Anaesthetists practice of intra-operative fluid management in the paediatric population in three academic hospitals

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Declaration

I, Klaudia Imiolo Bruckmann, declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in Anaesthesiology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University

.....[signature of candidate]

.....day of .....[month], 2018

Abstract

Background. Peri-operative fluid management in paediatric surgical patients is an integral part of any anaesthetic and influences surgical outcome. This study assesses the practice of peri-operative paediatric fluid administration in the Department of Anaesthesiology.

Method. This prospective descriptive cross-sectional practice-based study used an anonymous self-administered questionnaire to assess the approach to fluid administration during the peri-operative period in the paediatric population by the anaesthetists at Wits. A total of 125 completed questionnaires were received which attained a 61.3 % response rate. The questionnaire aimed to assess the approach to intra-operative fluid administration in both stable and unstable paediatric patients, knowledge of existing guidelines concerning peri-operative paediatric fluid administration, the approach to managing blood glucose intra-operatively and whether demographics, experience, training and designation influenced practice.

Results. Only 54.4% of the department knew of a recognized and published paediatric fluid protocol. Experience (p= 0.0856), training (p=0.2016) and designation (p= 0.2915) had no influence over the use of a specific formula for fluid calculation in paediatric patients. The two most commonly used formulae for maintenance was the 2:1:0.5 rule used by 38.7% and the 4:2:1 rule used by 37.1% of the study population. The majority of participants used a balanced crystalloid solution when administering intra-operative maintenance fluid but 13.7% still used hypotonic solutions. There was no clear preference between crystalloids (50.8%) and colloids (45.2%) when treating a haemodynamically unstable paediatric patient, specialists were however significantly more likely to use a colloid for resuscitation when compared to non-specialists (p=0.003).

Conclusion. This study revealed that there is no standard guideline when prescribing paediatric fluid intra-operatively at the Department of Anaesthesiology at Wits. Some anaesthetists practice unsafe fluid administration. Departmental

guidelines do not exist and there should be a framework for safe practice put in place.

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Abbreviations

Wits: University of the Witwatersrand

CHBAH: Chris Hani Baragwanath Academic Hospital

HJH: Helen Joseph Hospital

CMJAH: Charlotte Maxeke Johannesburg Academic Hospital

RMMCH: Rahima Moosa Mother and Child Hospital

APA: Association of Paediatric Anaesthesia

APAGBI: Association of Paediatric Anaesthesia of Great Britain and Ireland

AWMF: Association of the Scientific Medical Societies in Germany

HGT: Blood glucose

ICU: Intensive Care Unit

Cons: Consultant

Reg12: Junior registrar having 1-2 years of experience

Reg35: Senior registrar having 3-5 years of experience

MO: Medical Officer (including career medical officers)

CHAPTER ONE: OVERVIEW OF STUDY

1.1 Introduction

This chapter will provide an overview of the study. This includes the background to the study, the aims and objectives, definitions relevant to this study, a short description of the methodology, the significance as well as validity and reliability of the research undertaken. The study limitations and ethical considerations will also be discussed.

1.2 Background

Peri-operative fluid management in paediatric surgical patients is an integral part of any anaesthetic and influences surgical outcome. Inappropriate peri-operative intravenous fluid administration may lead to significant morbidity and mortality (1). There is no consensus on clinical practice for peri-operative fluid administration in children, largely accounted for by the lack of comparative paediatric research (2). A meta-analysis has shown that the use of protocols for peri-operative haemodynamic support improves patient outcomes (3). There are no guidelines available at the Department of Anaesthesiology at the University of the Witwatersrand (Wits) concerning paediatric peri-operative fluid administration and thus practice may vary amongst individuals.

The goal of intravascular fluid therapy is to maintain intravascular volume, electrolyte balance, cardiac output and ultimately achieve adequate tissue perfusion and meet basal metabolic requirements (2). The most common form of fluid replacement currently used intra-operatively takes into account replacement of preoperative losses, maintenance and replacement of intra-operative losses (4). Fixed volume replacement such as the Holiday and Segar (6) (4:2:1) formula are used to calculate maintenance for hospitalised paediatric patients. Lindahl et al and Holiday et al (5, 6) have since shown that anaesthetised patients have lower

metabolic requirements and generally less peri-operative losses than previously thought and as a result will require 50% less fluid than that originally calculated by the 4:2:1 approach (5). It has also been demonstrated in adult studies that protocol-based fluid restriction reduced the incidence of peri-operative complications but this has not been proven in any paediatric studies (7).

Fluid deficits that occur peri-operatively are influenced by sensible losses, insensible losses and on the duration of starvation period prior to surgery. The new starvation guidelines allow for clear fluid intake up to 2 hours before induction of anaesthesia. Breast milk may be taken up to four hours before surgery and six hours of fasting is required after formula milk and light meals (8). If the new starvation guidelines are adhered to, intravascular volume will be near normal at the time of surgical induction. The replacement of the losses during this period is not necessary unless fasting is prolonged (2, 8). If the starvation period is longer than required, the hydration status of the patient should be assessed and fluid replaced accordingly and plasma glucose should also be checked.

Glucose monitoring peri-operatively is important as hypoglycaemia may go undetected under anaesthesia. Paediatric patients have a physiological predisposition to hypoglycaemia. Therefore, intra-operative administration of either 1- 2.5% dextrose in a balanced solution or using a glucose free balanced solution is accepted practice provided meticulous glucose monitoring is done intra-operatively (9).

Intra-operative losses include sensible losses, insensible losses, blood loss and fluid shifts. Fluid shift is the movement of fluid between the different physiological fluid compartments, this previously included “third space” losses. Literature regarding adult patients has concluded that the “third space” does not exist and should no longer be considered when replacing intra-operative losses (10). Sensible and insensible losses have now been proven to be less than previously thought and may lead to excessive fluid administration if replaced (11).

Excess fluid may damage the glycocalyx and cause gastrointestinal oedema, coagulation abnormalities and fluid overload (12). These detrimental effects

where shown by Lowell et al (13). They showed that 40% of post-surgical adult patients admitted to the Intensive Care Unit (ICU) had a 10% increase in body weight that was attributed to intra-operative fluid administration and this contributed to a worse outcome.

Some adult studies have shown that restrictive fluid administration is safer than liberal fluid administration (14). A protocol-based fluid restriction strategy reduces the incidence of peri-operative complications such as cardiopulmonary events and paralytic ileus. It also improves wound healing and anastomotic integrity, all of which leads to a reduced length of hospital stay (7). However, patients in whom fluids are excessively restricted are at risk of hypovolaemia which may lead to poor tissue perfusion, post-operative nausea and vomiting, decreased cardiac output and multi organ dysfunction (12). Conversely, the FEAST trial which was based on septic paediatric patients showed that fluid boluses resulted in a worse outcome when compared to those who received no fluid boluses (15). There are some criticisms of the FEAST trial, one of which is that the severely hypotensive children were immediately allocated to the group receiving fluid boluses, which suggests that this group of patients had a poorer prognosis from the onset and this may have contributed to a biased result. However, it is not only the volume, but also the type of fluid that one chooses to administer peri-operatively that will have an impact on outcome.

A survey published in the British Journal of Anaesthesia in 2006 by Way et al (16) found that a large number of anaesthetists working in the United Kingdom (UK) still used inappropriate practices of intravenous fluid administration in the paediatric population. There were more than 50 cases reported of serious morbidity or mortality in previously healthy children associated with post-operative hyponatraemia after administration of unsuitable hypotonic intravenous fluid during major and minor surgeries. Many studies now suggest that an isotonic balanced solution should be used peri-operatively and these come in the form of crystalloids and colloids (16).

There has been much debate in recent literature as to whether colloids are more harmful than crystalloids. A systematic review from 2012 revealed that there is no

statistically significant evidence that colloids reduce mortality when compared to crystalloids (17). Published adult studies, including the CHEST trial (17), have indicated that 90 day mortality is not significantly affected by the type of fluid used but renal replacement therapy was increased with the use of HES's. The results of that study were contradicted by the 6s trial (18) which showed a higher mortality rate at 90 days with the use of HES's and the CRYSTAL (18) study which showed improved survival with the use of colloids at 90 days (17, 18). The limitations when comparing these studies is that the study design of all these trials differ and were only conducted on adult ICU patients. There are many physiological differences between adults and children and extrapolation of this data to paediatric fluid replacement needs to be carefully considered.

Due to the lack of consensus in the literature and limited paediatric data regarding peri-operative fluid management, consideration needs to be given to whether departmental guidelines should be implemented. A good starting point is to audit the practices of current practitioners and see whether there is a need to implement a framework for safe practice. Audits asses variation in practice and influence implementation and changes of guidelines (19). Guideline driven practice is effective in changing patient outcome and standardising patient care.

1.3 Problem statement

Fluid replacement and maintenance intra-operatively is a large contributor to post-operative morbidity and mortality. Inappropriate administration of intravenous fluids by the anaesthetist may cause peri-operative complications and lengthen hospital stay. It is imperative that meticulous care is taken in assessing paediatric fluid needs and replacing fluids correctly to avoid adverse outcomes related to intra-operative fluid management.

Guidelines in the UK for paediatric fluid administration have changed from using a hypotonic solution of 0.18% normal saline and 4% dextrose to the more isotonic balanced solutions such as Ringer's lactate due to the incidence of hyponatraemia. Fixed formula replacement is still being widely used. It is unknown

what peri-operative fluid practices are undertaken at Wits as there is no departmental guideline available for the management of paediatric fluids intra-operatively.

1.4 Aim and Objectives

1.4.1 Aim

The aim of this study was to determine the practice of intra-operative paediatric fluid management amongst anaesthetists working in the Department of Anaesthesiology at Wits.

1.4.2 Objectives

The primary objectives of this study were as follows:

- To describe the approach to intra-operative fluid management in haemodynamically stable paediatric patients
- To describe the approach to intra-operative fluid management of haemodynamically unstable paediatric patients
- To describe the demographic factors influencing paediatric fluid management
- To describe the use of dextrose intra-operatively

The secondary objective was:

- To describe awareness of intra-operative paediatric fluid guidelines

1.5 Research definitions

Anaesthetist: A qualified doctor working in the Department of Anaesthesiology

Junior registrar: A medical doctor that has been part of the post graduate training program in anaesthesiology for 1-2 years

Senior registrar: A medical doctor that has been part of a post graduate training program in anaesthesiology for 3-5 years

Medical officer: A doctor working as an anaesthetist for less than 10 years under the supervision of a specialist but not part of a registrar training program

Career medical officer: A medical officer practicing anaesthesiology for more than 10 years but for the purpose of this study will be considered as medical officer's

Consultant: An anaesthetist registered with the Health Professions Council of South Africa (HPCSA) as a specialist

Paediatric population: A child between the ages of one month to eighteen years

Protocol: A systematic approach to a course of medical treatment

Guideline: A recommendation to a course of medical treatment

1.6 Ethical considerations

Approval to conduct the study was obtained from the Human Research Ethics Committee (Medical) and the Postgraduate Committee at Wits (Appendix 1). The study was conducted according to the principles of the Declaration of Helsinki (28) and the South African Guidelines for Good Clinical Practice (29). Participation was

completely voluntary and consent was implied by completion of the questionnaire. Consent to using parts of the questionnaire that was published by Way et al (16) had been obtained and granted by the original author of the survey (Appendix 5).

1.7 Research Methodology

1.7.1 Study design

The study was a descriptive cross-sectional practice-based study using an anonymous self-administered questionnaire (Appendix 4).

1.7.2 Demarcation of study field

The study was conducted in the Department of Anaesthesiology at Wits, Johannesburg, South Africa. All anaesthetists working at the Department of Anaesthesiology at Wits were invited to participate in the study.

1.7.3 Study sample

The study population consisted of all anaesthetists working in the Department of Anaesthesiology at Wits. This consisted of 214 anaesthetists, of these, 10 attended the postgraduate meeting and were ineligible to fill out the questionnaire. Another 2 consultants reviewed the questionnaire during its development and were also excluded from participating in the survey. Thus 202 anaesthetists were available to be surveyed.

1.7.4 Sampling method

In this study a convenience sampling method was used.

1.7.5 Inclusion and exclusion criteria

Inclusion and exclusion criteria were set.

1.7.6 Development of questionnaire

A questionnaire was developed for data collection. The questionnaire consisted of three sections of questions as well as vignettes. A similar survey was conducted in the UK by Way et al. (16) and some of the questionnaire (Appendix 4) was developed from that original survey and written permission was granted by the authors to use content from the original survey and adapt the questions to the types of fluids available in South Africa (Appendix 5). Further questions were developed based on the literature available on the topic thereby ensuring content validity.

1.7.7 Data collection process

Questionnaires were numbered in order to keep track of the number of distributed questionnaires, these were then distributed at random and not according to the numerical system to ensure the participants did not feel that they could be identified. Data was collected at the departmental academic meetings. The chairperson was approached for permission to address the meeting. The researcher was present to explain the aim of the study and invite participation. An information sheet (Appendix 3) explaining the purpose of the study was attached to the questionnaire. The researcher was present throughout the filling out of the questionnaires to address any queries. Participants had the option of not filling out the questionnaire. The blank questionnaires were tallied to determine response rate but were not included in the study.

1.7.8 Data analysis

Data was entered on a REDCap (Research Electronic Data Capture) database and then transferred to a Microsoft Excel® spread-sheet and analysed. Descriptive statistics were used. Categorical data was summarised using frequencies and percentages. Data was assessed to ascertain whether demographic differences

influenced practice. Wilcoxon Mann Whitney U test, Chi^2 and Fishers exact tests were used for that purpose. A p value of <0.05 was viewed as significant.

1.8 Significance of the study

Studies have shown that some post-operative morbidity and mortality can be attributed to the anaesthetist's choice of fluid and the amount administered intra-operatively (7). A study published in 2006 by Way et al (16) confirmed that 60.1% of anaesthetists practicing in two training areas in the UK were still administering inappropriate fluids to paediatric patients (16). It is currently unknown whether safe and knowledgeable practice is being followed by individual anaesthetists at Wits. The outcome of this study may determine the need for departmental guidelines for intra-operative paediatric fluid management.

1.9 Validity and reliability of the study

Various methods were used to ensure validity and reliability, these included:

- Using parts of a questionnaire that has been administered and published in the UK
- Face value was maintained by having four specialist consultants both in state and private practice critique the questionnaire
- Content validity of the questionnaire was insured by a thorough literature review and scrutiny by senior qualified anaesthetists
- Having the researcher available for queries during completion of the questionnaire
- Maintaining anonymity and a neutral non-coercing environment
- Checking every tenth data entry point for accuracy
- Statistical analysis done with a biostatistician

1.10 Research report outline

This research report will have the following outline:

Chapter 1: Overview of the study
Chapter 2: Literature review
Chapter 3: Methodology
Chapter 4: Results and discussion
Chapter 5: Summary, limitations, recommendations and conclusion

1.11 Summary

This chapter gave an outline of the study background, aims and objectives, the problem statement and significance of the study, ethical considerations, demarcation of the study sample, the methodology and summarised the outline of this research report**.**

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

Peri-operative fluid management in surgical patients has been the focus of considerable debate. This is an integral part of any anaesthetic and influences surgical outcome. Inappropriate peri-operative intravenous fluid administration may lead to significant morbidity and mortality (1, 30). There is no consensus on clinical practice largely accounted for by the lack of comparative paediatric research (2, 31, 32). There are also no guidelines available at the Department of Anaesthesiology at Wits concerning paediatric peri-operative fluid administration. This section will review the literature pertaining to intra-operative fluid administration.

2.2 Background

A Survey published in the British Journal of Anaesthesia by Way et al (16) found that a large number of anaesthetists working in the UK still used inappropriate practices of intravenous fluid administration in the paediatric population. There were more than 50 case reports of serious morbidity or mortality in previously healthy children associated with hyponatraemia after peri-operative administration of hypotonic intravenous fluid (16). Both type and volume of fluid are important considerations when fluid prescription is undertaken. Way et al (16) showed that despite new awareness promoting isotonic solutions for maintenance, 60.1% of anaesthetists still administered hypotonic intravenous fluid intra-operatively and 75.2% did so post-operatively. As much as 11.1% of respondents in that study would also use a hypotonic solution to treat intra-operative hypovolaemia. Way et al (16) also showed that the volume administered for maintenance was calculated using the Holiday and Segar (6) formula by 81.8% of the participants and 67.7% of anaesthetists surveyed had no departmental guidelines to follow.

Due to the lack of comparative paediatric trials, guidelines are based on physiological knowledge, expert opinion and extrapolation from the adult

literature (32). Extrapolation from adult literature may not be appropriate due to the anatomical and physiological differences between the adult and paediatric population. Children have proportionately larger body surface areas and volumes of total body water that change with age, they also have higher metabolic rates, respiratory rates and heart rates with immature central temperature regulation and thus they lose heat and fluid much quicker than adults. In the infant kidney, the nephron is only fully functional at the age of 6 months and this affects sodium load handling in these younger children. Infants also have an increased parasympathetic tone and metabolic rate. These key differences may cause them to respond to intravenous fluids differently to adults (32). For these reasons it may be beneficial to have a guideline for paediatric fluid practice.

A Survey published in 2011 suggested that better standardization of intra-operative fluid practice may lead to better outcomes (106). A survey done by Cannesson et al. (106) compared fluid practices amongst the members of the American Society of Anaesthesiologists (ASA) and European Society of Anaesthesiology (ESA) (106). The survey concluded that standardised fluid therapy is not widely practiced and only 6% of the ASA respondents had a departmental protocol (3). Similar findings were described by Way et al (16) where 67.6% of their UK respondents had no departmental protocol for fluid administration in children.

In the absence of local guidelines, the Association of Paediatric Anaesthesia (APA) of Great Britain and Ireland consensus guidelines on peri-operative fluid management in children v1.1 (26), which was last reviewed in 2010, was used as a guide for correct practice along with more recent literature on the topic. Another guideline that will be referred to was published in 2006 and revised in 2016 by the Scientific Working Group for Paediatric Anaesthesia of the German Society for Anaesthesiology and Intensive Care Medicine (AWMF) (30).

2.3 Physiology of fluid and fluid compartments in the human body

The different body compartments contain different proportions of fluid; these compartments are described as intracellular and extracellular. The extracellular compartment is further divided into the intravascular (plasma) and extravascular compartments. The extravascular compartment is also composed of a “functional” interstitial space and the “non-functional” transcellular space which includes gastrointestinal fluid, ocular fluid and cerebrospinal fluid (7). Two thirds of the body’s fluid volume is contained intracellularly and one third is found in the extracellular space. Of the extracellular fluid, about two thirds is interstitial and the rest consists of plasma and transcellular fluid (Figure1) (7). Fluid shifts between all these compartments influence the fluid balance of paediatric patients. This balance is also dependent on cellular integrity, as it is this integrity that separates the different compartments (7, 33).

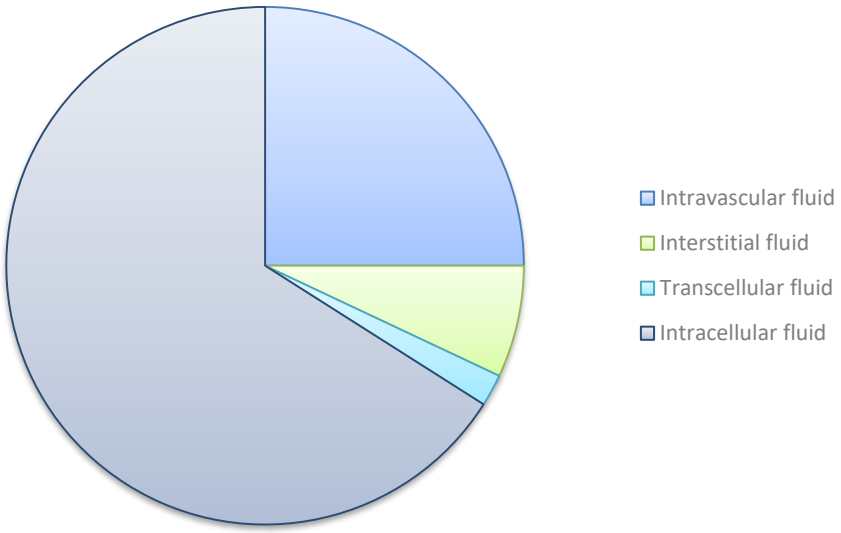

Figure 1. Body fluid compartments. (7)

The vascular barrier was described in 1896 by Ernest Starling (7, 33). His model describes the intravascular space as having a high hydrostatic pressure and a high apposing oncotic pressure, whereas the extravascular space has a low hydrostatic and oncotic pressure. Movement of fluid, as described by Ernest Starling, across a capillary is determined by Starling’s law as shown below (7,34):

$Q = k\ A\ [(Pc - Pi) - \sigma' (\pi c - \pi i)]$ (34)

Q = Net flow of fluid
k = Hydraulic conductivity coefficient (Index of pore size)
A = Area of the membrane concerned
Pc = Capillary hydrostatic pressure
Pi = Interstitial hydrostatic pressure
σ' = Protein reflectance coefficient
πc = Capillary oncotic pressure
πi = Interstitial oncotic pressure

These forces result in a small net loss of fluid into the interstitial space that is returned to the vasculature by the lymphatic system (7). If this theory is applied, over hydration with a crystalloid should in time be corrected by the lymphatic system, however, this does not always occur. It is now recognised that inflammation and damage caused to the vascular barrier will increase the amount of fluid escaping the vascular compartment.

Studies have shown that Starlings equation is not physiologically applicable and that an additional barrier, called the glycocalyx, exists between the lumen of the vessel and the endothelium. The glycocalyx contains glycoproteins, glycosaminoglycans and proteoglycans and these form a negatively charged surface to enhance the endothelial barrier (7,35-36). The oncotic pressure gradient is now believed to be between the plasma and the subglycocalyx and not the interstitial space as described by Starling. Disruption of this layer may cause local hypercoagulability, reduced vascular responsiveness and loss of fluids and protein from the intravascular space resulting in tissue oedema (7, 36). It has also been suggested that colloids may cause degradation of the glycocalyx and that preoperative fluid loading with hydroxyethyl starches (HES) may not be as beneficial as previously thought (37). Chappell et al (37) reported that hypervolaemia caused by HES causes a rise in atrial natriuretic peptide which is thought to be implicated in glycocalyx destruction (37). The anaesthetist has significant influence over preservation of this barrier by avoiding ischaemia,

hypervolaemia and hyperglycaemia (36). All these factors may be influenced by appropriate fluid practices.

2.4 Fluid Management

2.4.1 Fluid Replacement and maintenance

The goal of fluid therapy is to maintain intravascular volume, electrolyte balance, and cardiac output and ultimately achieve adequate tissue perfusion. Intra-operative fluid administration also needs to meet the basal metabolic requirements (2). The most common form of fluid replacement currently used intra-operatively considers replacement of preoperative losses, maintenance and replacement of intra-operative losses which includes blood loss (4, 38).

There are different methods of determining the volumes required for maintenance in children. One method is using body surface area and extrapolations from nomograms to determine fluid volumes required, however this carries with it the tediousness of measuring weight and height as well as a reported 15% error rate yielding unreliable results (39). Using caloric requirements or weights are the more common methods used in clinical practice. For many years the Holiday and Segar (4:2:1) formula was used to calculate maintenance fluids in children. They suggested a hypotonic solution should be administered by calculating a patients hourly fluid requirement according to their weight (2). Holiday and Segar (6) measured the caloric requirements to sustain basal metabolic rates in paediatric hospitalised patients. They devised that 100kcal per kg is required for the first 10kg of body weight, 50kcal/kg for the next 10kg of body weight and 20kcal/kg for every kg above 20kg of body weight is required to support caloric requirements per day (40, 41). This formula is also known as the 4:2:1 rule where fluid volume is calculated as follows: 4ml/kg is administered for the first 10kg of body weight, 2ml/kg for the next 10kg and 1ml/kg for every kg of body weight thereafter to calculate hourly fluid maintenance requirements (40).

Fixed volume replacement such as the Holiday and Segar formula are used to guide maintenance in many guidelines, more recently however Lindahl et al (5) as well as Holiday et al (6) showed that using this formula for anaesthetized paediatric patients overestimated the energy expenditure and thus electrolyte and fluid requirements by as much as 50%. Also, anti-diuretic hormone (ADH) secretion is increased peri-operatively as a result of the surgical stress response, reducing urinary losses and evaporative losses during anaesthesia when using a closed humidified breathing system, giving even further reasons to reduce the amount of maintenance fluid previously recommended (42, 43). In a resting state 80% of the bodies needs are driven by the heart, liver, kidneys and brain and these organs only contribute 7% to total body mass, thus using total body weight may contribute to inaccurate fluid estimation (43).

A large proportion of the caloric needs estimated by Holiday and Segar also took into account the need for growth, which in an anaesthetised child, is unnecessary to consider (43). It has since been accepted that anaesthetised paediatric patients will generally require 50% less fluid than that calculated by Holiday and Segar (5, 43-45) and thus the adoption of the 2:1:0.5 rule. However, the APAGBI guideline still refers to the 4:2:1 rule to calculate maintenance and suggest using a balanced isotonic solution. The AWMF guidelines recommend an infusion of 10ml/kg/hr of a 1-2,5% solution of dextrose in a balanced crystalloid for intra-operative maintenance and this is justified by taking into account both pre-operative and post-operative losses. The APAGBI and AWMF guidelines recommended that these rates should be adjusted according to the individual patient's intra-operative needs (26, 30). Fluid requirements will change according to peri-operative losses, surgical losses and fasting time and thus one formula cannot be applied universally but should be adjusted continuously according to one's clinical assessment of the patient.

2.4.2 Fluids and fasting

The primary reason for pre-operative fasting is to reduce the risk of aspiration. The risk of aspiration in the paediatric population is 0.0001-0.001% and most patients

suffering from aspiration have a predisposing factor such as gastro-oesophageal reflux or impaired coughing reflex (46, 47). The amount of deficit that occurs from the fasting period can be debated. A review of 25 studies showed that there is no benefit in fasting clear fluids for more than 2 hours pre-operatively. The children that were fasted for longer than 2 hours did not have lower gastric volumes or higher gastric Ph values (48). In 1999 the ASA published new acceptable starvation periods. Minimum fasting periods vary with food consistency. Six hours of starvation is required after intake of nonhuman milk, formula milk and light meals. Four hours of fasting is required after breast milk and 2 hours after the intake of a clear liquid (49, 50). These guidelines are aimed to reduce the risk of peri-operative hypovolaemia, hypotension and hypoglycaemia whilst reducing pre-operative irritability in children and the risk of regurgitation and aspiration of gastric content.

During the fasting period both sensible and insensible losses are not being replaced and thus may need to be replaced intravenously during the peri-operative period to compensate for any fluid deficits. Fluid deficits are calculated by multiplying the child's hourly requirements by the number of hours fasted. Berry et al (51) described that replacement of this deficit should be over the first 3 hours of anaesthesia, giving 50% over the first hour and the other 50% over the next 2 hours . Current evidence shows that replacing the fluid deficit incurred during the starvation period to be unnecessary unless this period is prolonged (11). This is largely due to the belief that the losses during this period are much less than previously thought and in fact a healthy patient should be normovolaemic after an overnight fast (11, 43). Jacob et al (11) showed that even a prolonged pre-operative fast of 10 hours in healthy adult patients resulted in normovolaemia at induction of anaesthesia (11). However, this period should always be kept to a minimum to avoid dehydration and ketogenesis, particularly in children (30).

Whether this data can be extrapolated to the paediatric population is questionable as hypotension has been found to be significant in infants presenting for anaesthesia that have been starved for more than 8 hours (52). Thus, we conclude that the duration of fasting may influence intravascular volume in children and will need to be considered when prescribing intra-operative fluids. There is no

data that determines exactly how much intravascular deficit occurs after a starvation period and it probably varies significantly between patients.

2.4.3 The “third space”

Historically, the “third space’ was thought to be a compartment where fluid could accumulate, and thus it formed part of fluid replacement strategies. It was believed to be functionally separate to the extracellular space and accounted for the unexplained peri-operative fluid shifts. Using tracer techniques fluid shifts have been quantified and what was previously believed to be the third space could not be identified (10). It is widely accepted that the concept of the “third space” has never been proven and is now considered to not exist and does not need to be included as a separate compartment when calculating volume replacement (7, 53).

2.4.4 Detrimental effects of inappropriate fluid administration

Inappropriate fluid replacement may be detrimental to a patient’s outcome. Excess fluid administration may damage the glycocalyx and cause gastrointestinal oedema, coagulation abnormalities and hypervolaemia (12). Lowell et al (13) showed that weight gain in post-operative adult ICU patients correlated positively with mortality. A less than 10% gain in weight corresponded to a mortality of less than 10%. A 10-20% weight gain increased mortality to 32% and a weight gain of more than 20% reflected a mortality of 100% (13). Other studies have also shown poor outcomes associated with a positive fluid balance in ICU patients making it crucial to revisit intra-operative fluid management (54, 55). On the other hand, patients in whom intravenous fluids are excessively restricted are at risk of hypovolaemia leading to poor tissue perfusion, an increased risk of post-operative nausea and vomiting, poor wound healing, decreased cardiac output, shock and multi organ dysfunction (12, 56). Thus, a perfect balance needs to be achieved.

2.5 Fluid resuscitation

2.5.1 The colloids versus crystalloid debate

Chappell et al (7) suggested that the fluid lost from the extravascular space, such as caused by dehydration, should be replaced with a crystalloid because a large proportion of this fluid will redistribute to the interstitial space. On the other hand, volume lost from the intravascular space, such as that caused by haemorrhage, should be replaced with a colloid as this will replenish this space more effectively (7). This theory largely supported the announcement by Twingley and Hillman (57) in 1985 where they explored the distribution of crystalloids throughout the extracellular space and their inability to maintain intravascular volume as effectively as colloids. Historically it was also believed that two to four times more crystalloid volume was required to achieve the same plasma expansion effect as a colloid. This ratio has been shown to be less than this and is now closer to one and a half times the volume of blood lost (58-60). Beyer et al (61) showed that in septic shock, there was no difference in time to reversal of shock between the two fluid types and only a marginally larger volume was required with the crystalloids (60, 61). The crystalloid versus colloid debate has continued since the 1980s and is still to reach a conclusion. However, several recent meta-analyses have shown no mortality benefit with either solution (18, 62, 63).

Colloids have a higher oncotic pressure when compared to crystalloids and as a result stay in the intravascular space for longer and to a greater proportion than a crystalloid fluid that exerts less oncotic pressure. However, the literature is contradictory as to which one is better for resuscitation. A systemic review from 2012 reviewed 78 trials and revealed that there is no statistically significant evidence that colloids reduce mortality when compared to crystalloids (64). The CRISTAL trial investigated 2857 hypovolaemic patients in 57 ICU’s on 3 different continents. The patients enrolled in this trial presented with sepsis and trauma or both but had not received prior fluid resuscitation. The conclusion reached by this study was that there was no significant difference in mortality at 28 days in critically ill patient receiving colloids (synthetic and non-synthetic colloids) compared to those receiving crystalloids (saline or Ringer’s lactate). However, the

90 day survival rate was higher in the colloid group (65). The flaw in this study design was that all colloids were grouped together and analysed as a group rather than assessing each colloid on its own merit.

The 6S study was conducted on 798 severely septic patients that were requiring fluid resuscitation in ICU, however many patients were already resuscitated prior to their ICU admission and trial enrollment. This trial compared Ringer's acetate to 6% HES 130/0.42 and found that the HES group would require more renal replacement therapy (RRT) and blood products and that mortality at 90 days was increased when using HES (66). The criticism of this trial was that some patients received more than the maximum dose of fluid allowed by the study design and these patients were not excluded from data analysis. The criteria used to initiate RRT were also not defined in this study which may have led to bias. Comparatively, the CHEST trial studied 7000 ICU patients requiring fluid resuscitation and compared 6% HES to 0.9% saline to determine whether there was a difference in 90 day mortality and to assess the incidence of renal injury and failure. This study, asserts no significant difference in mortality at 90 days but an increased incidence of renal dysfunction in the saline group and an increased requirement for RRT in the HES group (17). However, one of the criticisms of this trial is that patients who had received fluid resuscitation with crystalloids or HES before admission to ICU were not excluded from the study and patients were entered into the study only after being volume resuscitated. The adult SAFE trial enrolled 6997 patients who needed fluid resuscitation in ICU and compared 4% albumin to 0.9% normal saline. This trial also concluded that there was no benefit of one fluid over another in mortality outcomes in ICU at 28 days but in this study the volume of saline administered exceeded that of albumin and may not have been fairly compared (15, 67). Again, these studies are not homogenous in their designs and leave the reader wanting.

All these trials have shortfalls and much criticism and debate has arisen about the conclusions reached by these studies and in the end have left us with no definitive answer when it comes to the colloid versus crystalloid debate. These trials have also been conducted in adults and, once again, their findings may not apply to the paediatric population because of the physiological differences between the two

patient groups. There was one large paediatric study that was done in a resource poor setting on children presenting with sepsis and septic shock in Sub-Saharan Africa. The FEAST study was conducted in African children with severe infections and febrile disease (15). Patients were divided into those who received either 5% albumin boluses, 0.9% saline boluses and those who received no fluid bolus (control group). Only a minority of children presented with severe hypotension and these were immediately assigned to one of the bolus groups which may have influenced the poorer outcome of this group as these patients were significantly more ill than those assigned to the control group. It was established that there was a higher survival rate in the control group and that fluid boluses with either the colloid or crystalloid yielded higher mortality rates. It was found that there was no significant difference in outcome when comparing the two groups that received the different fluid boluses. The FEAST trial (15) has since had much criticism but the one message that one can take away from it is that fluid administration is not innocuous. A study by Chappell et al (37) reported that any cause of hypervolaemia regardless of the fluid used will cause a rise in atrial naturetic peptide and thus cause damage to the glycocalyx and may contribute negatively to morbidity and mortality. This study also supports the implementation of a fluid management strategy to guide appropriate fluid prescription and limit inappropriate fluid bolus administration.

2.5.2 Colloids

There are different types of colloids available and they may be categorised into synthetic colloids such as gelatins and hydroxyethyl starches (HES) and non-synthetic colloids such as albumin and fresh frozen plasma. They each differ in composition and side effect profile. The ideal colloid does not exist, and many possess undesirable characteristics such as tissue accumulation, coagulation abnormalities, disruption of blood cross matching, disease transmission and allergic reactions. Research conducted to assess the effectiveness of different colloids in adult patients has been done to help guide correct fluid choices but has also found to be contradictory and confusing at best with no definitive conclusion on which fluid choice is best in each situation (65-70). Furthermore, a review by

Bunn et al (68) in 2003 showed there to be no difference in effectiveness or safety between the different synthetic and non -synthetic colloids.

HESs are described by their concentration (6% or 10%), molecular weights (70kDa, 200kDa and 450kDa), molar substitutions and their C2/C6 ratio. The concentration describes the volume effect that the colloid will have, with 6% being iso-oncotic in plasma which means that the administration of 1 liter would be required to replace 1 liter of intravascular losses whereas the 10% solution has a much greater volume effect. The molecular weight of a HES represents an average of the mass of all the different sized molecules within the solution. Unlike albumin, HESs are polydisperse systems and the molecular weight will determine how easily the kidneys can excrete the particle. The smaller the molecular weight (below 60kDa) the faster it is cleared by the kidneys and once this happens the osmotic effect of the colloid is lost (69). The larger particles in the solution need to undergo degradation before excretion. The molar substitution represents how easily these particles can be degraded and is determined by the addition of the hydroxyethel groups to the original structure. The lower the substitution (0.45-0.58) the easier they are to break down whereas the higher substitutions (0.62-0.70) are more resistant to degradation and are retained for longer in the intravascular space and as a result retain their volume affect for much longer. It is these HES with high molar substitutions that tend to deposit in tissues and contribute to liver and renal dysfunction (70).

The C2/C6 ratio describes the position at which the hydroxyethyl substitution has occurred on the molecule. Those on C2 are more resistant to enzymatic degradation than those on C6, thus the particles with higher C2/C6 ratios will survive for much longer in vivo. Coagulopathy has been reported with all colloids but HES's are the main culprits. HES's have also been shown to be the only colloid to cause pruritis. Due to all these adverse effects, many institutions do not consider HES's to be their first choice for paediatric patients especially those that are critically ill or have renal injury (32, 70). However, in 2008, HES's 130/0.4 were studied in paediatric surgical patients that were under the age of 2 years and having non cardiac surgery. The researches in this study enrolled 81 patients at multiple centers in France that presented for elective surgery and administered

16ml/kg of either albumin or HES. HES's were shown to be as safe as albumin in this trial (71).There is still no consensus in the medical fraternity as to which colloid is best suited to the paediatric patient but If HES's are to be used it is advised to not exceed the maximum dose of 30ml/kg (72, 73).

Gelatins are large molecular weight proteins formed by hydrolysis of collagen. There are three types that are available; succinylated, urea cross-linked and oxypolygelatins (69). These have the smallest molecular weights when compared to other synthetic colloids and plasma expansion will not directly reflect the volume infused because of its metabolism, excretion and translocation into the interstitial space. Apart from being allergenic and causing some increase in bleeding, gelatins are considered to have few other side effects and are considered by some to be the preferred synthetic colloid to use in the paediatric population (32).

Albumin has been the most widely used and studied colloid in paediatric patients (70). It has one polypeptide chain that weighs 90kDa. Its ability to plasma expand depends on how quickly this amino acid gets degraded. The 4% solution causes an 80% plasma expansion whereas the hyperoncotic 20% solution will have a much greater volume expansion affect reaching 400% (69). In a systemic review done by Narron et al (70) the conclusion was drawn that albumin was the safest colloid causing the least adverse events, however cost limits its widespread use. Fresh frozen plasma, a hypertonic colloid, was found to be the least safe colloid to administer. Its use is associated with an increased risk of infection, transfusion reactions, acute lung injury, anaphylaxis and hypernatraemia and thus it is not recommended for the sole purpose of volume expansion (32). Dextrans are polysaccharides produced by bacterial enzyme dextran sucrose. The 6% solution has an average molecular weight of 70kDa and the 10% solution has molecules weighting 40kDa and thus the latter has a lower volume expansion affect (69). These colloids are mainly used for improvement in microcirculatory flow and not for fluid resuscitation per se and therefore will not be discussed further in this dissertation (69).

Gelofusin reportedly causes more allergic reactions when compared to other synthetic colloids, however, this has not been studied in paediatric patients (112).

Gelofusin seems to be a safe synthetic colloid to consider in paediatric patients due to its minimal side effect profile. Both HES and gelofusin may alter blood coagulation but with moderate doses (10-20ml/kg) this side effect appears to be uncommon (30). In studies conducted in cardiac paediatric patients requiring more than 20ml/kg of HES, no renal failure or increased blood loss was recorded and thus third generation HES are the preferred synthetic colloid to be used in paediatric patients according to the AWMF (113). As one can deduct from this discussion, there is little consensus amongst authors about which fluid is best for resuscitation. One must bear in mind that each fluid has an indication, dose and side effects and these should always be considered.

2.5.3 Crystalloids

The type of crystalloid used also has an impact on patient outcome. It is acknowledged that the incorrect intra-operative fluid used by anaesthetists may contribute to hyponatraemia, hyperglycaemia, acid base disturbances, coagulation disturbances and thus morbidity and mortality (69). An ideal crystalloid needs to have certain desirable characteristics: the fluid should not accumulate in tissue, should not alter electrolyte or acid base status, should not affect coagulation and should be affordable with a long shelf life. Unfortunately, just as with the colloids, no such ideal fluid is currently available. Being cognisant of the individual characteristics such as electrolyte content, tonicity and osmolarity of fluids is what should currently guide clinical practice and is vital in making the correct choice for a particular circumstance (69).

Tonicity refers to the molecules in a solution that exert an osmotic force across a membrane. A fluid can be described as hypotonic, isotonic or hypertonic and these terms describe the direction in which water would tend to travel if separated from another solution by a permeable membrane. In contrast osmolarity describes a characteristic of a single solution, and it is the number of osmoles (osmotically active particles) per liter of a solution, this includes those molecules that do not cross a membrane and hence exert an osmotic gradient as well as those molecules that cross a membrane freely (43). Fluids that are hypotonic will

redistribute between the intracellular and extracellular space accordingly. The electrolyte free portion will enter the cells and the rest will proportionately distribute between the intravascular, interstitial and transcellular space. Hypotonic solutions such as those used in the UK (0.18% Saline with 4% dextrose) are prone to cause hyponatraemia because of their excessive free water distribution. This is also seen with infusions of 5% dextrose water and therefore these solutions are not recommended for intravascular volume expansion (16, 43). Neville et al also found that the type and not necessarily the amount of fluid administered influenced peri-operative hyponatraemia (74).

Hyponatraemia may affect patient outcome. Way et al (16) reported more than 50 cases in the UK of serious morbidity or mortality in previously healthy children associated with hyponatraemia after administration of unsuitable intravenous fluid during major and minor surgery (16). In 1957 Holiday et al (5) suggested that a 0.2% saline solution with 5% dextrose was the ideal fluid for in hospital paediatric patients (43). Since then this recipe has been critiqued for causing iatrogenic hyponatraemia. Foster et al (45) along with many other authors concluded that hypotonic fluids in paediatric patients increase the risk of hyponatraemia and should not be used routinely for maintenance (45, 75). It is now accepted that an isotonic solution should be used for maintenance (16, 76, 77). The RCPCH in Great Britain had published their concerns with the use of hypotonic solutions in 2003 following several cases of death or adverse outcomes in children from iatrogenic hyponatraemia (26). Composition of commonly available fluid types is shown in Table 1.

Table 1. Comparison of fluid composition (74-76)

	Balsol/ Plasmalyte B	Ringer's lactate	5% Maintelyte (paediaric maintelyte)	Half Darrows dextrose	Normal saline
PH	7.4	6.0	4.0	5	5.5
Na+	130	131	35	60	154
K+	4	5.0	12	17	
Ca2+		1.8			
Mg2+	1.5		2.5		
Cl-	110	112	47	51	154
Lactate		29			
Acetate	23			26	
Glucose			55g/l	50g/l	
Osmolarity	294	273	372	434	308

Another important characteristic that has shown benefits when administering fluids is the electrolyte content of a solution. A balanced crystalloid solution is a solution that "mimics the ionic make-up of the aqueous fraction of blood" and this includes the electrolyte content and the ph (77). This type of solution has been shown to cause less renal injury, electrolyte disturbances and less adverse effects on coagulation and post-operative infections as well as less damage to the glycocalyx (77).

A 0.9% saline solution (non-balanced solution) has potential unwanted adverse effects, some of these include hyperchloraemic metabolic acidosis, hyperkalaemia due to cellular shifts, kidney injury, damage to the endothelial vessel layer and deleterious effects on inflammation and coagulation (76). A balanced solution such as Ringer's lactate however is not without side effects. The lactate gets metabolised in the liver to glucose and this needs to be considered when treating diabetic patients. Acetate, as found in balsol solutions, seems to be a better additive as it is metabolised by various tissues to bicarbonate and has been shown

to stabilize ph faster than lactate, however, it may cause vasodilatation and cardiac depression (76-78).

Fluids that are hypotonic (5% maintelyte and half Darrows dextrose) will redistribute between the intracellular and extracellular space accordingly. The electrolyte free portion will enter the cells and the rest will proportionately distribute between the intravascular, interstitial and transcellular space and thus have little effect on volume expansion because of their free water distribution. Therefore, these hypotonic, unbalanced solutions should be discouraged from being used peri-operatively. A balanced solution is one with appropriate amounts of electrolytes (76). An isotonic and balanced solution has been shown to cause less renal injury, electrolyte disturbances, coagulation abnormalities and is associated with less post-operative infections. There is also less damage to the glycocalyx reducing the amount of extravasation and tissue oedema (77). For these reasons a balanced isotonic solution should always be used peri-operatively.

A balanced salt solution should replace 0.9% normal saline as the fluid of choice for maintenance and resuscitation (78). Santi et al (76) discussed this in the paediatric population and drew the same conclusion that a “balanced salt crystalloids, although more expensive, should be preferred for volume resuscitation and maintenance of fluids in the peri-operative period.” The authors conclude that fluids should be treated like any other drug that is prescribed to a child and thus the correct dose containing the right amount of electrolytes should be given at an appropriate rate. Side effects of fluid administration should also be continuously assessed.

2.6 Glucose management

Part of intra-operative care is ensuring adequate glucose control as this also contributes to the integrity of the glycocalyx. Anaesthesia lowers the metabolic rate and in turn glucose requirements. Surgery increases the stress response and with it comes an increase in glucose levels due to neurohormonal changes that occur by release of glucagon, growth hormone, catecholamines, interleukin 1, interleukin

6 and tumour necrosis factor alpha that increase glycolysis and gluconeogenesis (79). Finding a balance between these two dynamics as well as the deficit that comes with starvation makes intra-operative glucose control complex.

It is possible to manage most small paediatric surgical cases without having to add dextrose into the intravenous solutions, however there are certain patients that are at increased risk of hypoglycaemia such as those that are starved for prolonged periods, malnourished children, children receiving parenteral nutrition and children undergoing surgeries that continue for long periods of time (>3hrs) (80-82). The pre-prepared glucose containing solutions that are available have low sodium contents and once the glucose is metabolised, the remaining solution becomes hypotonic and may further increase the risk of causing hyponatraemia (81). Hyponatraemia may lead to cerebral oedema, respiratory depression and death. A retrospective review of 24 412 medical records by Arieff et al (83) found that the rate of iatrogenic hyponatraemia in previously well surgical patients was 0.34% of which 8.4% resulted in death. The risk of administering unnecessary amounts of glucose containing solutions is that of hyperglycaemia, particularly with a concomitant stress response that occurs with surgery. Hyperglycaemia will cause an osmotic diuresis which may contribute to increased fluid loss and hypovolaemia (84).

In the 1900's Karelitz and Schick (84) described that children "fall into a restful sleep" by adding glucose to an intravenous infusion. For a few decades it became common practice to routinely administer dextrose to paediatric patients intra-operatively, until it was recognised that hyperglycaemia in the peri-operative period increased morbidity and mortality (85). Hanazkli et al (86) believed that a post-surgical blood glucose of more than 7,7mmol/l is a risk to surgical site infection and thus influences patient outcome. This sentiment was echoed by Sathya et al (87) who concluded that there was a correlation between blood glucose levels of more than 11,1mmol/l and infection risks (86, 88).

A study conducted in Malaysia aimed to investigate the risk of hyperglycaemia in children peri-operatively having received only Ringers lactate versus those receiving 5% dextrose in Ringer's lactate. This study found that children receiving

5% dextrose in Ringer's lactate were more likely to be hyperglycaemic (>11mmol/l) intra-operatively than those receiving Ringer's lactate alone but this did not extend into the post-operative period (9). Mierzewska-Schmidt (89) found that post-operative hyperglycaemia was detected in 94% of children and hyponatraemia in 36% of children receiving 5% dextrose water intra-operatively. None of the children who received Ringer's lactate in this study developed hyponatraemia or hyperglycaemia. Consequently, both these studies and others recommend using non-glucose containing fluids for routine maintenance and replacement of intra-operative losses (41, 85, 89). If a dextrose containing solution is chosen then an isotonic balanced solution with 1-2.5% of glucose is recommended as a safe infusion for maintenance fluid intra-operatively (4, 90).Whether a glucose free solution or a glucose containing solution is chosen for intra-operative maintenance, monitoring of blood glucose is required in order to ensure that normoglycaemia is maintained (91-93).

Hypoglycaemia may cause permanent neurodevelopmental damage and has been linked to poor patient outcome in the intensive care setting and increases the risk of mortality (94). Burns et al (95) conducted a study in 2008 in London where magnetic resonance imaging was used to prove that cerebral damage occurs in hypoglycaemic neonates. This study found that 94% of hypoglycaemic neonates had white matter changes and this later manifested as developmental impairments on follow up (95). Routinely administering either a 1- 2.5% dextrose in a balanced solution or using a glucose free balanced solution is acceptable (91-93, 96). In surgeries that are under an hour and appropriate starvation periods were adhered to no background infusion of glucose is necessary (30). Currently there is no consensus in clinical practice as to whether it is necessary to replace glucose routinely in paediatric surgical patients. The only way to ensure normoglycaemia is through testing blood glucose levels and treating the patient accordingly.

The preoperative fasting period may influence the need for glucose supplementation. There is conflicting evidence in the literature about intra-operative glucose administration according to starvation periods. Thomas et al (97) found that children under the age of 4 that were fasted for more than 6 hours may become hypoglycaemic and irritable. The same result was not demonstrated

by Nilsson et al (93) who studied children between the ages of 2 weeks and 22 months and discovered that there was no correlation between hypoglycaemia and time of preoperative starvation. The new starvation guidelines safely minimise the starvation period prei-operatively. In the South African public hospital setting, the starvation periods are not adhered to for various reasons resulting in our surgical patients being starved far longer than intended. This is due to many factors ranging from incorrect starvation orders prescribed by doctors, to poor execution of starvation guidelines by nursing staff, to unexpected changes in surgical schedules (98).

A study conducted at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) by T. Fitchat (98) found that 30.8% of the paediatric surgical patients had a blood glucose of < 4.1mmol/l on induction of anaesthesia and nearly 10% had a blood glucose level <3.1mmol/l. This study did not mention the starvation periods related to these glucose levels. A follow up study at CMJAH by C. Lee (82) looked at starvation periods and measured blood glucose levels in children who had been given apple juice 2 hours prior to surgery and compared them to a control group that did not receive apple juice. This study showed that paediatric patients presenting for surgery at CMJAH were starved between 5 hours 21 minutes and 21 hours 57 minutes. The mean blood glucose in the two groups was not much different at 4.06mmol/l and 4.26mmol/l respectively, however hypoglycaemia (less than 3.5mmol/l) was significantly reduced in those receiving apple juice. These prolonged starvation times are not unique to South Africa. A study conducted in India found that their surgical patients were being starved an average of 11 hours 25 minutes for solids and 9 hours 25 minutes for liquids (8).

In the UK, starvation periods were found to vary between 3 hours and 12 minutes and 8 hours and 48 minutes in children presenting for surgery (93). It was demonstrated in this study that there was no significant correlation between starvation period and hypoglycaemia, however this was a small sample size (70 patients) and hypoglycaemia was defined as a blood glucose level of less than 2.2mmol/l, which is out of keeping with most definitions. The more widely accepted definition of hypoglycaemia in children is a blood glucose concentration of less than 3.5mmol/l. The starvation periods in this study were also notably different to

those encountered at CMJAH, with only 4 out of the 70 patients being starved for more than 8 hrs. Similarly, Redfern et al (99) found that although an overnight fast may produce lower blood glucose levels than a morning fast, neither is likely to produce hypoglycaemia in children aged between 1-5 years. Fasting not only affects glucose levels but may also influence intravascular volumes. Although some studies have shown that intravascular volume status is unaffected by an overnight fast in adult patients (11), this may not apply to paediatric patients and may necessitate a careful evaluation of children presenting for surgery after an extended fasting period.

2.7 Assessment of volume status and goal directed fluid administration

The assessment of volume status of a child is difficult to perform since most assessment tools have been created mainly for use in adult patients and are unreliable or untested in the paediatric population. The most accurate method to determine fluid status in children is by working out the weight gain or loss perioperatively. This correlates well with the fluid status and is seen as the gold standard in monitoring fluid status in a child (41). Children are rarely weighed post-operatively making this method of determining fluid requirements unfeasible in our setting. This leads us to rely mainly on taking a history, looking for clinical signs and symptoms of fluid status and in rare instances using haemodynamic monitors in assessing fluid status.

A systemic review studying children aged one month to five years showed that the most reliable clinical signs of dehydration are capillary refill times of longer than 3 seconds, abnormal respiration and reduced skin turgor, however many studies have revealed the limitations of using clinical signs to determine the degree of dehydration in children (100). This review also concluded that a combination of signs yielded a more accurate estimation of dehydration than any single sign on its own (100). To assist with clinical features, another good monitoring tool for adequacy of volume status is the urine output. It has been shown to be give a fair reflection of fluid status providing the normal homeostatic mechanisms of fluid handling by the body including the renal function remains intact. In the paediatric

population a urine output of 1-2 ml/kg/hr, dependant on the age, is considered to indicate an adequate fluid status (41). In paediatric patients the use of dynamic and static haemodynamic measures to guide fluid requirements is fraught with challenges. Some challenges include the fact that many of the cardiac output monitoring tools are not validated for children and that the normal haemodynamic target ranges change with age making it difficult for clinicians to manage

The lack of validated measures for fluid responsiveness in children makes the task of goal directed fluid therapy (GDT) in the paediatric patient difficult. GDT consists of having haemodynamic monitors or their surrogates guiding fluid and inotrope therapy in haemodynamically unstable patients. A systemic review by Cecconi et al (101) claimed that GDT had mortality benefits when applied to extremely high risk adult patients. This conclusion was also established in the paediatric population with septic shock in ICU (102). Children who had monitoring of central venous oxygen saturations had better outcomes than those without this monitoring (103), however this result was not duplicated in other trials. Paul et al (104) conducted a randomized control trial that had enrolled 1260 septic patients that required fluid resuscitation and ascertained that early GDT showed no benefit over the usual forms of managing fluid resuscitation since the 90 day mortality rates were similar in both group.

The purpose of administering fluid boluses would be to improve oxygen delivery at the tissue level by increasing the cardiac output to the microcirculation, but this is very difficult to assess clinically. Mean arterial pressure is often a goal that is targeted. Unfortunately, mean arterial pressures only indicate what is happening at the macrocirculatory level which does not always reflect microcirculatory blood flow. Better indicators of microcirculatory blood flow, potentially revealing a supply and demand problem would be the use of mixed venous oxygen saturation and lactate but these are late signs of poor organ perfusion (20).

Most commonly used methods of measuring fluid responsiveness often assess heart-lung interaction and have been shown to be well validated in adults. Inspiration induces an increased intrathoracic pressure which will reduce venous return in fluid replete patients and is compensated normally by increasing the

systemic vascular resistance to maintain a normal stroke volume. This is exaggerated in hypovolaemic patients who would then respond positively to a fluid bolus (20). In practice if the stroke volume increases by 13-15% or more after a fluid bolus, the patient is deemed to be fluid responsive. However, when the cardiac myocyte is over stretched by administering too much fluid there will no longer be enough cross-linked actin and myosin fiber interaction to contract forcefully and the stoke volume will decrease (25). Preload is determined by the pressure gradient between the right atrium and the mean systemic filling pressure (MSFP) (20). The MSFP is largely regulated by the tone of the splanchnic venous vasculature as it contains 20% of the circulating volume and is very responsive to sympathetic stimulation. Because preload is not the only determinant of stroke volume, these parameters are not always accurate in indicating fluid responsiveness (20).

Echocardiography and Sonography are also used to assess haemodynamic status. These assess the cardiac function and determine inferior vena cava collapsibility as a surrogate for fluid status but there is again limited evidence for the use of these methods to determine fluid responsiveness in the paediatric population (25). Most other dynamic monitors such as pulse pressure variation, systolic pressure variation, stroke volume variation, end expiratory occlusion test and passive leg raise test, are also not validated for use in children and thus have limited value in this setting. A systematic review by Gan et al. (25) showed that the only dynamic variable of value in predicting fluid responsiveness in paediatric patients was respiratory variation in aortic blood flow peak velocity. Gan et al (25) also showed that static measurements such as heart rate, systolic pressure, CVP, left ventricular end diastolic volume seen on echocardiography did not show to predict fluid responsiveness in paediatric patients. The same review showed that Inferior vena cava diameter yielded contradictory results (25).

When considering these forms of haemodynamic monitoring the benefits should always outweigh the risks and cost. These conflicting results suggests the use of an individualised fluid therapy approach should be utilised to improve outcome of the children with haemodynamic instability and limit the detrimental effects of excessive fluid administration.

2.8 Conclusion

A paucity of paediatric based research limits our ability to confidently use literature to guide practice. Practice protocols are based on the few comparable paediatric trials, extrapolation from adult literature and expert opinion (32). Fluid administration should be considered as a drug and thus its use needs to be based according to their indications, contraindications and side effects. Timely optimisation of peri-operative tissue perfusion and fluid therapy improves peri-operative outcome in surgical patients. There are still no definitive answers when it comes to which solution (colloids versus crystalloid) is the optimal fluid type for resuscitation but we are certain that a balanced isotonic solution would have a better side effect profile than unbalanced fluid. In the haemodynamically unstable patient, large volumes of intravenous fluids may be justified, however once resuscitation is established liberal fluid administration and fluid overload should be guarded against as this contributes to increasing mortality (105).

CHAPTER 3: RESEARCH DESIGN AND METHODOLOGY

3.1 Introduction

In this chapter the problem statement, aims and objectives, ethical considerations, research methodology and the validity and reliability of the research report will be discussed in more detail.

3.2 Problem statement

Fluid replacement and maintenance intra-operatively is a large contributor to post-operative (consistency) morbidity and mortality. Inappropriate administration of intravenous fluids by the anaesthetist may cause peri-operative complications and lengthen hospital stay. It is imperative that meticulous care is taken in assessing paediatric fluid needs and replacing fluids correctly to avoid adverse outcomes related to intra-operative fluid management.

Guidelines in the UK for paediatric fluid administration have changed from using a hypotonic solution of 0.18% normal saline and 4% dextrose to the more isotonic balanced solutions such as Ringer's lactate due to the incidence of hyponatraemia. Fixed formula replacement is still being widely used. It is unknown what peri-operative fluid practices are undertaken at Wits as there is no departmental guideline available for the management of paediatric fluids intra-operatively.

3.3 Aim and objectives

3.3.1 Aim

The aim of this study was to determine the practice of paediatric fluid administration intra-operatively amongst anaesthetists working in the Department of Anaesthesiology at Wits.

3.3.2 Objectives

The primary objectives of this study were as follows:

- To describe the approach to intra-operative fluid management in haemodynamically stable paediatric patients
- To describe the approach to intra-operative fluid management of haemodynamically unstable paediatric patients
- To describe the demographic factors influencing paediatric fluid management
- To describe the use of dextrose intra-operatively

The secondary objective was:

- To describe awareness of intra-operative paediatric fluid guidelines

3.4 Ethical considerations

Approval to conduct the study was obtained from the Human Research Ethics Committee (Medical) and the Postgraduate Committee at Wits (Appendix 1). Participation was voluntary, and consent was implied by completion of the questionnaire (Appendix 4). No identifying information was requested of the participants and questionnaires were returned in a sealed envelope. Only the researcher and supervisor have access to the raw data. These measures ensure anonymity and confidentiality.

An information letter (Appendix 3) was provided for those who chose to partake in the study to explain the purpose of the study. Consent to use the questionnaire was obtained and granted by the original author of the survey (Appendix 5).
The study was conducted according to the principles of the Declaration of Helsinki (28) and the South African Guidelines for Good Clinical Practice (29).

3.5 Methodology

3.5.1 Demarcation of study field

The study was conducted in the Department of Anaesthesiology at Wits, Johannesburg, South Africa. The department consists of 73 Consultants, 110 Registrars, 12 Career Medical Officers, and 19 Medical Officers. The following academic hospitals constitute the department:

- Charlotte Maxeke Johannesburg Academic Hospital
- Chris Hani Baragwanath Academic Hospital
- Helen Joseph Hospital
- Rahima Moosa Mother and Child hospital

3.5.2 Study design

The study was a descriptive cross-sectional practice-based study using an anonymous self-administered questionnaire (Appendix 4). A descriptive study answers a specific question to describe a population's characteristics (21).

3.5.3 Study population

The study population consisted of all anaesthetists working in the Department of Anaesthesiology at Wits.

3.5.4 Sample size

The department consists of 214 anaesthetists of which 10 were excluded from the study because of their presence at the postgraduate meeting and thus had prior exposure to the questionnaire, as were a further 2 consultants who had reviewed the questionnaire during its development. Approximately 30% of the department's anaesthetists are unavailable at any given time due to leave, emergency theatres and other elective lists that need staffing and rotations being attended outside of

Johannesburg. A response rate of 60% (121 anaesthetists) of the eligible number of anaesthetists was targeted. This percentage has been described by Schutt et al (22) as acceptable for questionnaire based research. To achieve this yield, data was collected over several months. 135 Questionnaires were distributed and 125 of these were returned which equated to a realization of 92.5% of questionnaires returned and an overall sample size of 61.3%.

3.5.5 Sample method

In this study a convenience sampling method was used. Convenience sampling involves the sampling of participants who are readily available to the researcher (23). All available anaesthetists that met the inclusion criteria were invited to participate in the study.

3.5.6 Inclusion and exclusion criteria

The following inclusion and exclusion criteria were used:

Inclusion criteria:

- All anaesthetists working in the Department of Anaesthesiology at Wits
- Completed and partially complete questionnaires

Exclusion criteria:

- Illegible questionnaires
- Interns
- Anaesthetists not willing to participate in the survey
- Anaesthetists who took part in the post graduate meeting
- Anaesthetists who had seen the questionnaire during its development process

3.6 Data collection

3.6.1 Development of questionnaire

A questionnaire was developed for data collection. Self-report techniques are commonly used when the objective is to determine population practices (21). The survey determined participants' practice of intra-operative paediatric fluid administration and was collected simultaneously from large groups (24).

The questionnaire consists of questions as well as vignettes. These offer high internal and external validity of survey research in order to show predictors of clinician behavior (25). A similar survey was conducted by Way et al (16). No such survey has been conducted in South Africa and it is undocumented what is practiced by anaesthetists working at the Department of Anaesthesiology at Wits. Some of the questionnaire (Appendix 4) was developed by Way et al. and written permission was granted by the authors to use content from the original survey and adapt the questions to the types of fluids available in South Africa (Appendix 5). Further questions were developed based on the literature available on the topic thereby ensuring content validity. Face validity was ensured by including suggestions and criticisms by three senior consultants practicing paediatric anaesthesiology in the state sector as well as one consultant practicing paediatric anaesthesiology in the private sector. The questionnaire consisted of three sections and took approximately 15 minutes to complete.

Section one incorporated demographic details:

- Years of experience
- Professional designation
- Experience with paediatric anaesthesia

Section two addressed the use of existing guidelines and formulas used for intra-operative paediatric fluid administration:

- Awareness of paediatric fluid administration guidelines
- Guidelines used to guide practice

- Formulas applied to determine volume of fluid required intra-operatively

The third section determined the practice of paediatric fluid administration in various clinical scenarios using vignettes:

- Methods used for determining volume and type of fluid administered to both haemodynamically stable and unstable paediatric patients
- Practice of dextrose administration intra-operatively

In the absence of local guidelines, the Association of Paediatric Anaesthesia (APA) of Great Britain and Ireland consensus guidelines on peri-operative fluid management in children v1.1 (26) will be used as a guideline for standard practice. More recent guidelines were released by the Association of the Scientific Medical Societies in Germany (AWMF) in 2016 and these will also be referenced when describing acceptable practice, along with more recent literature on the topic.

3.6.2 Data collection process

Data was collected from November 2016 to April 2017. Questionnaires were numbered to keep track of the number of questionnaires distributed and returned. The questionnaires were distributed at random and not according to the numerical system to ensure that participants do not feel at risk of being discriminated against. Data was collected at the departmental academic meetings. The chairperson was approached for permission to address the meeting. The researcher explained the aim of the study and invited participation. An information sheet (Appendix 3) explaining the purpose of the study was attached to the questionnaire. The researcher was present throughout the filling out of the questionnaire to address any queries. Blank questionnaires were counted to determine response rate but were not included in other statistical calculations. No identifying information was requested of the participants and questionnaires were returned in a sealed envelope. Only the researcher and supervisor have access to

the raw data. These measures ensure anonymity and confidentiality. Data will be stored securely for six years after completion of the study.

3.7 Data analysis

Data was entered on a REDcap data base as well as a Microsoft Excel® spread-sheet. Descriptive statistics were used. Categorical data was summarised using frequencies and percentages. Comparative data was analysed using the chi^2, Fishers Exact and Wilcoxin Mann Whitney U tests. A *p*-value of less than 0.05 was regarded as being statistically significant. The assistance of a statistician was sought to assist with data analysis.

The Wilcoxin Mann Whitney U test was used to assess whether years of experience affected the knowledge of guidelines and practice of intra-operative fluid management, because this data was not normally distributed. The Fishers Exact and Chi^2 tests were used respectively to analyse whether paediatric training or designation influenced the knowledge and practice of intra-operative fluid management in paediatric patients.

3.8 Validity and reliability of the study

Validity of a study, according to Botma et al (27) refers to “the degree to which a measurement represents a true value” and reliability is “the consistency of the measure achieved” based on the study design.

This study maintained validity and reliability by:

- Using parts of a questionnaire that has been administered and published in the UK
- Face value was maintained by having four specialist consultants both in state and private practice critique the questionnaire

- Content validity of the questionnaire was insured by a thorough literature review and scrutiny by senior qualified anaesthetists
- Having the researcher available for queries during completion of the questionnaire
- Maintaining anonymity and a neutral non-coercing environment
- Checking every tenth data entry point for accuracy
- Statistical analysis done with a biostatistician

3.9 Summary

In this chapter the problem statement, aim and study objective, ethical considerations, research methodology, data analysis and validity and reliability were discussed. In the next chapter results of the study will be presented and discussed.

CHAPTER 4: RESULTS AND DISCUSSION

4.1 Introduction

In this chapter the results of this study will be presented. The Data presented will include analysis of the demographics of the study population and will address each objective individually.

To assess whether safe fluid practices are being followed the following objectives were investigated:

The primary objectives of the study were:

- To describe the approach to intra-operative fluid management of haemodynamically stable paediatric patients
- To describe the approach to intra-operative fluid management of haemodynamically unstable paediatric patients
- To describe the demographic factors influencing paediatric fluid management
- To describe the use of dextrose intra-operatively

The secondary objective was:

- To describe awareness of intra-operative paediatric fluid guidelines

4.2 Results

4.2.1 Demographic data

There were 214 anaesthetists in the Department of Anaesthetics at Wits, ranging from new medical officers to consultants. Of these, ten staff members were on the post graduate committee and had prior knowledge of the study and questionnaire and were therefore not eligible to complete the questionnaire. A further two

consultants had reviewed the questionnaire during its development and were therefore also excluded. This resulted in only 202 of the 214 staff members being eligible to partake in the study. A total of 135 questionnaires were distributed and all 135 were returned, but only 125 were completed or partially completed. This represents 61.8% of the department. A 60% response rate would be a fair representation of the department.

When analysing the study population according to designation (Figure 2), 37 (29.6%) were consultants, 34 (27.2%) were senior registrars, 33 (26.4%) were junior registrars, and 21 (16.8%) were medical officers (MO).

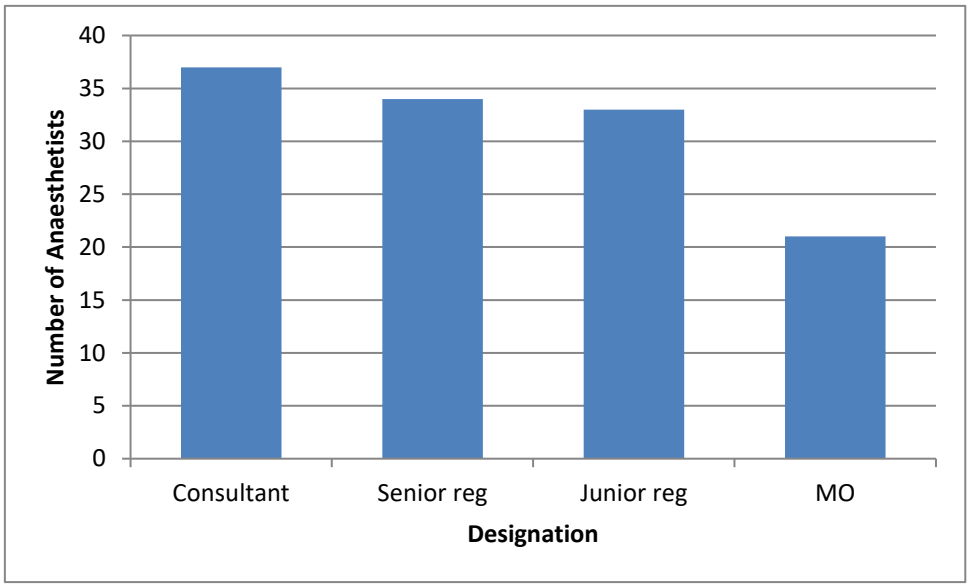

Figure 2. Number of participants representing each designation

The study population had a wide range of anaesthetic experience ranging from four months to 32 years. The mean number of years of experience at the Department of Anaesthesiology at Wits was 6.02 years (SD=5.67).

Of the 125 completed questionnaires received, one respondent did not anaesthetise children and was excluded from further data analysis. Of those that returned completed or partially completed questionnaires, 102 (82.3%) participants anaesthetised children more than 5 times a month and 22 (17.6%) did so fewer than 5 times a month. This cut off (five times a month) was chosen arbitrarily as

this was felt to be a significant enough amount of cases to warrant being familiar and confident with the intra-operative management of paediatric patients.

The registrar program is designed in such a way that most junior trainees get a formal paediatric teaching block early in their training in order to equip them with the necassary skills going forward. The training block can either be done at CHBAH or CMJAH where teaching is informal and largely undertaken in theatre on an indiviual basis. At the time of this study 82 (66.1%) participants had completed this training. However, having had this training did not strongly influence a particular practice (p=0.0713) and this may be accounted for by the fact that there is no standardisation of teaching.

4.2.2 The approach to intra-operative fluid management of haemodynamically stable paediatric patients

The objective was to review the participant's approach to fluid management in a patient that is haemodynamically stable and presents for surgery. The questions asked were whether the starvation period for such a patient was being replaced intra-operatively, whether participants routinely replaced surgical losses, administered a maintenance fluid and whether they viewed the third space as a real entity.

Formulas used for fluid management

The goal of intra-operative fluid maintenance is to maintain a normal fluid, electrolyte and energy state to meet the body's requirements and maintain adequate organ perfusion. The most popular formula, which was used by 48 (38.7%) people who participated in the survey, was the 2:1:0.5 rule as suggested by Lindahl et al and Holiday et al (5, 6). 46 (37.1%) of the participants used the older formula suggested by Holiday and Segar, the 4:2:1 rule (5). The rest of the formulas used by the anaesthetists partaking in the study are not recognised in the

literature and are perhaps anecdotal formulas that are used and taught by individual anaesthetists (Figure 3).

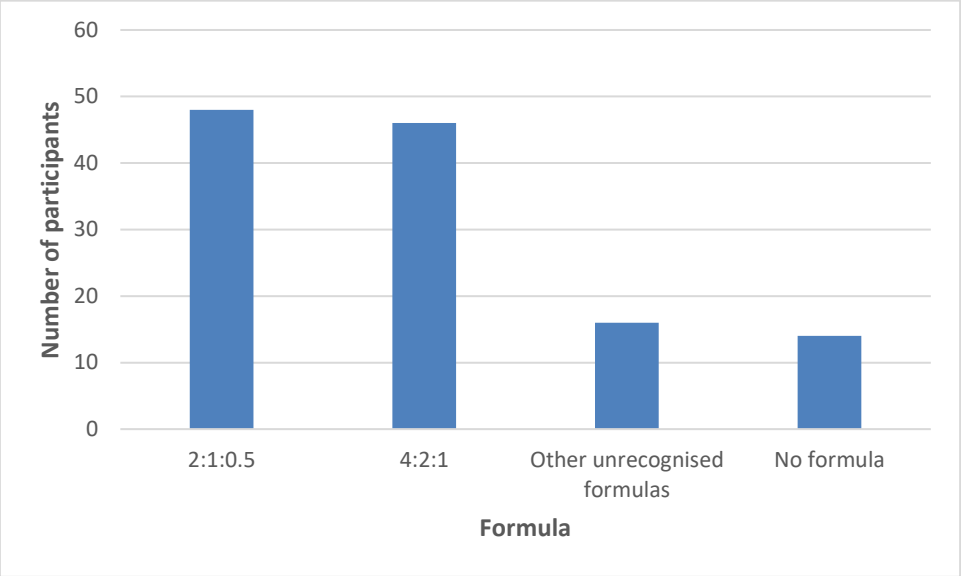

Figure 3. Formulas used to calculate fluid maintenance

The Approach to replacing fluids intra-operatively for two different starvation periods

The clinical scenario presented in the survey was a child requiring surgery that was starved for either 2 hours or 12 hours and it aimed to evaluate the practices of fluid replacement for the two different starvation periods with the expectation that the length of the starvation period would not influence the replacement of maintenance and surgical losses intra-operatively as these are independent of fasting.

Intravenous fluids where used as replacement for the two hour starvation period by 21 (17.8%) participants, which is not necessary as intravascular volume should not have changed with a two hour fast. For a patient that was fasted for 12 hrs, replacement fluids were administered by 111 (89.5%) anaesthetists. This fluid management is appropriate as one can assume that some level of dehydration would have occurred during this prolonged time (Figure 4). The remaining 13 (10.5%) participants would not replace a 12 hour starvation period.

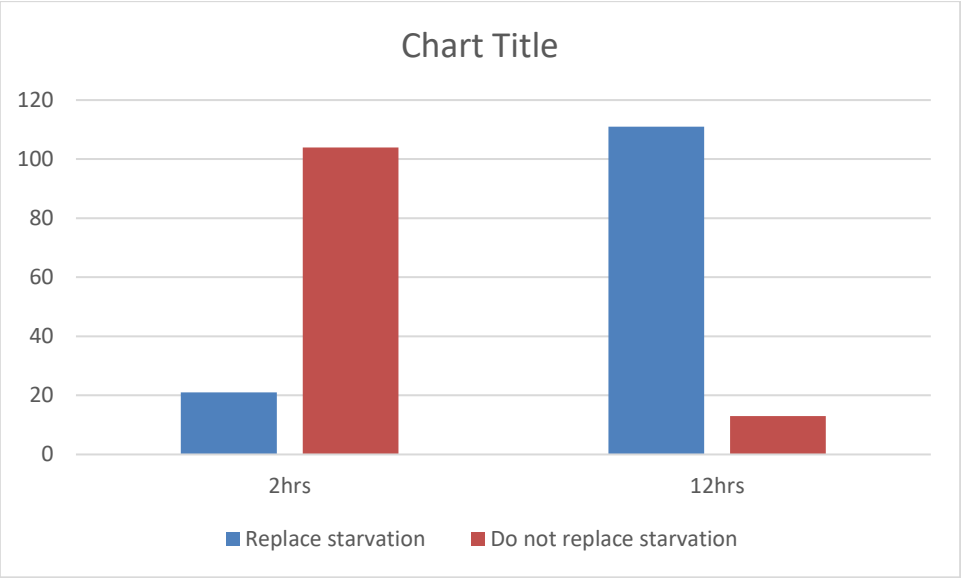

Figure 4. Replacement of starvation period

The same scenario also aimed to ascertain how other fluids were being replaced peri-operatively, such as maintenance and surgical losses (blood, nasogastric losses etc.). It was expected that participants would replace these losses regardless of the duration of starvation, surprisingly this was not the case and the starvation period appeared to influence the replacement of intra-operative losses. For the 12 hour starvation period as many as 7 (5.7%) participants would not give maintenance fluid intra-operatively and 10 (8.1 %) would not replace surgical losses (Figure 5). For the 2 hour starvation period, 20 (16.2%) survey participants would not give maintenance fluid intra-operatively and 9 (7.3%) would not replace surgical losses. It was also revealed that 41 (33.3 %) and 48 (41.3%) participants would still replace third space losses for the 2 hour and 12 hour starvation periods respectively.

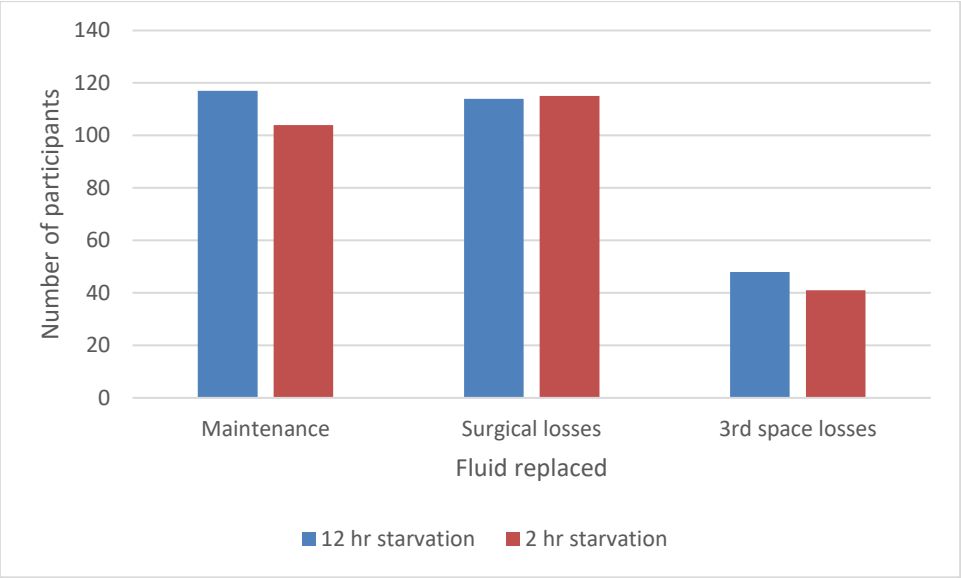

Figure 5. Fluid replacement for maintenance, surgical and 3rd space loss in different starvation periods.

Types of fluids used

It is recommended that isotonic balanced solutions be used peri-operatively. Although it is not our institution's practice to use hypotonic solutions peri-operatively, the practice of fluid prescription has never been assessed. The questionnaire explored this by asking participants to simply state what is done in terms of choice of fluid therapy for intra-operative maintenance. Balsol and Ringer's lactate were the preferred fluids for intra-operative maintenance used by 68 (54.8%) and 25 (29.0%) participants respectively. Fluids used less often were; paediatric maintelyte which was used by 12 (9.6%) survey participants, half Darrows dextrose was used by 5 (4.0%) and the least utilised fluid was normal saline used by 2 (1.6%) participants (Figure 6).

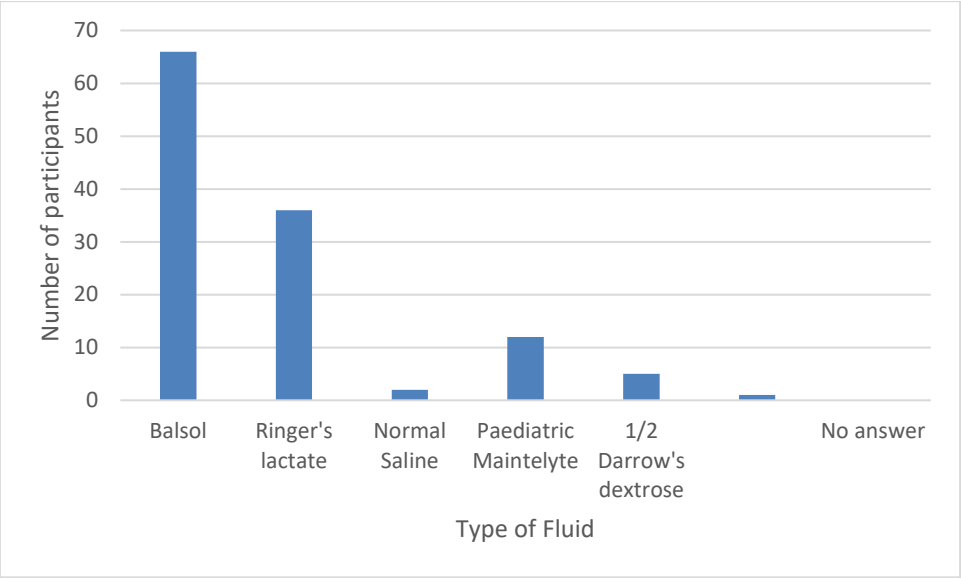

Figure 6. Types of fluid used for intra-operative maintenance

4.2.3 The approach to intra-operative fluid management of haemodynamically unstable paediatric patients

Anaesthetsits are not only expected to maintain a normal physiological state in healthy patients coming for surgery but also often encounter patients that are haemodynamically unstable peri-operatively. The first drug that is often prescribed to manage haemodynamic instability is clear fluid. The appropriate end point of this therapy is to restore adequate cardiac output and tissue perfusion.

The management of a bleeding patient

The vignette designed to address the fluid management of an unstable patient was one of a previously stable patient that began to bleed significantly intra-operatively and required immediate fluid resuscitation.

In this scenario,102 (86.2%) participants would have given a 10-20ml/kg bolus of fluid, 3 (2.4 %) would initially give a 40ml/kg bolus and 13 (10.5%) would administer 200 milliliters of fluid (Figure 7).

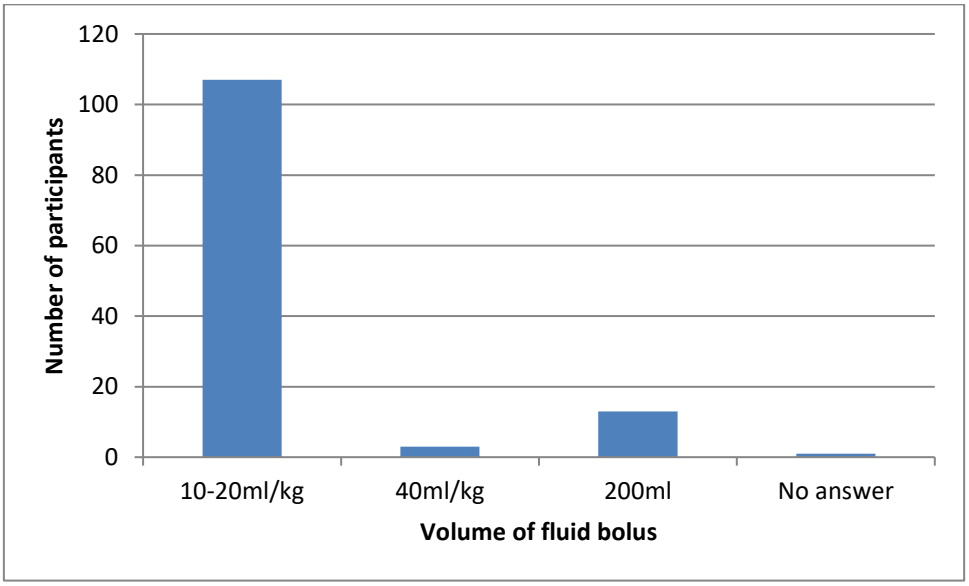

Figure 7. Volumes used for hypovolaemic resuscitation.

Types of fluid used for resuscitation

In this study crystalloids and colloids seem to be used in almost equal amounts, with 66 (53.2%) anaesthetists preferring to use a crystalloid bolus and 56 (45.2%) tend to use a colloid bolus to treat haemodynamic instability caused by acute blood loss in a child. Of the crystalloids used, 65 (53.2%) participants preferred to use a balanced solution (Ringer's lactate or balsol) and 3 (2.4%) would use normal saline. Of the synthetic colloids used, voluven was used by 40 (32.8%) of the participants, 3 (2.4%) used gelofusin and 1 (0.8%) preferred volulyte. Of the natural colloids, 11 (8.87%) participants would use blood whereas 2 (1.6%) preferred to use albumin (Figure 8).

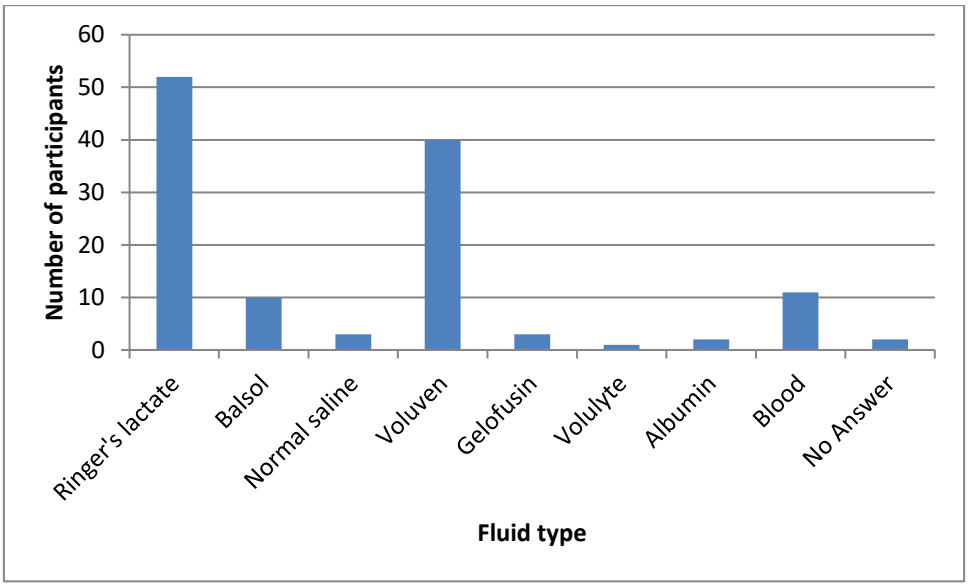

Figure 8. Types of fluid used for bolus administration in haemodynamically unstable patients.

Management of a dehydrated child

This situation is different from the acute blood loss scenario discussed above because dehydration is not only intravascular but also extravascular fluid depletion. This vignette was testing whether participants could assess the degree of dehydration correctly and which fluid type would be used to replace the pre-operative losses in a dehydrated child.

Although the most accurate way to determine dehydration is to monitor a change in a patient's weight, this is impractical in theatre. Other signs are open to subjectivity and therefore a combination of signs yields a more accurate estimation of dehydration rather than any single sign on its own. All participants could pick up clinical signs of dehydration and 108 (87.1%) participants assessed the child correctly as being >10% dehydrated and 16 (12.9%) assessed the child to be 5-10% dehydrated according to the signs given in the scenario.

Participants were then asked what volume and type of fluid they would use to resuscitate this severely dehydrated patient. Of the participants that answered this question, 104 (83.8%) would have given a 10-20ml/kg bolus of crystalloid,14 (11.2%) would have given a 10-20ml/kg colloid bolus and one (0, 8%) would have

given a 5ml/kg crystalloid bolus (Figure 9). One (0, 8%) anaesthetist would have not given this child any fluid bolus.

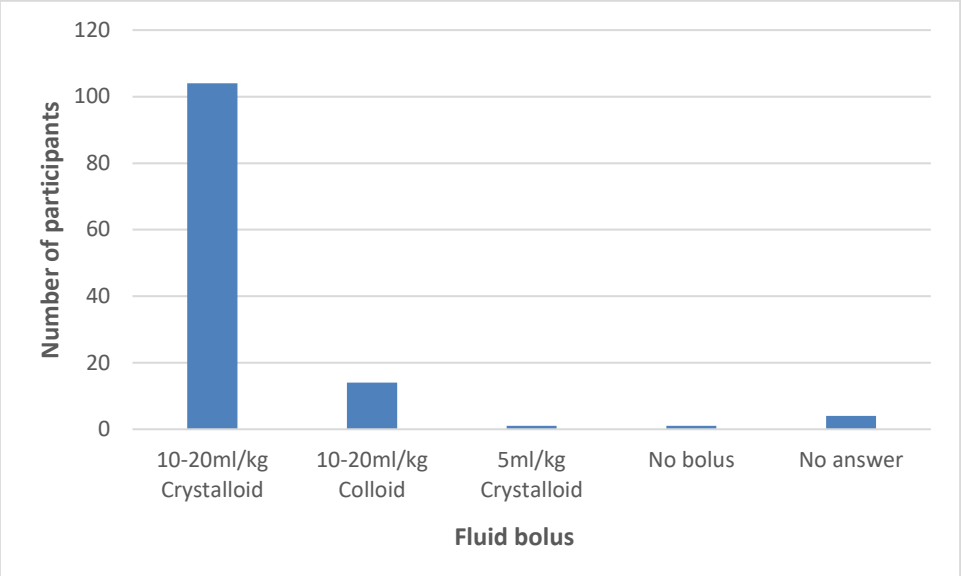

Figure 9. Volumes used for fluid resuscitation.

4.2.4 To describe the demographic factors influencing paediatric fluid management.

The researcher was interested in ascertaining whether designation, experience and training influenced the approach used for fluid maintenance intra-operatively. It was concluded that years of experience had no influence over a preferred formula used (p=0.0856). Having had paediatric training during registrar time also failed to influence the use of a specific formula (p=0.2016) and this may reflect inconsistent teaching of registrars doing the paediatric block on this topic. The only significant difference was amongst the junior and senior registrar groups. The registrars with 3-5 year of experience used the 2:1:0.5 rule much more readily than the registrars with 1-2 years of experience who preferred to use the 4:2:1 rule for maintenance intra-operatively (p=0.0239).

When assessing the types of fluids used for maintenance intra-operatively, consultants were far more likely to use isotonic solutions when compare to the non-specialists in the department (p= 0.0212). Years of experience (p= 0.083) and

training (p=0.187) did not influence the type of fluid used for maintenance. It was also found that consultants were significantly more likely to use a colloid for initial fluid resuscitation of a haemodynamically unstable patient with blood loss when compared to non-specialists who preferred to use crystalloids (p=0.003). Having done the paediatric rotation did not influence participants opinions on whether to use colloids or crystalloid for resuscitation (p=0.0713). Designation seems to be the only factor that influences fluid practice in this study.

4.2.5 To describe the use of dextrose intra-operatively.

Hypoglycaemia may go undetected under anaesthesia and peri-operative glucose requirements are largely unpredictable and vary greatly amongst paediatric groups. It is recommended that blood glucose be checked regularly, and glucose administration adjusted to maintain normoglycaemia. The scenario presented to the participants was a child that presented to theatre with a blood glucose of 2mmol/l and it aimed to determine the approach to glucose replacement.

Management of hypoglycaemia varied amongst anaesthetists (Figure 10). As few as 56 (45.1%) participants would have treated this patient's hypoglycaemia with 2ml/kg of 10% dextrose which is recommended by most guidelines. The majority of participants did not manage hypoglycaemia correctly and would have given 2ml/kg of 50% dextrose, this concentration of dextrose is hyperosmolar and may cause phlebitis and thrombosis in the vessel and thus is not recommended in paediatric patients. Another 13 (10.5%) anaesthetists would have only added a 5% dextrose solution to the maintenance infusion of fluid without administering an additional bolus whereas 2 (1.6%) participants would not have treated the glucose level of 2mmol/l.

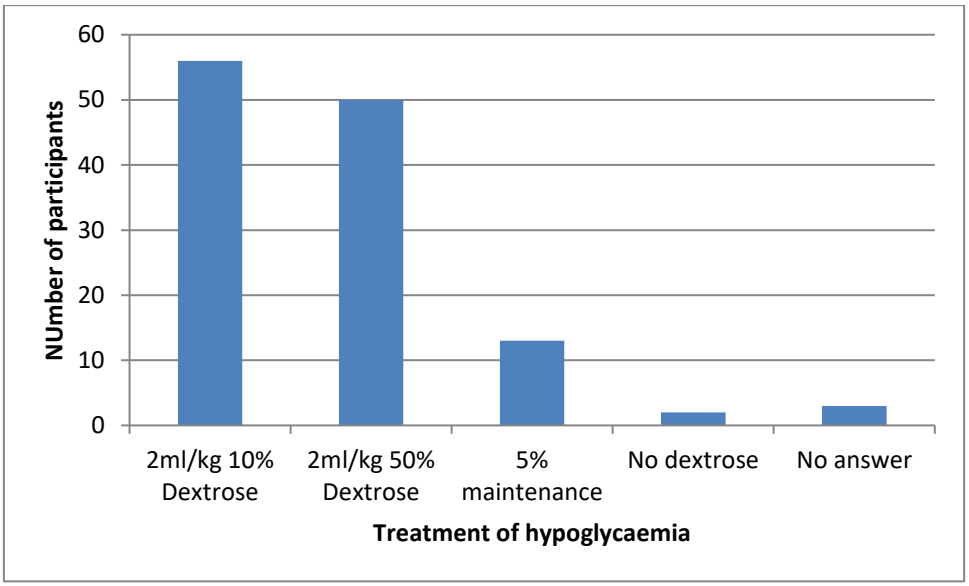

Figure 10. Approach to managing hypoglycaemia.

The second scenario related to blood glucose management and questioned the participant on their management of an 18 month old child that was starved for 10 hours pre-operatively. At the Department of Anaesthesiology at Wits, as many as 84 (68.2%) respondents routinely measured the blood glucose level and administered dextrose according to need. A minority of participants routinely administered glucose without initially checking a blood glucose level, with 18 (14.5%) survey participants routinely administering a 1% dextrose solution, 15 (12.2%) used a 2% dextrose solution and 6 (4.9%) participants adding a 5% dextrose solution to their maintenance fluid (Figure 11). The pre-prepared glucose containing solutions that are available have low sodium contents and once the glucose is metabolised by the body, the remaining solution becomes hypotonic and may further increase the risk of causing hyponatraemia (81). For this reason, it is recommended that if a dextrose solution is to be given for maintenance it should be added to a balanced solution.

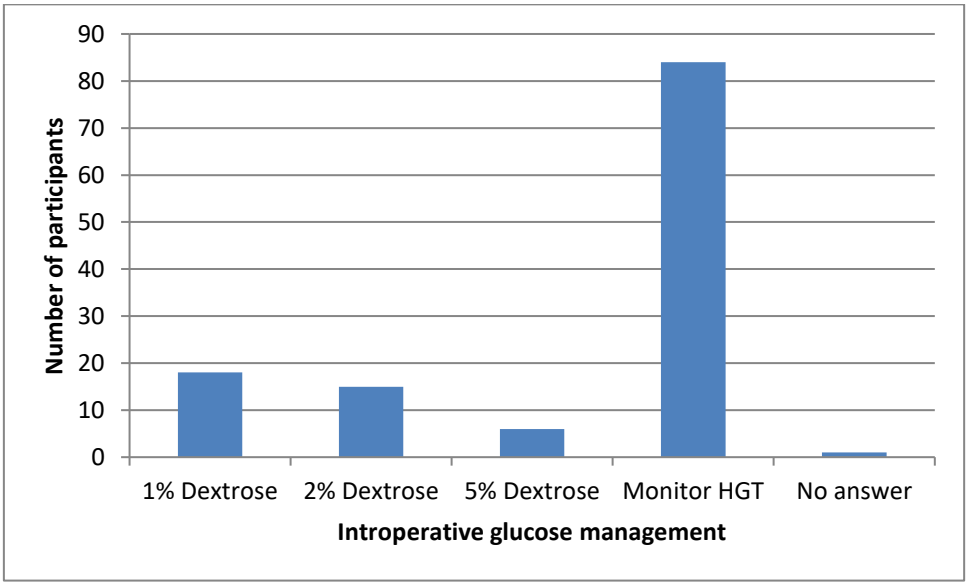

Figure 11. Approach to intra-operative glucose control.

At Wits the majority of anaesthetists prefer to monitor the blood glucose level and administer glucose as required rather than routinely running a background infusion of dextrose with their maintenance. It needs to be noted that certain paediatric patients are at increased risk of hypoglycaemia and administering a glucose containing solution does not necessarily protect this group against hypoglycaemia. For these at-risk patients extra vigilance and monitoring needs to be implemented. Normal plasma glucose levels are ideal and the only way to ensure that this is maintained is by testing the glucose level intra-operatively.

4.2.6 To describe awareness of intra-operative paediatric fluid guidelines

In the study population at Wits, 68 (54.8%) respondents were aware of some sort of international guideline that had guided their fluid administration. 24 (19.3%) anaesthetists in the department claim to have knowledge of the existence of departmental guidelines at Wits. There are no formal guidelines at any of the hospitals, but these participants may have been referring to notes that they have read or anecdotal information that they had received during their training. These results are in keeping with other international studies (106).

The Department of Anaesthesiology at Wits also does not have a standard protocol for paediatric peri-operative fluid administration and it has not adopted any international guideline. It is left up to the individual anaesthetist to choose which protocol they would prefer to follow. However, as seen from the survey results, just under half of the participants did not know of any international guideline and therefore it can be assumed that these individuals do not have any framework to guide their fluid administration.

4.2.7 Discussion

In 2006 Way et al. (16) conducted a survey to elicit whether safe fluid practices were being conducted in the UK after the RCPCH issued an alert of the dangers of using hypotonic solutions. That study showed that anaesthetists were still practicing dangerous fluid prescription and prompted the need to identify the peri-operative fluid management within the Department of Anaesthesiology at Wits.

This study assessed 124 anaesthetist's practice of intra-operative paediatric fluid management at the Department of Anaesthesiology at Wits. This corresponded to a response rate of 61.8% of the eligible anaesthetists within the Department of Anaesthesiology at Wits. Achieving a higher response rate was limited by the fact that the academic meetings were variably attended and some consultants had prior access to the questionnaire which made them illegible to participate in the study. It is important to note the designation of the participants in this study (Figure 2): 37 (29.6%) were consultants, 34 (27.2%) were senior registrars, 33 (26.4%) were junior registrars, and 21 (16.8%) were medical officers (MO). This is not a reflection of the spread of anesthetist within the department but only a rough reflection of the proportion of the designations that attend the academic meetings and thus had the opportunity to participate in the study. Therefore, the results cannot be generalised but may help identify areas that may need improvement with regard to peri-operative paediatric fluid management.

There are no departmental guidelines to assist in the prescribing of fluids to paediatric patients, as well as no consensus internationally on intra-operative fluid

management in paediatric patients. The results of this study show that this lack of consensus amongst peers regarding fluid administration has resulted in significant variation in fluid prescription. This variability may be due to the lack of paediatric based studies looking at peri-operative fluid management which results in the extrapolation of many principles from adult research. It is also heavily influenced by physiological differences amongst paediatric patients including their disease processes. Bearing all this in mind, it is recognised that fluid administration needs to be tailored to individual patient requirements and reassessed and adjusted continuously during the peri-operative period. This process could be more uniform by implementing appropriate guidelines for fluid management.

A survey done by Cannesson et al (106) compared fluid practices amongst the members of the ASA and ESA. The survey concluded that standardised fluid therapy is not widely practiced and only 6% of the ASA respondents had a departmental protocol (3). Similar findings were found by Way et al (16) where 67.6% of their UK respondents had no departmental protocol for fluid administration in children. In the study by Way et al (16), 68 (54.8%) anaesthetists were aware of some sort of international guideline that had guided their fluid prescribing practices in paediatric patients and 100 (79.7%) had no knowledge of the existence of departmental guidelines. These results are very similar to other international studies. The Department of Anaesthesiology at Wits also does not have a standard protocol for paediatric peri-operative fluid administration and it has not adopted any international guideline. It is left up to the individual anaesthetist to choose which protocol, if any, they would prefer to follow.

The RCPCH in Great Britain had published their concerns with the use of hypotonic solutions in 2003 following several cases of death or adverse outcomes in children from iatrogenic hyponatraemia and therefore recommended that isotonic balanced solutions be used peri-operatively (26). In contrast to the study conducted in 2006 by Way et al (16) where 60.1 % of participants still used hypotonic solution for maintenance, the majority, 104 (83.8%) participants in this study used isotonic balanced fluid. The other solutions that were used were paediatric maintelyte by 12 (9.6%) participants, half Darrows dextrose used by five (4.0%) participants and the least utilised fluid was normal saline, used by two

(1.6%) participants. Potential problems commonly described when using these solutions are hyperchloraemic metabolic acidosis when using normal saline and hyponatraemia when using half Darrows dextrose and paediatric maintelyte. Both these solutions are unbalanced hypotonic solutions with very little resemblance to plasma when comparing electrolyte content and result in excessive free water distribution which further worsens hyponatraemia (16, 43). Therefore, these hypotonic, unbalanced solutions should be discouraged from being used peri-operatively and instead isotonic solutions should be encouraged at all times.

By appropriate implementation of peri-operative fasting practices, one could minimize the inappropriate use of fluids or requirements intra-operatively. Duration of fasting influences intravascular volume as both sensible and insensible losses are not being replaced which may lead to hypovolaemia which results in organ hypoperfusion and in turn has negative consequences for oxygen delivery, wound healing, post-operative nausea and vomiting and cardiac function. A study done by C.A Lee (82) at CMJAH in 2010 showed that the mean fasting period for paediatric patients was 14.09 hours (SD= 3.37). These prolonged starvation periods should be strongly discouraged. The ASA created guidelines which encourage clear fluids to be taken orally up until 2 hours before the start of anaesthesia, however, this is rarely adhered to in the hospitals observed in this study and internationally (30, 82, 109).

Together with the fluid requirement from prolonged fasting, the maintenance and other fluid losses occurring intra-operatively need to be estimated and replaced. For the 2 hour starvation period 104 (83.3%) survey participants would have given maintenance fluid and 115 (92.7%) would replace surgical losses intra-operatively. When compared to a 12 hour starvation period 117 (94.3%) would administer maintenance fluid and 114 (91,9%) would replace surgical losses. The length of the starvation period should not influence one’s practice of replacing maintenance and surgical losses and all participants should have replaced these for both starvation periods. It is unclear why the length of starvation influenced these independent fluid losses. This may show a poor understanding by the participants of their own fluid practices or a poor understanding of the question asked in the survey.

Adult studies suggest that replacing the fluid deficit incurred during the starvation period is not necessary unless this period is prolonged for more than 8 hours (11, 52). In view of the physiological differences between children and adults it is unlikely that the same can be said for the paediatric patient. In this study, the calculated fluid deficit was replaced by 21 (17.8 %) participants after a 2 hour starvation period which is not necessary as intravascular volume should not have changed during this period. For a patient that was fasted for 12 hrs or more, 111 (89.5%) anaesthetists gave intravenous fluid intra-operatively to compensate for this prolonged fast. The remaining 13 (10.5%) anaesthetists would not replace fluids for a 12 hour starvation period which is concerning as this may lead to hypovolaemia and the sequelae thereof. There is no data that determines how much intravascular volume deficit occurs after a certain starvation period, this is probably since it is difficult to determine the wide variability in volume of distribution between compartments in individuals (30).

When approaching the intra-operative maintenance fluid requirements, the APAGBI (26) guidelines recommend using the Holiday and Segar (4:2:1) formula whereas the AWMF (90) guidelines suggest an infusion of 10ml/kg/hr. Although these values differ dramatically, these authors qualify their recommendation with the fact that the fluid status of the patient has to be reviewed regularly and the infusion rate adjusted according to the patient requirements. Even though these guidelines assist with intra-operative fluid management, Lindahl et al (5) suggested that using the 4:2:1 formula for anaesthetised paediatric patients overestimated the electrolyte and fluid requirements. This statement was later supported by Holiday (6), the original author of the 4:2:1 formula, who suggested that anaesthetised patients have a slower basal metabolic rate and an inappropriate secretion of anti-diuretic hormone (ADH) leading to less peri-operative losses than previously thought. This prompted a change in the original formula to what is now known as the 2:1:0.5 rule which reduces the original volume administered for maintenance by 50% (42). This revised formula and the formula proposed by Holiday and Segar where almost used equally between participants with 48 (38.7%) of participants using the 2:1:0.5 formula and 46 (37.1%) of participants using the 4:2:1 formula. This differed from the study by Way et al (16) in which 81.8% of the participants used the 4:2:1 calculation.

The remainder of participants in this study used formulas not recognised in the literature and which are perhaps anecdotally taught by individual anaesthetists. One participant used a 50 ml/hr infusion of fluid, which is not weight based and may be detrimental. Another participant uses goal directed fluid therapy (GDT) which would be a good approach in a hemodynamically unstable patient but would not have much benefit in the average child presenting for surgery. This approach comes with many limitations such as requiring haemodynamic monitoring and the patient described in the scenario was fluid replete and would not have significant haemodynamic changes with minor surgery. Goal directed therapy was not intended as treatment of an intra-operative fluid replete and haemodynamically stable patient (104, 107, 108). This variation in the approach to fluid replacement within the Department of Anaesthesiology at Wits reinforces the fact that there is lack of consensus and standardised teaching of staff on this topic.

It is currently widely accepted that the concept of the “third space” has never been proven and is now considered not to exist, therefore, it should not be included in the calculation of intra-operative fluid requirements (7, 53). The data in this study showed that at least 41 (34.7 %) participants would still replace third space losses which is no longer recommended and may promote excessive fluid administration and negatively affect the patients outcome. This may be due to certain gaps in the teaching program or perhaps not much emphasis is placed on this particular form of fluid replacement and thus individuals have not been updated on its proposed discontinuation.

Another important aspect when prescribing maintenance fluids is the glucose requirements of the patient peri-operatively. Glucose requirements are largely unpredictable and vary greatly amongst paediatric patients. It is well recognized in the literature to either administer a 1- 2.5% dextrose balanced glucose solution or to use a glucose free balanced solution, provided plasma glucose levels are monitored regularly (91-93, 96). It needs to be noted that certain paediatric patients are at increased risk of hypoglycaemia and for these patients extra vigilance and monitoring needs to be implemented. Those that are vulnerable to hypoglycaemia include malnourished children, children on total parenteral nutrition, those undergoing prolonged or major surgery, children that have a

neuraxial block and thus a reduced stress response as well as children that have been starved for prolonged periods of time. These at risk groups of children should have a background infusion of dextrose running and/or have their blood glucose checked more regularly. Appropriately starved patients that present for surgeries where the duration of theatre time is expected to be under an hour, would not require a background infusion of glucose during this period (30).

The routine use of a dextrose solution was implemented by 39 (31.5%) of the participants in this study, of which 33 (84.6%) used the correct percentage (1-2.5%) of dextrose according to the recommendations. The remainder of the participants chose to administer a 5% dextrose solution which may have the unfavorable effect of inducing intra-operative hyperglycaemia. If a dextrose solution is chosen, it is recommended that dextrose should be added to a balanced crystalloid solution, as using pre-prepared dextrose solutions carry the risk of inducing hyponatraemia due to their low sodium concentrations. Additionally, once the glucose is metabolised by the body, the remaining solution becomes hypotonic and may further contribute to hyponatraemia (81). At Wits the majority of anaesthetists, 85 (68.2%) prefer to only monitor the blood glucose level and replace as necessary, rather than routinely running a background infusion of dextrose. This is acceptable practice as monitoring blood glucose will prompt rapid detection of hypoglycemia if it occurs.

Once hypoglycaemia had occurred the management varied amongst anaesthetists considerably. As few as 56 (45.1%) participants would have correctly corrected a blood glucose of less than 3.5mmol/l with 2ml/kg of 10% dextrose, which is the recommended volume and concentration of dextrose to be infused according to most guidelines. A large proportion of participants 50 (40.3%) did not manage hypoglycaemia correctly and would have given 2ml/kg of 50% dextrose bolus. As this is a hyperosmolar concentration it is not recommended as an appropriate replacement solution since it may cause phlebitis, thrombosis and induce hyperglycaemia amongst other side effects. Of further concern is that 15 (12.1%) anaesthetists would not have corrected the hypoglycaemia at all which may lead to significant detrimental side effects such as seizures, long term cognitive impairment and even death. Therefore, it is imperative to standardise the

prevention and appropriate management of hypoglycaemia in the Department of Aanaesthesia at Wits.

Administering fluid for maintenance and insensible losses as well as monitoring glucose are all important aspects of peri-operative fluid management, however further fluid calculations may be required when considering a haemodynamically unstable patients. When presented with a haemodynamically unstable bleeding patient, the recommendations are to give a bolus of between 10-20 ml/kg of a balanced isotonic crystalloid which may be repeated up to three times to achieve the required haemodynamic goals which must include avoiding overloading the extravascular compartments (30, 90, 110). The majority, 102 (86.2%) participants in this study would have correctly given a 10-20ml/kg bolus of fluid whereas 13 (10.5%) participants would have given a 200ml bolus. Giving a 200ml bolus in this case would not have been incorrect as the patient's weight in the scenario was 15 kg and thus the 200ml bolus would have been 13.33 ml/kg. This question did not achieve what the researcher intended for it to establish, which was to ascertain whether anaesthetists were cognisant of the fact that fluid volume calculations in children need to be calculated according to weight. Although coincidentally in this scenario 200ml happens to be an adequate amount of fluid for a fluid bolus, administering fluids without bearing the child's weight in mind is dangerous and inappropriate practice. The remainder of participants would have administered 40ml/kg for an initial bolus which could lead to fluid accumulation and overload.

Excess fluid administration may damage the glycocalyx and cause gastrointestinal oedema, coagulation abnormalities, hypervolaemia and increase the risk of mortality (12). Lowell et al (13) showed that in an adult ICU population a weight gain of less than 10% corresponded to a mortality risk of less than 10%. Furthermore, he showed that a 10-20% weight gain increased the mortality risk to 32% and a weight gain of more than 20% placed you at a 100% mortality risk. This shows that appropriately dosing of fluid is essential to the outcome of a patient. The application of standardised fluid therapy protocols this excessive fluid administration can be avoided and has been shown to improve outcome (3).

In the setting of acute blood loss there is a shift of interstitial fluid into the intravascular space to restore adequate intravascular volume and thus maintain cardiac output. When approaching a patient's peri-operative fluid management, the goal is to maintain a normal fluid, electrolyte and energy state to maintain adequate organ perfusion. It is important to always consider the tonicity, the electrolyte content and the glucose content of the fluid utilized. The risk of using certain pre-prepared solutions such as hypotonic dextrose containing fluids need to be considered.

It seems rational to initially restore this volume loss with a crystalloid that is isotonic and electrolyte balanced. Colloids are recommended if crystalloids alone are not effective in restoring the perfusion pressures and if blood products are not indicated or available. In this study crystalloids and colloids seem to be used as the initial fluid choice in almost equal amounts, with 65 (53.2%) participants preferring to use a crystalloid bolus and 57 (45.2%) participants a colloid bolus to treat haemodynamic instability caused by acute blood loss. Although crystalloid solutions may cause significant haemodilution, interstitial oedema and thus reducing oxygenation to tissues (30, 111), albumin and synthetic colloids are associated with more side effects when compared to their crystalloid counterparts. Some adverse events that may occur with colloid use include tissue accumulation, coagulation abnormalities, interference with blood cross matching, renal dysfunction and allergic reactions, amongst others. However, crystalloids in excess may cause significant haemodilution, interstitial oedema and thus reduce oxygenation to tissues and thus the most appropriate fluid replacement for blood loss would in fact be blood product (30, 111).

In this study, 11 (8.87%) participants mentioned that they would administer blood in the scenario of acute blood loss. Blood was not a fluid that appeared on the list of choices in the survey question, however an "other" option was presented to participants to not limit the participant to the options in the questionnaire. Had it been an option, participants may have chosen blood more readily. Although the researcher acknowledges that there is no better substitute for blood loss, the objective of this section was to determine which immediately available clear fluid the participants would choose if blood products were not available, which is

usually the case with unanticipated blood loss. Albumin, volulyte and gelofusin are not readily available in our state hospitals and therefore may not be well known to many participants which would account for the low numbers using these products.

When confronted with a dehydrated patient intra-operatively a different approach needs to be considered since dehydration differs from acute blood loss in its distribution of fluid depletion. A dehydrated patient has both intravascular and interstitial fluid deficits concurrently. Administering a colloid to replace extravascular losses is futile as most of the fluid will remain in the intravascular compartment, leaving the interstitial compartment un-resuscitated. Chappell et al (7) suggested that the fluid lost from the extravascular space, such as caused by dehydration, should be replaced with a crystalloid because a large proportion of this fluid will redistribute to the interstitial space (7). In this study when presented with a severely dehydrated child, 104 (83.8%) participants would have correctly given a 10-20ml/kg bolus of crystalloid, and the remainder would have used a colloid. It may be rationalised that giving a colloid to replace extravascular losses is futile as most of the fluid will remain in the intravascular compartment and not redistribute quickly enough into the extravascular space as is required for such a patient. 1 (0, 8%) Anaesthetists would have not given this child any fluid bolus. It must be assumed that this survey participant misinterpreted the question as it is unlikely that a clinician would not replace fluid once this diagnosis has been made or worse, that the participant genuinely would not give a dehydrated child fluid.

Designation was the only factor that proved to influence fluid practices in the Department of Anaesthesiology at Wits. Experience and paediatric training did not seem to have an impact on the fluid choices. Senior registrars were more likely to use the 2:1:05 formula and junior registrars were more likely to use the 4:2:1 rule for calculating maintenance fluid (p=0.0239). This may have been influenced by the more senior registrars attending tutorials and conferences that may have influenced their clinical approach.

Designation was the only parameter that influenced certain fluid practices at the Department of Anaesthesiology at Wits. Consultants were more likely to use isotonic solutions for maintenance when compared to other designations

(*p*=0.0212) and they were more likely to use a colloid for resuscitation of acute haemorrhagic shock whereas other designations were inclined to use crystalloids (*p*=0.003). These results reflect the lack of consensus on fluid practices and this emphasizes that paediatric fluid administration is not standardised within the department of anaesthesia at Wits.

4.2.8 Conclusion

The use of standardised fluid protocols is limited because of the significant variability in fluid requirements amongst individual paediatric patients. It is difficult to study which fluid approach is best as there are many confounding factors that influence a patient's fluid needs and outcomes. A universal formula for fluid administration cannot be applied to all patients as it is limited by the fact that patients respond differently to fluid and not all patients require fluid, however the 2:1:0.5 rule seems to be an acceptable starting point for maintenance. There is no consensus in the management of both hemodynamically stable and unstable patients at the Department of Anaesthesiology at Wits and internationally and this is explained by the complexity of fluid management. Implementing a protocol would be futile but a guideline could be beneficial to ensure that a margin of safety is maintained and appropriate peri-operative fluid management adhered to. The results of this study have shown that although the majority of the fluid practices at the Department of Anaesthesiology at Wits are acceptable, some are dangerous and if not corrected may have detrimental outcomes.

CHAPTER 5: SUMMARY, LIMITATIONS, RECOMMENDATIONS AND CONCLUSION

5.1 Introduction

This chapter will present a summary of the aims and objectives, research method and results. The limitation of the study will also be discussed. Relevant recommendations with regards to the practice and guidelines of intra-operative paediatric fluid administration will be made. A conclusion will also be presented.

5.2 Study Summary

5.2.1 Aim

The aim of this study was to determine the practice of intra-operative paediatric fluid management amongst anaesthetists working in the Department of Anaesthesiology at Wits.

5.2.2 Objectives

The primary objectives were:

- To describe the approach to intra-operative fluid management of haemodynamically stable paediatric patients
- To describe the approach to intra-operative fluid management of haemodynamically unstable paediatric patients
- To describe the demographic factors influencing paediatric fluid management
- To describe the use of dextrose intra-operatively

The secondary objective was:

- To describe awareness on intra-operative paediatric fluid guidelines

5.2.3 Summary of methodology

This study was a prospective, observational, cross sectional study describing practice of paediatric fluid administration based on a questionnaire that was distributed. The sample population comprised of anaesthetists that practice at the department of Anaesthesiology at Wits that met the inclusion criteria. A sample size of 61.8% (125 participants) was attained.

The questionnaire consisted of questions as well as vignettes as these offer high internal and external validity in order to show multiple predictors of clinician behavior (23). The survey was adapted with permission from Way et al (16), they had conducted a similar survey in the United Kingdom (Appendix 5). Further questions were developed based on the literature available on the topic thereby ensuring content validity. Face validity was ensured by including suggestions axnd criticisms by four senior anaesthesiologists.

Data was collected from November 2016 to April 2017. The anaesthetists were invited to participate in the study when they attended the weekly academic meetings. A convenient sampling method was used and questionnaires were distributed at random to willing participants and these were filled out before the start of the meeting. Discussion amongst participants was not allowed. Questionnaires were returned in a sealed envelope to a collection box as to ensure anonymity and confidentiality. To further protect the participant from any discrimination, no identifying data was requested on the form.

Data was captured on a Redcap data base and analysis was done using Redcap and Microsoft Excel. Categorical data was summarised with percentages.

Comparisons were analysed using the Chi^2 and Fishers Exact for parametric data and for non-parametric data the Mann Whitney U test was utilised.

5.3 Summary of results

The most common form of fluid replacement discussed in the literature takes into account replacement of pre-operative losses, maintenance and replacement of intra-operative losses (4, 38). This study showed that the Department of Anaesthesiology at Wits by and large follows the same approach. The majority, 111 (95.8%) members of the department appropriately replaced a prolonged starvation period. Even though the concept of third space losses has been disproven, over 48 (40%) anaesthetists in the department still compensate for these losses (7, 53).

There are formulas that may be applied to guide maintenance requirements, however, the fluid status of the patient changes regularly and the rate of fluid administration must be adjusted accordingly. In this study the 2 most popular methods used for calculation of maintenance requirements were the 2:1:0.5 formula used by 48 (38.7%) and the 4:2:1 which was utilised by 46 (37.1%) participants. A significant contrast between the participants in the Way et al (16) study and those partaking in this study is that the majority of participants (67%) working in the UK in 2006 used hypotonic dextrose intra-operatively whereas 104 (86.2%) participants in our study preferred to use an isotonic balanced intravenous fluid. It needs to be mentioned that these two surveys were conducted 11 years apart and perhaps they should not be compared as much change occurs in that time period within the medical field. However, the researcher feels that comparing the studies allows us to prove that practice does in fact change when new literature emerges to suggests that prior practice was harmful.

It was also important to assess which fluids where used in the treatment of hemodynamic instability caused by hypovolaemia. When resuscitating acute hypovolaemia secondary to blood loss, 102 (86.2%) participants administered an adequate bolus of 10-20ml/kg but 13 (10.5%) would have placed patients at risk of

hypervolaemia by initiating a bolus of 40ml/kg. As many as 66 (53.2%) participants initially used a balanced isotonic crystalloid for their fluid bolus and 56 (45.2%) used a colloid, of which voluven was the most popular, used by 40 (32.8%) anaesthetists. In a severely dehydrated patient the majority of participants, 104 (83.8%) participants correctly resuscitated the patient with a crystalloid bolus of 10-20ml/kg but 14 (11.2%) would have incorrectly used a colloid.

There was a wide variation in fluid management practices and it was investigated whether designation, experience or training had any influence over any particular approach. When taking a look at the types of formulas used to calculate intra-operative fluid, it appears that designation (p= 0.2915), experience (p= 0.0856) nor training in paediatric anaesthesia (p=0.0713) had any influence over the method used for calculating intra-operative maintenance. This may reflect inadequate training or simply a lack of consensus due to the complexity of intra-operative fluid management.

Another aspect of fluid management that plays a major part in patient outcomes is the management of blood glucose levels. In this study, 84 (68.2%) of the participants did not routinely add or administer dextrose solutions with the maintenance fluid that they prescribe intra-operatively, but instead would check the patient's blood glucose levels and administer dextrose if required. When hypoglycemia was detected, 56 (45.1%) of participants would have corrected the glucose by giving a 2ml/kg bolus of 10% dextrose solution, as most guidelines recommend, but 50 (40.3%) would have given a bolus of 2ml/kg of a 50% dextrose solution. As many as 13 (10.7%) participants would have just added a 5% dextrose solution to the maintenance infusion without giving a bolus of dextrose intravenously.

In the studies conducted by Way et al (16) and Cannesson et al (106), the majority of the anaesthetic departments that their participants worked at had no departmental guidelines for haemodynamic management of high risk surgical patients. Similarly, the anaesthesiology department at Wits does not have a standard guideline for paediatric peri-operative fluid administration and has also not adopted any particular international guideline. It is left up to the individual

anaesthetist to choose which method of fluid management they prefer to follow. This may explain the large variation in fluid management as shown in the results of this study.

5.4 Limitations

This study is contextual to the department of anaesthesiology at Wits and therefore only represents a small geographic region. Practices in the rest of the country may not echo those found in this study. While the population of the department was 214 at the time of data collection, a sample of only 135 (61,8%) was achieved. Sample size was dependent on the attendance and willingness of participants at the departmental academic meetings and this might not adequately represent the knowledge of the whole department but rather the knowledge of those attending the meetings. Many of those that attended the meetings were people that had attended previous meetings and had already participated in the questionnaire. People excluded from completing the survey included those anaesthetists that had attended the post graduate meeting and thus had previously reviewed the protocol and questionnaire. This resulted in 12 consultants being immediately excluded from participating in the study. The results may have been different if these consultants were eligible to participate as many of them from part of the anaesthetic population that practice paediatric anaesthesia. However, including these consultants would have definitely led to bias and skewing of results because they knew the questions beforehand. Annual leave, maternity leave and anaesthetist attending outreach programs as well as those that don't attend meetings would have also missed the opportunity to participate.

Research suggests that this type of study design is a valid, reliable and practical method of collecting information about clinical practice (25) however, it needs to be acknowledged that this form of research has its own limitations. Although the questionnaire was adapted from a study already conducted in the UK, many questions were changed to suit the South African context and this may have compromised the validity of the survey. Even though it was reviewed by senior colleagues, it is not a standardised questionnaire and many of the questions may

have been misinterpreted by the participants. My assumption is that this holds true as some of the questions had unexpected results.

Another limitation to a survey type study is that the participant may be led to answer questions based on the choices available and not necessarily what the participant would have practiced in a real situation. Some participants may feel that none of the choices presented to them described their practice and therefore may have chosen the closest option. The majority of the study population are doctors that have only worked in the state sector and are not exposed to all the available fluids such as albumin and volulyte. Without having seen or used these fluids before, participants are less likely to have knowledge of their indications.

Another possible source of data contamination was the long duration of data collection. Data was collected over 6 months and the questionnaire may have been discussed outside of the meeting room.

Participants may not have any interest in this particular topic and as a result would not have read and answered the survey questions to the best of their ability. If participants got bored, tired or lost interest in answering accurately, the results would be affected, this is known as survey fatigue. This kind or error will then not reflect true practice as was intended by the study.

5.5 Recommendation

There is a variation in practice amongst the anaesthetists at Wits and there should be a framework in place to try limit incorrect practice and potential harm to the paediatric surgical patients. Anaesthetists at Wits should be made aware of international guidelines available concerning paediatric fluid protocols. It is my recommendation that a document should be made available pertaining to fluid replacement requirements peri-operatively. The replacement of the starvation period and maintenance fluid should be covered during each paediatric rotation within the registrar training program.

Further collaborative research should be conducted on a departmental, regional and national level including multi center analysis in order to establish national guidelines on peri-operative paediatric fluid administration.

5.6 Conclusion

Intravenous fluid is a drug. Prescribing this drug should always be indicated and dosing should be patient specific. Standardisation of fluid administration is very difficult because patients and surgeries will have unique fluid requirements that are influenced by multiple factors. It seems that paediatric fluid administration is not standardised within the department of anaesthesia at Wits. Although it is acknowledged that having everyone adhere to a strict fluid protocol is nonsensical, a framework of safe practice is necessary especially when considering the variation of knowledge and experience of anaesthetists working at the institution. There are currently no departmental guidelines to assist in standardising basic fluid principles.

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Appendix 1: Ethics approval

R14/49 Dr Klaudia Imiolo Bruckmann

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160675

NAME: (Principal Investigator)	Dr Klaudia Imiolo Bruckmann
DEPARTMENT:	Anaesthesiology University of the Witwatersrand Department of Anaesthesiology
PROJECT TITLE:	Anaesthetists' Practice of Intraoperative Fluid Management in the Paediatric Population at Three Academic Hospitals
DATE CONSIDERED:	24/06/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Des Lines
APPROVED BY:	Professor P. Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	15/07/2016

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004,10th floor, Senate House/2nd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. I/We fully understand the the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated,from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially review in June and will therefore be due in the month June each year.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 2: Graduate studies committee approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

18 August 2016
Person No: 0501017F
PAG

Dr KA Imiolo Bruckmann
P O Box 5283
Weltevreden Park
1709
South Africa

Dear Dr Imiolo Bruckmann

Master of Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *Anaesthetists' practice of intraoperative fluid management in the paediatric population at three academic hospitals* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Appendix 3: Participant information letter

Dear Colleague

My name is Klaudia, I am a registrar in the Wits Department of Anaesthesiology. I would like to invite you to take part in my MMed research survey entitled "Anaesthetists' practice of intra-operative fluid management in the paediatric population at three academic hospitals."

Fluid administration is an integral part of any anaesthetic and may influence the post-operative outcome of our patients. The objective of the study is to describe the practice of intra-operative fluid administration in the setting of paediatricanaesthesia within the Wits Department of Anaesthesiology. The study will aim to determine whether there is safe and appropriate practice in terms of fluid administration and in view of the results whether a guideline needs to be established.

The questionnaire will take approximately 15 minutes to complete. No incentives will be provided to complete the survey and participation is voluntary. Consent will be implied by the return of a completed questionnaire. There will be no judgment or penalty if you choose not to participate in the study. Information is kept anonymous and no personal information is required. Only the researcher and supervisors will have access to the raw data.
Complete the questions in the context of what you practice, sharing information between participants may skew results.

Thank you for taking time to read this information and for assisting me with my MMed study. If you have any questions please don't hesitate to contact me:
KlaudiaImioloBruckmann: 0822916421

Appendix 4: Questionnaire

Section 1: Demographics

1.1) Which hospital are you currently based at?

Charlotte Maxeke Johannesburg Academic Hospital	
Helen Joseph Hospital	
Chris Hani Baragwanath Academic Hospital	
RahimaMoosa Mother and Child Hospital	

1.2) How many years of anaesthetic experience do you have?

.....

1.3) Designation

Medical Officer	
Registrar (1-2 years)	
Registrar (3-5 years)	
Career medical officer/ consultant	

1.4) How frequently do you anaesthetise children?

I do not anaesthetise children	
<5 cases per month	
>5 cases per month	

If you do not practice paediatricanaesthesia you may stop the survey here and return it.

1.5) Have you had any specialist training in paediatricanaesthesia?

1.5.1) During registrar training or time as a medical officer:

Yes	
No	

1.5.2) After completion of registrar time (if applicable):

Yes	
No	

If you have answered yes to question 1.5 please give details of your training

.....

Section 2 : Knowledge of practice guidelines and formulas

2.1) Are you aware of any international or national intra-operative paediatric fluid prescribing protocol or guideline?

Yes	
No	

If you have answered yes to question 2.1 please specify which guidelines or formula's you are referring to.

.....

.....

2.2) Does your department have a guideline/protocol for intra-operative fluid management in paediatric patients?

Yes	
No	
I don't know	

Section 3: Practical approach to fluid therapy

3.1) A 3 year old boy with no co-morbidities weighing 15 kg has been booked for an elective inguinal mass to be excised.He is haemodynamically stable with no signs of dehydration and the surgery will last approximately 2 hours. His heart rate (HR) is 80 beats per minute (bpm), and his blood pressure (BP) is 92/45 mmHg with a mean arterial pressure (MAP) of 60 mmHg. You will be responsible for administering his anaesthetic.

3.1.1) What formula, if any, do you use to determine the volume of maintenance fluids to be given intra-operatively to a well paediatric surgical patient?

.....

3.1.2) Indicate with a tick what you would replace intra-operatively for the two different starvation periods:

	Received oral fluids 2 hours prior to surgery	Starved for 12 hours
Starvation period		
Maintenance		
Surgical losses		
3rd space losses		

3.1.3) Choose your one preferred intravenous fluid you would administer for maintenance fluid requirements?

a) Balsol (Plasmalyte B)
b) Half Darrows Dextrose
c) 5% maintelyte (paediatric maintelyte)
d) 0.9% Normal Saline
e) Ringers Lactate

f) Other

3.1.4) If you have answered “other” please specify:

.....

3.1.5) Would you routinely add dextrose to your chosen intravenous solution?

Yes	
No	

3.2) During the procedure the surgeon alerts you that he has mistakenly severed the femoral artery. You notice the patients HR (heart rate) has increased to 150 bpm and his BP (Blood Pressure) has dropped to 70/40 mmHg. You asses that he has lost 250 ml of blood and he is hypovolaemic.

3.2.1) What fluid do you choose to administer as an intravenous fluid bolus

a) 0.9% Normal Saline
b) Ringers Lactate
c) Voluven
d) Gelafusin
e) Albumin
f) Balsol
g) Other

3.2.2) If you have answered “other” please specify:

.....

3.2.3) Referring to the scenario in 3.2, what volume of an initial bolus would you administer?

a) 10 ml/kg
b) 20 ml/kg
c) 40 ml/kg
d) 200 ml Stat

3.3) You are consulted by the paediatric surgeon for a 6 month old girl with a possible bowel obstruction for emergency surgery. She has been vomiting and has not passed urine for the past 10 hours. You assess the patient clinically and she is lethargic, has sunken eyes, HR is 160 bpm and capillary refill time of 4 seconds.

3.4)

3.3.1) What would your clinical assessment and treatment be of her fluid status? Place a tick next to your choice:

Assesment:

Percentage (%) dehydrated	
<5%	
5%	
5-10%	
>10%	

Treatment:

Required Bolus	
No bolus is required	
Crystalloid bolus of 5ml/kg	
Crystaloid bolus of 10-20ml/kg	
Colloid bolus of 10-20ml/kg	

3.3.2) She has a blood glucose of 2.0 mmol/l. How would you replace the glucose?

Administer 5% dextrose with the maintenance fluid	
Administer a 2 ml/kg bolus of a 10% dextrose solution	
Administer a 2ml/kg bolus of a 50% dextrose solution	
No need to replace the glucose	

3.4. A healthy 18 month old child has been starved for 10 hours for a minor surgical procedure. What is your practice of dextrose administration intra-operatively?

Administer 1% dextrose with the maintenance fluid	
Administer 2% dextrose with the maintenance fluid	
Administer 5% dextrose with the maintenance fluid	
Check HGT's once and replace accordingly	
Monitor HGT's regularly and replace accordingly	
No need for dextrose administration	

3.5. On average how many hours are paediatric patients being starved at your current hospital prior to surgery?

.....
..

Appendix 5: Letter of permission

On 19 Jan 2016, at 18:23, KlaudiaImiolo<klaudiaimiolo@gmail.com> wrote:
Good Day Dr Walker
My name is KlaudiaImiolo, I am an Anaesthesiology Registrar at the University of Witwatersrand, Johannesburg, South Africa. I am doing research on our current practice of intra-operative fluid administration and came across your study in the British Journal of Anaesthesia 97 (3): 371–9 (2006) : **Peri-operative fluid therapy in children: a survey of current prescribing practice C. Way, R. Dhamrait, A. Wade and I. Walker.**
It was a very intriguing study and very similar to what I have wanted to establish in our own teaching hospitals. We currently have no data on our peri-operative fluid practices and I would like to base my research study on this. Would you be willing to grant me permission to use a similar survey to yours in my research which would be referenced accordingly?

Kindest Regards
Dr. K. Imiolo
MBBCh (WITS), DA (CMSA)

Jan 19

Isabeau Walker <Isabeau.Walker@gosh.nhs.uk>

Hi Klaudia - very happy! I'd be interested to hear what you find out.
All the best,
Isabeau