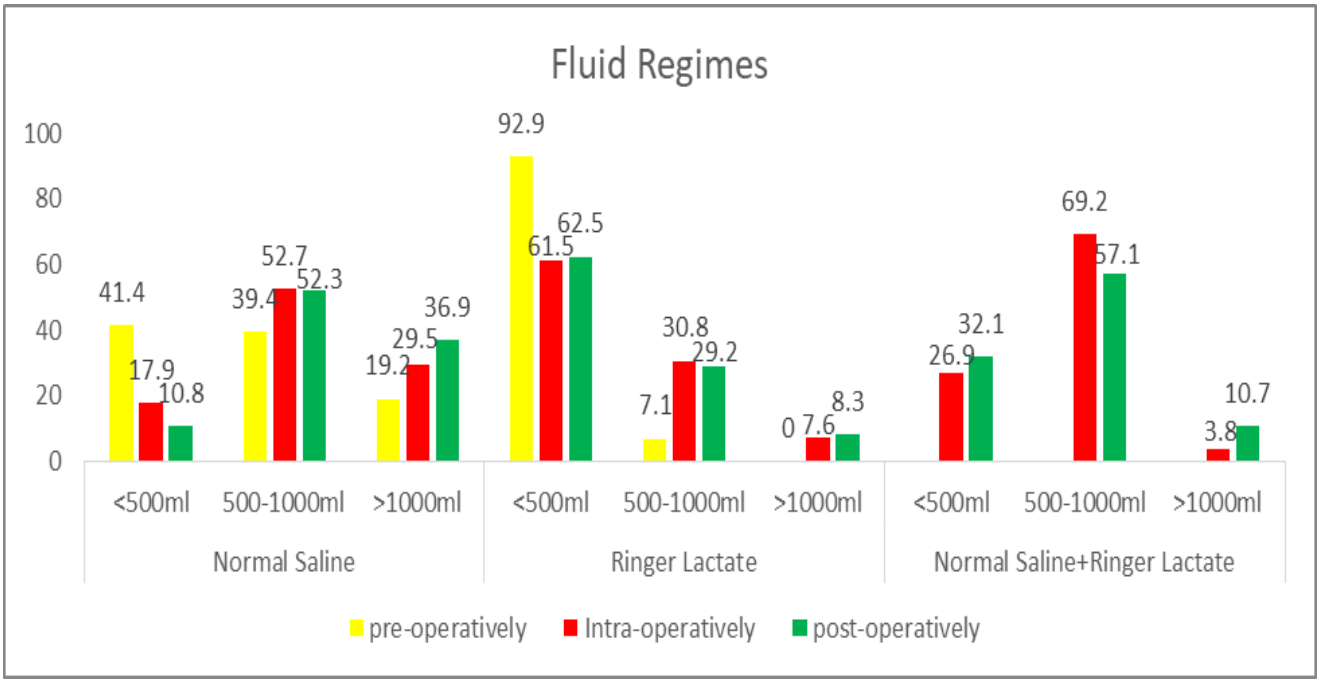


Figure 4: Fluids administered perioperatively

Table 9: Number of hours from the time of surgical incision

	Mean	Minimum	Maximum
Time to first flatus (hours)	7	1	36
Time to normal bowel sounds (hours)	10	1	54
Time to first defecation (hours)	32	4	85
Time to first rescue analgesia (hours)	11	1	52
Time to tolerance of first oral feed (hours)	14	4	36

The average time to occurrence of outcomes of interest from surgical incision time include: period of time to first flatus (7 hrs), duration of time to normal bowel sounds (10 hrs), the time taken to first rescue analgesia (11 hrs), period of time to first defeacation (32 hrs) and time taken to tolerance of first solid food (14 hrs) (Table 10).

27.3% (41 patients) of patients developed nausea postoperatively reducing to 18.6% (28 patients) and 14% (21 patients) in second and 3 third day respectively. Anti-emetics were administered to all patients who developed nausea. 14.6% (22 patients) vomited in the first postoperative day which reduced to 8.6% (13 patients) in the third postoperative day. Rescue analgesia was administered to 12.6% (19 patients) on the first postoperative day compared to 8% on the third day after surgery (Table 11).

Table 10: Occurrence of nausea and vomiting versus anti-emetics and rescue analgesia administration post operatively

		Day 1	Day 2	Day 3
No. Of times of anti-emetics in 24 hours	Valid N	42	28	24
	Mean	2	2	4
	Minimum	0	0	0
	Maximum	4	4	5
No. Of times of nausea in 24hrs.	Valid N	41	28	21
	Mean	2	2	2
	Minimum	0	0	0
	Maximum	5	3	4
No. Of times of vomiting in 24 hours	Valid N	22	15	13
	Mean	2	1	1
	Minimum	0	0	0
	Maximum	3	2	2
No. Of times of rescue analgesia in 24 hrs	Valid N	19	15	12
	Mean	1	1	1
	Minimum	0	0	0
	Maximum	3	2	1

Table 11: Age and BMI versus Ileus

		Time to flatus	Time to bowel movement	Time to defeacation	Time to first rescue analgesia	Time to oral feeding
		Mean	Mean	Mean	Mean	Mean
Age	Up to 1 day	28	28	29	29	28
	More than 1 day	30	31	28	30	39
p-value		0.106	0.804	0.567	0.207	0.314
BMI	Up to 1 day	29	29	30	30	29
	More than 1 day	28	30	29	31	32
p-value		0.314	0.743	0.518	0.473	0.565

Results of paired t-test carried out to find association between age and BMI on recovery of intestinal function after surgery revealed that they did not significantly influence ileus (outcomes of interest) post operatively (Table 12).

As shown in the table below, longer duration if surgery was associated with higher EBL but Pearson correlation test showed no significant statistical difference.

Table 12: Duration of surgery versus EBL

Duration of Surgery (Hrs)	EBL (Mean in mls)	P-Value
1.0 – 1.20	475	0.672
1.21 – 1.40	525	0.861
1.41 – 1.50	650	0.954

Table 13: Effect of intraoperative drugs on Ileus

		Time to flatus	Time to bowel movement	Time to defeacation	Time to first rescue analgesia	Time to oral feeding
		Mean	Mean	Mean	Mean	Mean
i. Fentanyl Dose	Up to 1 day	24	24	24	25	24
	More than 1 day	25	25	24	19	25
p-value		0.569	0.533	0.895	<0.0001	0.661
ii. Tramadol Dose	Up to 1 day	100	100	88	77	100
	More than 1 day	100	100	101	100	88
p-value		0.997	0.997	0.801	0.484	0.890
iii. Paracetamol Dose	Up to 1 day	14	14	12	19	12
	More than 1 day	7	7	14	1	1
p-value		0.703	0.708	0.811	0.500	0.721
iv. Diclofenac Dose	Up to 1 day	137	137	100	131	136
	More than 1 day	100	100	141	100	100
p-value		0.689	0.655	0.397	0.751	0.781

Effect of drugs given intraoperatively on recovery of intestinal function postoperatively was evaluated using paired t-test. Fentanyl significantly (p=<0.0001) reduced time to rescue analgesia postoperatively but did not have significant effect to recovery of gut after surgery. Other drugs had no significant effect on intestinal recovery after surgery (Table 14). On analysis of variance (ANOVA), postoperative crystalloids (normal saline >500mls in a day) significantly (p=0.021 and p=0.017) reduced the incidence of rescue analgesia administration in the second and third postoperative day respectively but had no significant effect on nausea and emesis.

		Normal Saline pre-operatively	Ringer Lactate pre-operatively	Normal Saline intra-operatively	Ringer Lactate intra-operatively	Normal Saline post-operative Day1	Ringer Lactate post-operative Day1
		Mean	Mean	Mean	Mean	Mean	Mean
No. Of times of antiemetics in 24 hours Day 1	<500ml	2	2	1	3	1	1
	500-1000ml	1	.	2	1	2	2
	>1000ml	1	.	2	1	2	.
p-value		0.334	-	0.829	0.427	0.765	0.234
No. Of times of antiemetics in 24 hours Day 2	<500ml	1	1	1	1	.	1
	500-1000ml	1	.	1	1	1	1
	>1000ml	0	.	1	.	1	.
p-value		0.034	-	0.274	0.347	0.160	-
No. Of times of antiemetics in 24 hours Day 3	<500ml	1	1	1	1	1	1
	500-1000ml	1	.	1	1	1	1
	>1000ml	1	.	1	.	1	.
p-value		0.340		0.507	-	0.507	-

		Normal Saline pre-operatively	Ringer Lactate pre-operatively	Normal Saline intra-operatively	Ringer Lactate intra-operatively	Normal Saline post-operative Day1	Ringer Lactate post-operative Day1
		Mean	Mean	Mean	Mean	Mean	Mean
No. Of times of nausea in 24hrs. Day 1	<500ml	2	2	1	2	3	2
	500-1000ml	1	.	2	2	2	3
	>1000ml	2	.	2	2	1	.
p-value		0.376	-	0.507	0.698	0.119	0.042
No. Of times of nausea in 24hrs. Day 2	<500ml	1	2	1	1	2	1
	500-1000ml	1	.	1	1	1	3
	>1000ml	1	.	2	3	1	.
p-value		0.832	-	0.404	0.061	0.650	0.130
No. Of times of nausea in 24hrs. Day 3	<500ml	2	2	.	1	.	2
	500-1000ml	5	.	1	2	1	3
	>1000ml	1	.	1	6	1	8
p-value		0.159		0.936	0.090	0.798	-

		Normal Saline pre-operatively	Ringer Lactate pre-operatively	Normal Saline intra-operatively	Ringer Lactate intra-operatively	Normal Saline post-operative Day1	Ringer Lactate post-operative Day1
		Mean	Mean	Mean	Mean	Mean	Mean
No. Of times of vomiting in 24 hours Day 1	<500ml	2	2	.	2	3	2
	500-1000ml	2	.	2	1	2	2
	>1000ml	2	.	2	2	1	.
p-value		0.724	-	0.869	0.385	0.101	0.342
No. Of times of vomiting in 24 hours Day 2	<500ml	1	1	1	1	1	2
	500-1000ml	2	.	1	1	1	1
	>1000ml	1	.	1	.	1	.
p-value		0.177	-	0.394	0.721	0.394	0.667
No. Of times of vomiting in 24 hours Day 3	<500ml	1	1	.	1	.	2
	500-1000ml	2	.	1	1	1	1
	>1000ml	0	.	1	.	1	.
p-value		0.125	-	0.162	0.541	0.211	-

		Normal Saline pre-operatively	Ringer Lactate pre-operatively	Normal Saline intra-operatively	Ringer Lactate intra-operatively	Normal Saline post-operative Day1	Ringer Lactate post-operative Day1
		Mean	Mean	Mean	Mean	Mean	Mean
No. Of times of rescue analgesia in 24 hrs Day 1	<500ml	2	1	1	2	1	1
	500-1000ml	1	.	2	1	1	3
	>1000ml	1	.	1	2	1	.
p-value		0.299	-		0.363	0.797	0.667
No. Of times of rescue analgesia in 24 hrs Day 2	<500ml	1	1	.	1	2	1
	500-1000ml	1	.	1	1	1	.
	>1000ml	1	.	1	.	1	.
p-value		-	-	-	-	0.021	-
No. Of times of rescue analgesia in 24 hrs Day 3	<500ml	1	1	.	1	.	1
	500-1000ml	1	.	1	1	1	.
	>1000ml	0	.	1	.	0	.
p-value		-	-	-	-	-	0.017

Table 14: Effect of Perioperative crystalloids on Intestinal recovery after surgery.

		Time to first flatus (hours)	Time to normal bowel sounds (hours)	Time to first defecation (hours)	Time to first rescue analgesia (hours)	Time to tolerance of first oral feed (hours)
Normal saline mls – preop	Pearson Correlation	0.146	0.171	-0.075	0.045	-0.197
	p-value	0.154	0.093	0.465	0.829	0.045
Ringers lactate mls - preop	Pearson Correlation	-0.148	-0.208	-0.11	0.[a]	-0.467
	p-value	0.615	0.476	0.708	<0.0001	0.092
Normal saline mls – intraop	Pearson Correlation	0.046	0.094	0.002	0.085	0.089
	p-value	0.631	0.327	0.979	0.655	0.355
Ringers lactate mls – intraop	Pearson Correlation	0.03	0.053	-0.098	-0.308	-0.04
	p-value	0.815	0.679	0.44	0.214	0.755
Normal saline + Ringers Lactate –intraop	Pearson Correlation	0.064	0.088	0.007	0.053	0,094
	p-value	0.437	0.621	0,932	0,556	0.236
Normal saline mls Post-operative day 1	Pearson Correlation	-0.102	-0.104	0.078	0.370*	0.102
	p-value	0.291	0.279	0.418	0.048	0.296
Ringer's lactate Post-operative day 1	Pearson Correlation	0.015	-0.116	-0.082	0.241	0.146
	p-value	0.918	0.433	0.579	0.335	0.334
Normal saline + Ringers Lactate -Post Operative day 1	Pearson Correlation	0.078	0,066	0.006	0.047	0.084
	p-value	0.381	0.687	0.743	0.772	0,194

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

a. Cannot be computed because at least one of the variables is constant.

Analysis by Pearson correlation test demonstrated that administration of normal saline preoperatively significantly (P = 0.045) influenced time to tolerance of first oral feed {with analysis of variance showing that the most significant volume of normal saline that shortened duration of time to first oral feed and period of time to normal bowel sounds was 500-1000mls in a day (p=0.011 and p=0.029 respectively) (Table 16) whereas normal saline in the first postoperative day prolonged time to first rescue analgesia in the first postoperative day (p=0.048). Crystalloids administered preoperatively had no significant effect to other outcomes of interest (Table 15). Other intraoperative and postoperative fluid volumes (normal saline given with ringers lactate and colloids) as well as EBL had no effect on the outcomes of interest.

Table 15: Effect of different fluid volumes on intestinal recovery postoperatively.

		Time to first flatus (hours)	**Time to normal bowel sounds (hours)**	**Time to first defecation (hours)**	**Time to first rescue analgesia (hours)**	**Time to tolerance of first oral feed (hours)**
		Mean	Mean	Mean	Mean	Mean
Estimated Blood Loss	<250ml	21	22	40	10	20
	250-500ml	7	10	32	11	14
	501-1000	8	10	32	10	14
	>1000	10	10	20	12	9
	p-value	0.275	0.552	0.457	0.991	0.600
Normal Saline preop	<500ml	8	10	35	12	14
	500-1000ml	5	8	31	13	13
	>1000ml	11	15	34	13	12
	p-value	0.011	0.029	0.297	0.954	0.261
Ringer Lactate preop	<500ml	9	11	29	13	15
	500-1000ml	4	4	26	.	5
	>1000ml	.	.	.	.	.
	p-value	0.615	0.476	0.708	-	0.092
Normal Saline intraop	<500ml	7	10	33	13	13
	500-1000ml	7	10	33	11	13
	>1000ml	8	12	33	15	14
	p-value	0.960	0.446	0.963	0.799	0.683
Ringer Lactate intraop	<500ml	7	9	34	14	13
	500-1000ml	9	11	31	11	12
	>1000ml	4	9	34	3	13
	p-value	0.373	0.661	0.485	0.434	0.780
Normal Saline post-operative Day1	<500ml	11	16	36	8	12
	500-1000ml	7	10	31	12	13
	>1000ml	6	10	35	18	14
	p-value	0.137	0.068	0.095	0.521	0.618
Ringer Lactate post-operative Day1	<500ml	5	9	34	11	12
	500-1000ml	9	11	33	12	12
	>1000ml	3	4	32	24	12
	p-value	0.123	0.279	0.827	0.616	0.939

Analysis of variance (ANOVA) revealed that patients operated on by consultants significantly (P=<0.001) tolerated first oral feeds earlier compared to patients operated on by registrars but the latter cadre achieved faster onset to first defeacation (P=0.016) compared to consultants. Achievement of shorter time to oral feeds in patients operated on by consultants could have been due to strict follow up of postoperative instructions.

Outcome	Service provider	Mean	Std. Deviation	p-value
Time to first flatus (hours)	Consultant	7.61	7.708	0.764
	Registrar part II	7.36	6.058	
	Registrar part I	5.20	2.775	
Time to normal bowel sounds (hours)	Consultant	10.69	8.757	0.640
	Registrar part II	9.69	6.528	
	Registrar part I	7.80	5.020	
Time to first defecation (hours)	Consultant	33.50	9.429	0.016
	Registrar part II	28.31	8.301	
	Registrar part I	31.40	9.762	
Time to first rescue analgesia (hours)	Consultant	12.47	12.409	0.305
	Registrar part II	7.00	3.490	
	Registrar part I	16.00	.	
Time to tolerance of first oral feed (hours)	Consultant	12.78	5.321	<0.0001
	Registrar part II	17.06	5.477	
	Registrar part I	19.40	2.510	

7.0 CHAPTER SEVEN: DISCUSSION

7.1 Prevalence of ileus after 3 days post caesarian delivery (5.6%)

The prevalence of ileus after caesarian delivery was 5.6%. This is similar to data analysis of abdominal surgery patients by *Tevis et al* whose prevalence was 5.3 to 24% (37). Time to first defeacation was considered as the clinical hall mark that best reflected recovery of gut after surgery which had been validated by *Vanbree et al* in a multicenter trial of segmental colectomy patients (39).

7.2 Predictive Factors associated with Postoperative Ileus after Caesarean Delivery.

The age and BMI of patients did not influence recovery of gut after surgery. This observation is similar to a randomized study by *Kathrine, H et al* where age and BMI had no effect on intestinal recovery post operatively in cholecystectomy patients (13).

Preoperative intravenous fluids (normal saline 501 – 1000 mls) significantly influenced duration of time to first flatus, period of time to normal bowel sounds and time to first oral feed. This suggests that hydration status of the patient preoperatively influences intestinal recovery postoperatively. Crystalloids (normal saline) administered in the first postoperative day prolonged time to first rescue analgesia but this could have been influenced by intraoperative fentanyl which was found to significantly prolong the time to rescue analgesia. Preoperative intravenous fluid regime data is lacking for comparison with this finding.

Intravenous crystalloids had no significant effect on intestinal function postoperatively. This is dissimilar to study by *Nisanevich, V et al* on laparatomy patients (colectomy, gastrectomy and cholecystectomy) which revealed that intraoperative restrictive fluid regime significantly shortened period of time to first flatus and duration of time to defeacation compared to liberal administration of fluids (29). Similar results on intraopearative fluid restriction with improved gastrointestinal recovery in comparison to liberal fluid administration were demonstrated by *Varadhan et al* using systematic meta-analysis on 801 patients who underwent open abdominal surgery (40).

Research Methodology utilized here varied from other studies because all patients received fluid volumes of the restrictive regimen, fluid administration was not goal guided by vital signs (central venous pressure) or invasive monitoring (stroke volume oesophageal Doppler

monitoring) and patients were not randomized in comparison to studies by *Pearse et al* and *Rahbari et al* which included goal directed therapy and use of different fluid regimes with patient randomization (31,33). Restrictive fluid regimes (especially with colloid) were demonstrated to be superior to liberal fluid regime in enhancing gut recovery after abdominal surgeries (colon resection, cholecystectomy, hepatectomy and gastrectomy).

Level of surgical competence was shown to influence recovery of intestinal function. Patients operated by consultants had significantly reduced time to tolerance of first oral feeds compared to patients operated by registrars. Since time to first flatus, time to normal bowel sounds and time to passing stool was not significantly different in all surgical cadres, the consultants instructions to feeding of patients could have influenced the time to first oral feed (considering they operated most of the patients).

7.3 Statistically Significant Association between Perioperative Intravenous Fluids and Recovery of Intestinal Function.

Pearson correlation test carried out to find any association between perioperative intravenous fluids and recovery of gut function after caesarean delivery showed statistically significant association between shortened time to tolerance of first oral feeds and administration of normal saline preoperatively (P=0.045) with a significantly lengthened time to first rescue analgesia in the first postoperative day (P=0.048) when 500 – 1000 mls was administered. Analysis of variance also revealed association between preoperative crystalloids administration (500-1000 mls) and shortened time to normal bowel sounds (P=0.029) and time to first flatus (0.011). This was most likely due to improved hydration status preoperatively.

8.0 CHAPTER EIGHT: CONCLUSIONS AND RECOMMENDATIONS

8.1 CONCLUSIONS

From this study, we can conclude that prevalence of postoperative ileus in the obstetric population is similar to that seen in abdominal surgery patients. There is a significant association between preoperative intravenous fluids administration and recovery of intestinal function postoperatively. We also noted that 500-1000mls of normal saline preoperatively led to enhanced recovery of intestinal function compared to other fluid volumes (reduced time to tolerance of oral feeds and reduced need for rescue analgesia). The level of competence of the surgeon had a positive influence on recovery of intestinal function postoperatively with patients operated on by consultants having shorter time to tolerance of oral feeds compared to those operated by registrars. For example, consultant's surgical practice in KNH of repairing the uterus without exteriorization might have contributed to enhanced gut recovery post-operatively.

8.2 RECOMMENDATIONS

1. Optimization of hydration status of patients preoperatively to improve intestinal recovery postoperatively.

2. A large randomized controlled study to better understand the effect of postoperative fluid volume on recovery of intestinal function.

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APPENDICES

Appendix I: Explanation and Consent for the Patient (English)

A PROSPECTIVE OBSERVATIONAL STUDY ON THE EFFECT OF PERI-OPERATIVE INTRAVENOUS FLUIDS ON RECOVERY OF INTESTINAL FUNCTION AFTER CAESAREAN DELIVERY UNDER SPINAL ANAESTHESIA

Study Site

Kenyatta National Hospital.

Background

My names are Dr. Vincent Mtongwe. I am pursuing anaesthesia course at the University of Nairobi as a postgraduate student, School of Medicine. I am conducting a study on "The effect of peri-operative intravenous fluids on recovery of intestinal function after caesarean delivery under spinal anaesthesia".

Purpose

The aim of this study is to establish how intravenous fluids administered for management during caesarean delivery under spinal anaesthesia and in the postnatal ward affect recovery of intestinal function post-operatively. This will help us improve the quality of care.

Procedure

If you agree to participate in this study, I will capture medical details from your hospital file, record the intravenous fluids given at surgery and in the postnatal wards. Follow up after surgery will be done in order to assess intravenous fluids affect recovery of intestinal function.

Participation

Participation in the study is voluntary and no rewards will be awarded. You will not incur any extra cost due to this study other than the usual cost of care at Kenyatta National Hospital. As a participant you will get explanation about the study and give informed written consent. You have a right to full information on the study

outcomes and free to with draw your participation at any time during the study without ant repercussions.

Risks of participation

There are no risks involved in this study since there is no intervention under study in patient management. Planned treatment will not be altered.

Confidentiality

All information gathered will be treated with utmost confidentiality. The patients name will not appear in any document.

Sharing of results

The results obtained from this study will be shared with other experts through formal platforms. For further information, issues or clarification you may contact KNH/UON – Ethics & Research Committee, P.O Box 20723-00202, Telephone number – 2726300-9.

CONSENT FORM

I……..……(Name) of ……..……
from ……. (area) hereby give written consent for the participation in the prospective observational study assessing effect of peri-operative intravenous fluids on recovery of gut function after caesarean delivery under spinal anaesthesia.
I have understood the information regarding the study. I have had my questions addressed.
I have the right to withdraw at any stage of the study.

Signed……. Date……

Appendix II: Explanation and Consent for the Patient (Swahili)

FOMU YA MAKUBALIANO YA KUJIUNGA NA UTAFITI

A PROSPECTIVE OBSERVATIONAL STUDY ON THE EFFECT OF PERI-OPERATIVE INTRAVENOUS FLUIDS ON RECOVERY OF INTESTINAL FUNCTION AFTER CAESAREAN DELIVERY UNDER SPINAL ANAESTHESIA

Utangulizi

Jina langu ni Vincent Mtongwe nafanya utafiti wa shahada ya juu katika "anaesthesia" kwenye Chuo Kikuu cha Nairobi. Fomu hii ya utafiti ni ya wale wagonjwa ambao wanahudumiwa katika hospitali kuu ya Kenyatta na wamealikwa kujiunga na utafiti.

Madhumuni ya utafiti

Malengo ya **utafiti** huu ni kudhibitisha athari ya maji ya mishipa katika kurejea kwa utenda kazi wa tumbo tangu wakati unapolazwa kwa wodi hadi siku tano baada ya operesheni wakati wa kujifungua mtoto.

Utaratibu

Ukikubali kushiriki katika utafiti huu, nitapekua faili yako ya hospitali, nitarekodi maji yote utakayo pewa katika mishipa ya damu wakati wa upasuaji na katika wodi utakayo lazwa baada ya upasuaji. Uchunguzi utaendelea katika wodi kwa minajili ya kudhibitisha athari ya maji ya mishipa katika kurejea kwa utenda kazi wa tumbo.

Madhumuni

Utafiti huu utasaidia madaktari kuboresha huduma zinazotolewa kwa wagonjwa katika wodi zinazolazwa akina mama baada ya kujifungua mtoto/watoto kwa njia ya operesheni. Kusajiliwa kwa utafiti huu ni kwa hiari yako. Hakuna malipo utakayo lipa zaidi ya malipo ya hospitali. Pia, hakuna pesa utakazo pewa kwa kushiriki na hakuna hatari inayotokana na kushiriki katika utafiti huu. Isitoshe, una ruhusa au uhuru wa kujiondoa kwa utafiti huu wakati wowote. Majina yako hayatatumika katika utafiti na usiri mkubwa utatumiwa katika utafiti. Utahitajika kuelewa kuhusu utafiti huu na kutia sahihi kubalio hili ili usajiliwe katika utafiti.

Usiri

Baada ya utafiti, uchambuzi wa takwimu utafanywa. Habari itachapishwa katika kitabu kitakachowekwa kwa maktaba ya Chuo Kikuu Cha Nairobi. Usiri mkubwa utatumika kwa kuziweka taarifa hizi.

Sasa, nitakupa nafasi ya kuuliza maswali yoyote uliyo nayo kuhusu utafiti huu na ikiwa utakubali kushiriki katika utafiti huu, utatia sahihi yako kwenye nafasi iliyotolewa kwenye fomu ya kubalio. Maswali yoyote kuhusu utafiti huu yanaweza kuelekezwa kwa "KNH-ERC, Hospitali ya Rufaa ya Kenyatta, Sanduku la Posta20723, Nairobi. Simu: 2726300-9".

FOMU YA IDHINI

Nambari ya Usajili…….. Mimi ni ……..(Jina) wa…….Kutoka……..(Sehemu).

Nimekubali kushiriki katika utafiti wa: "A Prospective observational study assessing the effect of perioperative intravenous fluids on recovery of intestinal function after cesarean delivery under spinal anaesthesia"

Ninaelewa ya kwamba uchunguzi utafanyika bila madhara yoyote kwa mgonjwa na pia ya kwamba, nina uhuru wa kujiuzulu kutoka kwa utafiti huu wakati wowote.

Nina thibitisha kwamba nimemueleza mgonjwa kikamilifu kuhusu utafiti huu na amekubali bila kushurutishwa.

Sahihi…….. Tarehe……

Appendix III: Research Questionnaire

Date: (DD/MM/YYYY) _____

TOPIC: A PROSPECTIVE OBSERVATIONAL STUDY ON THE EFFECT OF PERI-OPERATIVE INTRAVENOUS FLUIDS ON RECOVERY OF INTESTINAL FUNCTION AFTER CAESAREAN DELIVERY UNDER SPINAL ANAESTHESIA

Serial No.: …….....

A. DATA ABSTRACTION TOOL

Part 1: Demographic Data (Indicate)

1. Date of Birth [DD/MM/YYYY]: **…….....……**
2. Weight (kg)**…….....** Height (m) **…….....** BMI (kg/m2)**…….....**
3. Parity**…….....…** Gestation (weeks)**…….....**
4. What is the type of surgery? (Tick as appropriate)
   - i. Elective □
   - ii. Emergency □
5. What is the indication for caesarean section? (Tick as appropriate)
   - i. Non reassuring foetal state □
   - ii. Placenta Previa type IV □
   - iii. Placenta Abruption □
   - iv. Maternal request □
   - v. Breech presentation □
   - vi. Transverse lie □
   - vii. Others **…….....……**

6. What were the intra-operative complications? (Tick as appropriate)
   - i. Difficult foetal extraction □
   - ii. Extensive uterine incision □
   - iii. Bladder injury □
   - iv. Others **…….....……..……**

7. What was the surgical Incision time? **……..…** (am/pm) Duration of surgery?
   ……..…….(hrs) EBL? …… (mls) Entry time to PACU? ….……...(am/pm)
8. Which other co-morbidities does the patient have? (Tick as appropriate)
   i. Diabetes □
   ii. Hypertension □
   iii. Others **…….....…….....……..**
9. Who performed the surgery? (Tick as appropriate)
   Consultant □ Registrar part II □ Registrar part I □

Part 2: What analgesics were given intra-operatively?

1. Which medications has the patient been using before surgery, duration and dosages if any? (Tick as appropriate)
   i. Metoclopramide □ Dose (mg) …… Days……...……
   ii. Tramadol □ Dose (mg) …… Days ……..……
   iii. Morphine □ Dose (mg) …… Days …….……
   iv. Erythromycin □ Dose (mg) …… Days ……..**.....**
   v. Others (specify)…….**.....**
2. Which analgesic(s) were given intra-operatively? (Tick and indicate the dosages given)
   i. Fentanyl □ Dose……
   ii. Tramadol □ Dose……..……..……
   iii. Paracetamol □ Dose …….……..……
   iv. Diclofenac □ Dose…….....…….....
   v. Others, (specify)…….**.....**…….**.....**
3. How much intravenous fluids were administered before admission to theatre?
   i. Crystalloids (a) Normal saline 0.9% □ **……** (mls)
   (b) Ringers lactate □ **……** (mls)
   ii. Colloids □ **…….....** (mls)
   iii. Blood □ **…..... (mls)**
   iv. Blood products (specify) **…….** □ **……...…** (mls)
4. How much intravenous fluids were administered intra-operatively?
   i. Crystalloids (a) Normal saline 0.9% □ **……** (mls)
   (b) Ringers lactate □ **……..…** (mls)

ii. Colloids □ **……..** (mls)

iii. Blood □ **…..** (mls)

iv. Blood products (specify) **…….** □ **……..…** (mls)

5. Which other medications were used during surgery?

Indicate other medications and dosage used during surgery,

…….....…….....…….....

.....

Part 3: What were the Post-Operative Complications?

1. Indicate the complications observed post operatively; (Tick as appropriate)
   i. Surgical site pain □
   ii. Wound infection □
   iii. Wound dehiscence □
   iv. Others **…….....…….....……..**

Part 4: Which intravenous fluids were administered post operatively?

Type	**Post-operative day 1**	**Post-operative day 2**	**Post-operative day 3**
Colloids			
Normal saline 0.9%			
Ringer's lactate			
Blood transfusion			
Other blood products (specify)			

B. OUTCOMES OF ASSESSMENT TOOL

1. Outcomes of Assessment (Number of hours from the time of surgical incision)

Outcomes	**Hours**
Duration of time to first flatus	
Duration of time to normal bowel sounds	
Duration of time to first defecation	
Duration of time to first rescue analgesia	
Period of time to tolerance of 1st oral feed	

2. Outcomes of assessment (Number of times every 24 hrs of intervention/occurrence)

Outcomes	**Number of times every 24 hours Day 1**	**Day 2**	**Day 3**
No. Of times of anti-emetics in 24hours			
No. Of times of nausea in 24hrs.			
No. Of times of vomiting in 24 hours			
No. Of times of rescue analgesia in 24 hrs			

Appendix IV: Spinal Anaesthesia Protocol

Kenyatta National Hospital Maternity Theatre

PROTOCOL FOR SPINAL ANAESTHESIA AT THE KENYATTA NATIONAL HOSPITAL

1. Know the indications & contra-indications.
2. Inform the patient what you wish to do and have their co-operation.
3. Inform the rest of the team in theatre so you can be assisted appropriately.
4. Insert a good gauge I/V cannula (20 or larger).
5. Pre-load with ½ -1L N/saline / Hartman's over 30-60 mins.
6. Install your monitors (pulse, respiration, SPO2, BP and ECG) and take baseline readings.
7. Position the patient either sitting or lateral knee-chest. Make the patient comfortable.
8. Open your Spinal Tray & clean the site & drape.

   Spinal Tray should contain:

   a) Sterile towels for draping the patient.
   b) 2 gulley pots for holding cleaning solutions.
   c) Appropriate spinal needle (with introducer where required).
   d) 2 syringes & Needles
      i. 5ml syringe for infiltration of L.A to the site
      ii. 2ml syringe for administering the spinal medication
      iii. Sterile gauze pads for cleaning & dressing
9. Reconfirm the position of the patient (knee chest).
10. Identify the site: mid-line L3-4/ 4-5 & administer 3ml of 1% lignocaine using a gauze 21 needle to maximum depth. Withdraw the needle as you continue to administer L.A and raise a skin wheal.
11. Give 1-2 minutes for the L.A to take effect as you re-assure & position patient (if administered well, this usually covers one vertebra above & below, should you need to alter position of lumbar puncture).

12. While waiting for L.A to take effect, prepare your appropriate drug. You must have decided whether using plain or heavy L.A.
    a) Remember Heavy L.A is position dependent. The patient must be appropriately Positioned after injection to allow desired distribution.
    b) Bupivacaine is usually 0.5% concentration. The highest volume in tall patients will be 4ml (20mg). Most patients will require between 7.5mg (1.5mls) to 15 mg (3ml).
    c) Obstetric patients are more sensitive and will require between 10mg (2ml) to 12.5mg (2.5ml). Aim for a block up to T6. Test and record level of block.
    d) Additive: 25mg Fentanyl (0.5ml) is a useful additive to prevent the discomfort of gut handling during CS etc. This must still make up the total volume of 2-2.5 ml of drug injected into the spinal canal. Other drugs have been used as additives but its best to avoid them unless you have been trained to use them. The haphazard use of additives into the CSF may have disastrous results.
    e) Remember for CS the volume & position is critical to achieve a good or disastrous spinal block. Aim for a block up to T6.
13. Confirm the L.A. has taken effect and note level/site for the block.
    Insert the spinal needle. Usually there is a sudden give when the needle goes through the dura. Withdraw the stylet and check for CSF flow. Do not allow unnecessary drainage of CSF. Use the stylet to stop the flow temporarily, if you cannot administer the spinal drug immediately.
14. Administer the drug, dress the puncture site and position the patient appropriately to allow planned distribution of drugs. Rapid positioning after administration is critical if the drug used is hyperbaric (heavy).
15. Start your post-spinal monitoring & make adjustments accordingly. It is recommended to repeat BP readings at 1 minute intervals. You will need to respond rapidly to the initial changes in pulse & BP. Ask the patient to inform you immediately if nausea occurs. Nausea in spinal anesthesia is most likely due to hypotension. It is an early warning sign that you must not ignore.
16. Test the level of the block. The tilt of the bed may have to be adjusted if using hyperbaric Local Anesthetic to change drug distribution. This manipulation may only work within the first 10-20 minutes after administration of the L.A into the CSF.

17. Post-operative pain management -I/M Pethidine 1mg/kg 4-6 hourly, for 24 hours-Diclofenac suppository (or equivalent) stat & 12 hourly for 48 hours then oral analgesics. Follow up visit, within 24 hours.
18. Critical observation
    a) Pulse –symptomatic bradycardia –Atropine 0.1 -0.6mg.
    b) SPO2 saturation ≤ 90% -Increase the O2 flow.
    c) BP –symptomatic Hypotension -Ephedrine 5mg-10mg PRN (you may occasionally need an infusion)-Phenylephrine-Adrenaline.
    d) Respiration –falling respiratory rate (usually temporary)-Give oxygen. Assist with respiration briefly if required. Reassure.
    e) Total Spinal Anaesthesia
        i. Convulsions /loss of consciousness
        ii. Respiratory failure
        iii. Cardiovascular collapse -

        Intubate, ventilate, cardiac massage, vasopressors, anticonvulsants till vital signs stabilize.
    f) Post spinal headaches-May occur post-operatively are worse on standing & relieved by lying down.

        Management
        i. Bed rest
        ii. Plenty of fluids
        iii. Non-Steroidal Anti-inflammatory Drugs (NSAIDS)
        iv. Epidural blood patch as a last resort.

Post-Operatively, monitor BP ¼ hourly for 2hrs.

Positioning –make patient comfortable with pillow under the head.

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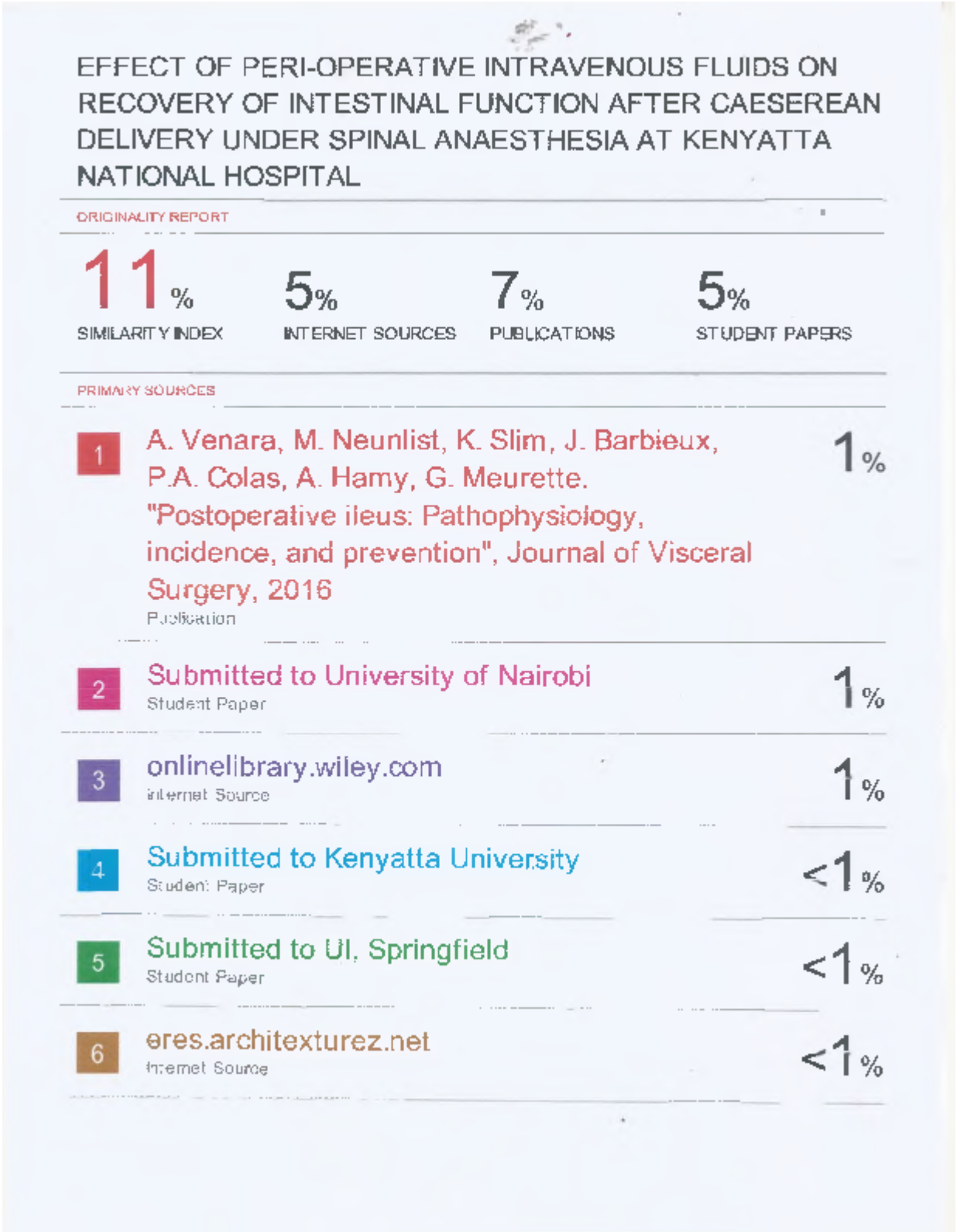
Appendix V: Anti-plagiarism Certificate



EFFECT OF PERI-OPERATIVE INTRAVENOUS FLUIDS ON RECOVERY OF INTESTINAL FUNCTION AFTER CAESEREAN DELIVERY UNDER SPINAL ANAESTHESIA AT KENYATTA NATIONAL HOSPITAL

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