
# An audit of uterotonic use for the prophylaxis and treatment of haemorrhage at caesarean delivery at Mowbray Maternity Hospital, Cape Town, South Africa

Thesis submitted in partial fulfilment for the
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## Abbreviations

| | |
|---|---|
| ACOG | American College of Obstetricians and Gynaecologists |
| BANC | Basic Antenatal Clinic |
| BLDACD | Bleeding associated with caesarean delivery |
| BMI | Body mass index |
| CD | Caesarean delivery |
| CEMD | Confidential Enquiry into Maternal Deaths |
| GA | General anaesthetic |
| GSH | Groote Schuur Hospital |
| IM | Intramuscular |
| IU | International Units |
| IV | Intravenous injection |
| MMH | Mowbray Maternity Hospital |
| MMR | Maternal Mortality Ratio |
| MOU | Midwife Obstetric Unit |
| MRL | Modified ringers lactate |
| NCCEMD | National Committee for Confidential Enquiry into Maternal Deaths |
| NDOH | National Department of Health, South Africa |
| OH | Obstetric Haemorrhage |
| PPH | Postpartum Haemorrhage |
| RANZCOG | Royal Australian and New Zealand College of Obstetricians and Gynaecologists |
| RCOG | Royal College of Obstetricians and Gynaecologists |
| SA | South Africa |
| SDG | Sustainable Development Goals |
| SOGC | Society of Obstetricians and Gynaecologists of Canada |
| TXA | Tranexamic acid |
| UK | United Kingdom |
| VBAC | Vaginal delivery after CD |
| WHO | World Health Organization |

# Abstract

Obstetric Haemorrhage is the leading cause of maternal death globally (1) and the third leading cause of death in South Africa (2). Concern has been expressed in South Africa that bleeding associated with caesarean delivery (CD) accounts for one-third of haemorrhage deaths and this has increased over the last ten years (3). The underlying cause of bleeding at CD is commonly uterine atony, and the majority of the CDs were performed at district hospitals (2,3,4). The Saving Mothers Reports describe inadequate use and documentation of uterotonics to prevent or treat bleeding at CD and have promoted the development of a standardised national protocol. While there is international agreement on the dosage and administration route for oxytocin to prevent OH after vaginal delivery, there is lack of consensus or standardisation of protocols for its prophylactic use at CD, with marked differences between country and facility protocols. Anaesthetists are concerned about the hypotensive effect of high dose intravenous boluses of oxytocin, particularly in women under spinal anaesthesia, and some maternal mortalities in the United Kingdom have been partially attributed to this (5). Hence it is important to balance safety with efficacy by promoting the lowest effective doses to minimise side effects but enable uterine contraction.

**Aim**

The aim of this study was to perform a clinical audit of the documented use of uterotonics at CD at MMH to see how it adheres to the national protocol; and as a secondary outcome to measure the rate of haemorrhage at CD.

**Methods**

This was a retrospective folder review of women who delivered by CD at MMH during the months of June and July 2017, including both elective and emergency operations. Information was obtained from women's folders kept in the medical records department, using especially designed data extraction sheets. Data analysis was by simple descriptive statistics.

**Results**

Three hundred and nineteen (319) folders from the study period were interrogated. This included 239 emergency CDs (75%) and 80 elective CDs (25%). They were all performed by obstetric registrars or medical officers with 89% being done under spinal anesthesia. Prophylactic oxytocin boluses at CD were given in 302 (94.7%) women but there was no documentation of its use in 17 (5.3%). One of the 302 women had a high dose IV bolus (7.5 IU) but the remainder had boluses below 5 IU. There were 75 women (23.5%) patients who received the national recommended dose of 2.5 IU IVI while 227 (71.1%) received

alternative low dose boluses which were all less than 5 IU. The dose most commonly given was 3 IU; to 169 patients (53%) as a single or divided dose. There was wide variation in the dosage of prophylactic infusions with only 18 (5.6%) patients receiving the recommended intraoperative 7.5 IU infusion, while 221 (66.5%) received alternate infusion doses. Only 49 (15%) were discharged from theatre recovery to the postnatal ward with a prophylactic infusion running. In total 65 (20.4%) of the women received a 20 IU oxytocin infusion but it was unclear whether this was for prophylaxis or treatment. No intramuscular doses of oxytocin or syntometrine were given for prophylaxis. Among the 319 CDs, 13 (4.1%) had documented blood loss over 1000 ml and 24 (7.5%) had uterine atony reported by the surgeon. The most common treatment was 20 IU infusion followed by misoprostol (13 women), syntometrine (three women) and tranexamic acid (one woman). Additional surgical measures required were B-Lynch compression suture for one, and haemostatic sutures for two. There were no re-look laparotomies or hysterectomies during the study period and there were no major morbidity or mortalities from either CD or from anaesthetic complications.

**Discussion**

Low dose bolus oxytocin and infusion is widely used at CD post fetal delivery at MMH, although the dose of 3 IU was most commonly used in contrast to the recommended 2.5 IU in the national protocol. There was variation in the usage and dosage of prophylactic oxytocin infusion. The rate of PPH in the subjects was low (4.1%) with the low dose prophylactic regimens used, suggesting that they were effective, although this may also have been contributed to by the skill of the surgeons. Consensus is needed among anaesthetists and standardisation of protocols on oxytocin prophylaxis at CD, particularly for training doctors working in district hospitals. Repeating this audit in district hospitals where there are higher CD case fatality rates would be important to shed light on practice in such facilities and improve healthcare delivery.

## Table of Contents

# List of Tables

# List of Figures

# Chapter 1: Introduction

## 1.1 Background

Obstetric haemorrhage (OH) remains an important cause of maternal morbidity and mortality globally. It is estimated that up to 800 women die per day worldwide as a consequence of pregnancy and childbirth, with haemorrhage accounting for two-thirds of these deaths (3). Most of this bleeding is related to uterine atony. In South Africa, OH has featured among the top three causes of maternal mortality in recent triennial publications of the Saving Mothers Reports which describe findings of the Confidential Enquiry into Maternal Deaths in South Africa (CEMD) (2,4,5). An important component of this problem is bleeding at caesarean delivery (CD) which has increased markedly in the last ten years as a cause of maternal death. Bleeding during or after caesarean delivery (BLDACD) accounts for nearly a third of deaths related to obstetric haemorrhage (221 deaths during 2011-2013) and this occurs mainly at level one and two hospitals (6). The mortality rate due to BLDACD is markedly lower in the Western Cape compared to the rest of South Africa and this is reflected in the statistics of Mowbray Maternity Hospital (MMH) where in three years there have been two deaths from this condition out of 15000 CDs. Nearly 5000 CDs are performed annually at MMH with a case fatality rate of 16.6 per 10000 CS compared to 33.6 in South Africa for a similar time period.

A common cause of CD associated bleeding is uterine atony. One of the measures put in place to prevent or treat bleeding at CD includes the routine and therapeutic use of various uterotonic drugs to aid uterine contractility. There has been widespread discussion and conflicting views between obstetricians and anaesthetists about safe but effective doses particularly of oxytocin, but also of misoprostol and ergometrine. Obstetricians promote the use of prophylactic oxytocin at CD, but anaesthetists are concerned about the potential of high dose intravenous boluses to cause hypotension (7,8). The 2011-2013 triennial Saving Mothers Report reports that inadequate doses of uterotonics were administered in many of the deaths from BLDACD, but also that in many case files there was no documentation concerning if and what uterotonic was administered (2). Protocols have been put in place, disseminated and published by the National Committee on Confidential Enquiry into Maternal Deaths (NCCEMD) for the Department of Health on the prevention and management of BLDACD (9). These include an updated consensus policy on recommended use of uterotonics at CD (10).

## 1.2 Rationale for current study

There is a dearth of studies that have audited uterotonic use in maternity units especially, in Sub-Saharan Africa or other low resource settings where the burden of OH is greatest. There is not much literature addressing the compliance of maternity units to set protocols for the

prophylaxis and treatment of PPH, particularly at CD. An audit of oxytocin use in a tertiary level hospital in Botswana found that there were no standardised protocols for oxytocin use at CD and as a result prescribing practice differed significantly among the healthcare workers, with some giving as high as 20 IU intravenous bolus of oxytocin (11).

The other concern raised by the Saving Mothers Report (2011-2013) was that documentation was poor, which made it difficult to properly assess whether uterotonics were administered as per protocols. A study on peripartum hysterectomy in the UK found that some women who had a hysterectomy as treatment for PPH did not have any uterotonic administered to them, while another subset (23%) of women in the same study had only one uterotonic given before hysterectomy (12). This may reflect lack of documentation as in South Africa, or that it was not given or not thought to be indicated.

The question for this study is whether MMH is documenting the administration of uterotonics at CD and adhering to the recommended protocols for their use in prophylaxis and treatment of PPH. The hypothesis for the current study is that MMH is using adequate uterotonic therapy both for prophylaxis and treatment and documenting their administration.

# Chapter 2. Literature Review

## 2.1 Introduction

Maternal mortality is defined by the World Health Organization (WHO) as the death of a woman while pregnant or within 42 days after termination of a pregnancy, no matter how long the gestation was or where the pregnancy was located, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes (13). Maternal mortality has for a long time been a bane of many health systems globally. The developed world has led the way in reducing the scourge of mothers dying in delivery, while the developing countries continue to report ongoing maternal deaths. Estimates by the WHO show that an alarming 99% (302,000) of all maternal deaths in the world in 2015 occurred in developing countries, with the Sub-Saharan African region alone accounting for 66% of the deaths (14), many of which were preventable.

The impact of maternal deaths on society is dire and the effects are felt and are more pronounced in the developing world than the developed world (15). Studies in East Africa have shown that the consequences of a maternal death or disabling injury secondary to pregnancy complications not only impact the immediate grieving family but the community as well. The impact is felt not only in the immediate future but for generations to come (15). Some of the issues include financial instability in the household and for the relatives who have to take over the care of orphaned children, which comes with great financial burden. There is also disruption of schooling and education and increased mortality among children whose mothers have died, related to difficulty managing the household by the bereaved fathers. Similar findings were found in a study from rural China (16).

Efforts have previously been made to address maternal deaths globally, for example, the 1987 Safe Motherhood Conference, and the 1995 Beijing World Congress on Women, but they have had little impact. The issue of maternal and reproductive health was brought into the spotlight when the United Nations met in the groundbreaking Millennium Summit in the year 2000 and proclaimed the Millennium Development Goals, one of which, Goal 5, was the improvement of maternal health (17). The target was reduction of maternal deaths by 75% by the year 2015. Overall maternal deaths decreased from 532,000 in 1990 to 303,000 in 2015. Global MMR declined by 45% with slowest improvements in countries of Sub-Saharan Africa (1,18). Only eight nations managed to achieve a 75% reduction in maternal deaths, of which one, Rwanda, is on the African continent (3).

As 2015 came to an end, a transition to a new set of United Nations goals, commonly known as the Sustainable Development Goals (SDG), came into being. There are 17 SDGs which are tied to 169 targets. Goal 3 of the SDGs is geared at ensuring healthy lives and the promotion of well-being for all. With respect to maternal mortality, the target is reduction by the year 2030 of the global MMR to 70 deaths per 100,000 live births, with no country having an MMR of more than 140 (1).

Of the many causes of maternal death and severe morbidity, obstetric haemorrhage is the leading cause of maternal deaths globally. A reported 127,000 women die yearly from obstetric haemorrhage and the rates are 14 times higher in developing countries compared to developed countries. The 2011-2013 triennial report on maternal deaths from the United Kingdom (UK) indicated that 13 women died as a result of OH (19); this compares with 684 deaths in South Africa in the same time period (2). The concerning aspect of deaths resulting from obstetric haemorrhage in South Africa is that the majority (89%) during 2011-2013 were preventable.

Postpartum haemorrhage (PPH) is the most common type of obstetric haemorrhage. The number of women dying from PPH is greatest in low resource settings compared to well-resourced countries where PPH tends to be a more frequent cause of morbidity than mortality (20). In Uganda, PPH causes 25% of all maternal deaths, whereas in the United States it is the fourth leading cause of maternal death, accounting for 13.4% of maternal deaths. PPH occurring at or after CD has been implicated in a rising number of maternal deaths in South Africa. In three successive triennial reports a steady increase in deaths at or during CD has been reported, with 221 deaths in the last report (2011-2013), compared to 180 in the previous report period (5). Caesarean delivery rates are increasing globally and in South Africa, with the potential to increase the problem of bleeding at CD. This is particularly relevant in South Africa where CDs are performed at all levels of care, including by non-specialist doctors at district hospitals.

Uterine atony has been identified as a leading cause of PPH after vaginal delivery and also at CD. Uterine atony is defined as the failure of the uterus to have sustained, proper haemostatic contractions. The causes of uterine atony include uterine over-distension (multiple gestation), intrinsic uterine dysfunction (prolonged labour), retained products of conception, abnormal placentation and iatrogenic causes such as volatile anaesthetics. In one large population based retrospective study of 649,000 childbirths (vaginal, instrumental, elective and emergency CD) from Ireland, uterine atony was responsible for 75.7% of PPH diagnoses (21). Other common causes include genital tract trauma and rarely, coagulation disorders.

The routine use of uterotonics at delivery has been advocated by many international societies and organisations as one of the measures for combating uterine atony and thus ameliorating the risk of PPH. However, it has been noted by several investigators that uterotonics are not routinely administered to all patients which thus puts parturients at risk for PPH (2,12). Documentation of uterotonic use at CD is a particular problem. According to the authors of the Saving Mothers Report 2011-2013, several issues regarding the administration of uterotonics at CD were identified from folder reviews of maternal deaths attributed to PPH:

a) poor documentation of whether any uterotonics were given;
b) inadequate doses of uterotonics were administered,
c) poor documentation of the route, timing or if any repeat doses were given; and
d) inadequate documentation as to whether any additional uterotonics were given.

There are several uterotonic medications available to healthcare workers managing patients at delivery in South Africa.

## 2.2 Oxytocin

Oxytocin is a neuropeptide that was discovered and synthesised in the early 1950s. It is produced in the paraventricular nuclei in the hypothalamus and released in a pulsatile manner by the posterior pituitary into the circulation where it binds to its receptor on uterine muscle cells and acts via intracellular messenger systems to increase the concentration of intracellular calcium. Intracellular calcium activates calmodulin and myosin light chain kinase leading to uterine muscle contraction. Oxytocin is widely distributed in the extracellular space and is metabolised by the gastrointestinal enzyme chymotrypsin. In the pregnant subject oxytocinase is produced early in the pregnancy and metabolises oxytocin.

Prophylactic uterotonic (oxytocin) use after vaginal delivery is a well-established obstetric practice with robust evidence to back up its use (22). Oxytocin has been found to reduce the risk of PPH by at least 40% and is the drug of choice when compared to placebo following vaginal delivery (23). Thus 10 IU IMI oxytocin is recommended by the WHO and the South African National Department of Health (DOH) as the uterotonic of choice for the prophylaxis of postpartum haemorrhage after vaginal delivery (22,24). However, the optimal route of administration and dose of prophylactic oxytocin at CD where there is intravenous access, has been less studied. Globally there are wide variations in the use of oxytocin at CD and even where guidelines exist, surveys among obstetric practitioners have revealed inconsistencies in usage (25).

### 2.2.1 Haemodynamic effects of oxytocin

Concerns have been raised about the side effect profile (26) of oxytocin by the anaesthetic community, especially its effects on haemodynamic instability and water intoxication. Intravenous boluses of oxytocin are known to cause hypotension especially when 10 IU oxytocin IVI or more are given rapidly as a bolus (26). Oxytocin causes hypotension by transiently relaxing vascular smooth musculature via triggering the nitric oxide pathway. This results in the mean arterial blood pressure decreasing and associated with a reflex tachycardia and increase in cardiac output which are easily tolerated by the well woman undergoing CD; however, these can cause significant harm in those not able to compensate adequately, like cardiac or hypovolemic patients. Studies comparing bolus administration versus infusion have consistently showed that the haemodynamic changes are not profound when oxytocin is given as an infusion (27). Oxytocin can also cause myocardial ischemia, arrhythmias, headache, nausea, flushing and vomiting. Also of concern is that prolonged use of high doses of oxytocin in infusions may cause minor activation of vasopressor and antidiuretic hormones which may produce water intoxication, hypotension and hyponatremia (28,29).

Spinal anaesthesia is the most commonly used mode of anaesthesia for obstetrics in primary and regional hospitals in South Africa (30). Hypotension and bradycardia are common side effects of spinal anaesthesia as a result of anaesthetized sympathetic innervation (31). This hypotension may be potentiated by oxytocin use, especially at high doses, and blood loss that occurs at CD.

There have been reports from the UK of deaths that were attributed to oxytocin; these, however, were in haemodynamically unstable women (32). In some of the cases reviewed in the UK incidences of healthcare providers giving higher than recommended doses of oxytocin were encountered (33). These side effects can be counteracted by infusing oxytocin with isotonic solutions like ringer's lactate and normal saline.

### 2.2.2 International guidelines on oxytocin use at CD

The Royal College of Obstetricians and Gynaecologists (RCOG) and the British National Formulary in the UK recommend for PPH prophylaxis at CD, that 5 IU oxytocin be given by slow intravenous injection (34,35).

In the United States of America, the American College of Obstetricians and Gynaecologists (ACOG) does not specify the agent, dose or route of administration for PPH prophylaxis at CD, but rather advises that individual obstetric units should have guidelines for the routine administration of uterotonics in the immediate postpartum period (36). For acute medical management of PPH caused by uterine atony, ACOG state that the choice of the uterotonic agent, bar any known contraindications, is at the discretion of the practitioner because no one

agent has been shown to be superior to another for the treatment of uterine atony. With specific regard to oxytocin, ACOG recommends an infusion of oxytocin 10 – 40 IU in 500 – 1000 ml as a continuous infusion or 10 IU IMI (36).

The Society of Obstetricians and Gynaecologists of Canada (SOGC) recommends oxytocin for vaginal deliveries while carbetocin 100 micrograms IVI slow infusion over one minute is recommended for PPH prevention at CD and in women with at least one risk factor for PPH (37).

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) recommends oxytocin as the prophylactic uterotonic for both vaginal and CD, however neither the dose nor route is specified (38).

The WHO recommends either IM or IV 10 IU oxytocin for the prevention of PPH after vaginal delivery; and intravenous oxytocin for the treatment of PPH by slow bolus at CD, but does not specify the dose (22).

The use of 5 IU oxytocin bolus, as recommended by the RCOG, has been suggested to be too high by some authorities, given the above side effect profile of the drug. Doses as low as 0.5 – 3 IU have been found to be sufficient to cause adequate uterine contractions (39,40).

In South Africa, the dosing of oxytocin and indeed a stepwise approach to administration of uterotonics at CD was described in the PPH monograph (8) and updated after consensus was reached among anaesthetists and agreed upon with obstetricians (10). It is reproduced in Table 2.1 below. The recommendation at CD is for oxytocin 2.5 IU IVI to be given as a slow bolus over 30 seconds which should be repeated if the uterus remains atonic. It should be followed by 7.5 IU IVI in the remaining IV fluid as an infusion. A further infusion of 20 IU in a 1000 ml running at 125 ml over eight hours would then be administered as a prophylactic postpartum infusion. The South African guideline also gives an option for intramuscular use of oxytocin at CD and syntometrine post CD in women with no contraindications to the latter and in situations where IV infusions cannot be maintained.

In one trial, the administration of an oxytocin bolus and subsequent infusion have been found to be superior to an oxytocin bolus only in that there was no need for additional uterotonic use in the bolus and infusion arm compared to oxytocin bolus alone (41).

**Table 2.1: Recommended algorithm for use of oxytocin and other agents at CD in South Africa (10)**

| Stage | Option 1<br>***(Suitable for units equipped with volumetric pumps, syringe drivers and trained anaesthetists)*** | Option 2<br>***(Suitable for resource constrained units)*** |
|---|---|---|
| **Step 1:**<br>*All Cases* | 1. Oxytocin 2.5iu ivi slow bolus (over 30 secs)<br>2. Oxytocin 7.5 iu in remaining ivi fluid to running in<br>3. Oxytocin infusion 20iu/1000mls@125mls/hr | 1. Syntometrine ® 1 amp in left deltoid after delivery baby (be aware of contraindications)<br>***If contraindicated***<br>Syntocinon 10 iu in left deltoid after delivery baby (repeat at 4 hours in ward) |
| **Step 2:**<br>*Ongoing uterine atony at 3 minutes* | 1. Repeat oxytocin 2.5iu ivi slow bolus (over 30 secs)<br>2. Oxytocin infusion 20iu/1000mls@125mls/hr | Ensure total misoprostol dose is 600 mcg in last eight hours |
| **Step 3:**<br>*Actively Bleeding cases* | 1. Ergometrine 0.2mg ivi slow bolus repeated up to 1.0 mg<br>**Or**<br>Syntometrine 0.1mg/1iu ivi slow bolus (over 30 secs) repeated up to 0.5 mg/5iu<br>2. Oxytocin infusion 40iu/1000mls@125mls/hr<br>3. Cyclokapron 1g ivi<br>4. Check coagulation profile<br>5. Administer blood and FDP/FFP | 1. Repeat IMI dose in Right deltoid<br>2. Cyclokapron 1g ivi<br>3. Check coagulation profile<br>4. Administer blood and FDP/FFP products<br>5. Inform referral hospital of problem |
| **Step 4:**<br>*Resistant Bleeding Cases* | 1. Ensure total misoprostol dose is 600 mcg in last eight hours<br>2. Consider intramyometrial Prostaglandin F2 alpha (250 mcg)<br>3. Check fibrinogen levels<br>4. Follow massive transfusion protocol | Pack uterus and transfer |

Most international guidelines, including the South African guidelines, recommend a 20 – 40 IU oxytocin infusion as the first measure for treating PPH due to uterine atony (8,10,11,21,30,31,32). In the setting of acute postpartum haemorrhage, oxytocin is ideal since it has a fast onset of action of three to five minutes, when given intravenously (42) while its half-life is 10 minutes.

## 2.3 Misoprostol

While oxytocin is the drug of choice for PPH prophylaxis, one of its main drawbacks is the requirement for strict cold chain, need for parenteral administration, need for sterile equipment and trained personnel, thus making it unsuitable for many low resource settings. An alternative, second line uterotonic in low resource settings is misoprostol. Misoprostol is a prostaglandin E1 analogue that is used off label to cause uterine contractions. Initially registered for gastrointestinal peptic ulcer disease caused by nonsteroidal anti-inflammatory use, misoprostol has widespread evidence based use in terminations of pregnancy, induction of labour, and can be considered in the treatment and prophylaxis of PPH. Evidence shows it is inferior to oxytocin when given both for PPH prophylaxis and treatment (43). Its main advantage is ease of use, no need for the cold chain, wide availability, low cost and no need for special equipment or specialised personnel. However, its side effect profile includes shivering which can occur in up to 75% of recipients and raising of maternal temperature (28,44). The onset of action of misoprostol given orally is eight minutes, while by other routes it is even slower (11 minutes, 20 minutes, 100 minutes for sublingual, vaginal and rectal, respectively) (45), however it has longer duration of action, up to four hours when administered rectally and vaginally. This long duration of action certainly has advantages for areas where postpartum monitoring of patients is not ideal. Poor monitoring of patients postpartum by nursing personnel has been identified in previous Saving Mothers Reports as one of the contributing factors in PPH related deaths.

## 2.4 Carbetocin

Carbetocin, 1-desamino-1-monocarbo-(2-*O*-methyltyrosine)-oxytocin, is a synthetic oxytocin analogue (46) which has a longer half-life of 40 minutes compared to oxytocin. It is indicated for PPH prophylaxis at CD after delivery of the placenta and can be administered either intravenously or intramuscularly at a dose of 100 micrograms. Rhythmic uterine contractions last 60 minutes after IV administration and 120 minutes after intramuscular administration (47). The side effect profile of carbetocin is similar to that of oxytocin and randomised controlled trials comparing the two show that one dose of parenteral carbetocin is as effective as an infusion of continuous oxytocin in maintaining uterine tone, and is more reliable than an oxytocin infusion which is difficult to maintain with limited staff numbers (48). Because of the prolonged duration of action, monitoring of patients postoperatively on carbetocin is not labour intensive. A new formulation of carbetocin that is stable at room temperature and thus does not require refrigeration has been under investigation in a large randomized non inferiority trial to compare it with oxytocin (CHAMPION trial) (49). The recently published results show that heat stable carbetocin is not inferior to oxytocin in preventing blood loss of 500 ml or in the use of additional

uterotonic agents. It is also not inferior in preventing blood loss ≥ 1000 ml, although the study was not powered for this finding because of low rates of this event.

## 2.5 Ergometrine

Ergometrine is an ergot derivative that has agonist properties at alpha adrenergic receptors thus causes sustained uterine contraction. It has a short onset of action within a minute of intramuscular injection and has a long half-life of up to two hours. It is indicated for the prophylaxis and treatment of PPH, however it has side effects which have led to a reduction in its use. These include nausea and emesis, and it is contraindicated in hypertensive and cardiac patients. However, where no contraindication exists it is very effective and is the second line agent for treating uterine atony in the South African protocol. Ergometrine is often combined with oxytocin as syntometrine (5 IU oxytocin and 0.5 mg ergometrine) and this combination has been found to be superior to oxytocin administered alone (50). The time of onset of syntometrine is shorter when administered intramuscularly than that of ergometrine alone and it has a longer duration of action. Syntometrine compared to oxytocin alone, has been found in a randomised controlled trial on CD PPH prophylaxis in Pretoria, South Africa to reduce by more than half the need for postpartum transfusion based on clinical need (51). Syntometrine or ergometrine can also replace a post CD oxytocin infusion in low resource settings where there is no capacity to maintain an infusion in a postnatal ward.

## 2.6 Tranexamic acid

The use of tranexamic acid, a systematic antifibrinolytic medication which can be administered IV for the prevention of PPH, was recently investigated in the World Maternal Antifibrinolytic (WOMAN) trial. Results show that there is a significant reduction in the number of deaths from PPH and in the number of laparotomies performed to control bleeding in women given tranexamic acid early (within three hours) after delivery compared to placebo (52). Also of note, is that thromboembolic events in both arms of the WOMAN trial were similar. Tranexamic acid has been used in non-obstetric trauma patients to prevent fibrinolysis and results of a large CRASH 2 trial showed a reduction in mortality in this patient group (53). A systematic review of tranexamic acid use preoperatively before skin incision showed a significant decrease in blood loss with no differences in thromboembolic episodes between controls and the treatment arms. The WHO has in the past (2012) recommended the use of tranexamic acid when uterotonics fail to control bleeding, with a caveat that the recommendation was based on moderate strength evidence. With the recent release of the WOMAN trial results, there is now more robust evidence to incorporate parenteral tranexamic acid into obstetric protocols for PPH treatment (54). More work still needs to be done on the use of oral tranexamic acid for use in less well-

resourced settings. At the time of conducting this study, TXA use for PPH was not widespread in South Africa and it was not available at primary care.

## 2.7 Surgical technique

Haemorrhage at or after CD can also be prevented by good surgical technique at the primary surgery. Care should be taken with incisions on the abdomen and uterine walls to avoid extension of incisions and to ensure good hemostasis. Uterine incision should be extended by blunt dissection instead of sharp extension because of decreased blood loss, decreased postpartum haemorrhage and need for transfusion. Placental delivery should be by controlled cord traction instead of manual removal, with a uterotonic given to all women at placental delivery. Where there is poor response to uterotonics and tranexamic acid, insertion of uterine compression sutures such as the B-Lynch suture, assist in maintaining uterine compression. Uterine balloon tamponade is valuable where there is placental site bleeding such as in cases of placenta previa (9). Uterine artery ligation is another surgical measure that reduces uterine bleeding allowing conservation of the uterus. If bleeding is noted after the CD, a relook laparotomy is strongly encouraged and should be undertaken. The goal of the surgeon at the relook laparotomy is to try and stop bleeding by using the least invasive methods possible (uterine artery ligation, balloon tamponade, compression sutures) progressing eventually to hysterectomy. However, the surgeon should not feel compelled to go through all the different steps first before performing a lifesaving hysterectomy (55,56).

# Chapter 3: Aims and Objectives

## 3.1 Overall aim

The aim of this study was to perform an audit of prophylactic and therapeutic use of uterotonic medications at CD.

## 3.2 Specific primary objectives

1. To describe the uterotonic drugs, dosages and routes of administration given for PPH prophylaxis to women having CD.
2. To describe the uterotonic drugs, dosages and routes of administration given for management of PPH in women having CD.

## 3.3 Specific secondary objectives

3. To determine the proportion of CD women who developed postpartum haemorrhage, and its management.
4. To determine how MMH practices adhere to the national recommendations on uterotonic use for PPH prevention and management at CD.

# Chapter 4: Methodology

## 4.1. Study design

This was a retrospective descriptive clinical audit.

## 4.2. Study setting

The study was conducted at MMH in Cape Town. MMH is a 130 bed, regional/secondary level hospital in the Metro West Health District that offers maternity and neonatal services to a catchment area served by five midwife obstetric units (MOUs). These currently are False Bay, Gugulethu, Mitchell's Plain, Hanover Park and Retreat. MMH conducts on average 850-900 deliveries per month with 45% of these being CDs (57). As a teaching hospital, obstetric services are consultant led with registrars/residents, medical officers and junior doctors (interns, community service doctors) in training making up the bulk of the medical team. The majority of the CDs are performed by the registrars and medical officers; as is usually the case in comparable South African hospitals. All non-specialist doctors need to be accredited by a consultant before they can perform CDs independently. A consultant obstetrician is always available, onsite during daylight hours, and afterhours on standby off site to come to assist with difficult CDs and perform peripartum hysterectomies where necessary. Similarly, consultant anaesthetists are on site during the working day to assist anaesthetic registrars and medical officers who perform the majority of anaesthetics and are available for problems after hours.

The population profile served by MMH is diverse. The women are from different socioeconomic backgrounds, mainly low to middle income and of varying racial, religious and national backgrounds.

Obstetric care in South Africa is provided free of charge in the Public Sector. On recognising that they are pregnant, women are encouraged to 'book' or register for antenatal care at an MOU or Basic Antenatal Clinic (BANC) nearest to them. MOUs, as the name suggests, are midwife run and led, with support outreach visits from their referral hospitals. Basic obstetric care and deliveries are performed at the MOUs. Any complicated women either antenatally, intrapartum or postpartum are referred onwards to higher levels of care as per local protocols that are widely distributed in the MOUs. Secondary level referrals are sent to MMH which may in part explain the high CD rate described above. Women with previous CD, as an example, are managed at the MOUs until the $36^{th}$ to $37^{th}$ week of gestation whereupon they are referred to level 2 for further care. Those requiring sub-specialist obstetric care, input from other medical disciplines or critical care are stabilised at MMH and then referred to the tertiary obstetric unit at Groote Schuur Hospital (GSH).

## 4.3. Study population

Inclusion criteria: The study population was women who delivered by CD performed at MMH during June and July 2017. February and August were excluded as potential months because they are the times when new obstetric and anaesthetic doctors commence at MMH and may not yet be familiar with protocols. The study population included both elective and emergency CDs.

Exclusion criteria: Women having vaginal delivery during the same time period.

## 4.4. Data collection

The cases were identified retrospectively from the theatre register, and the women's files were retrieved from the medical records of MMH and also from GSH if the women had any reason to be referred there postoperatively.

The following data were abstracted from the files and entered onto a purpose designed data collection sheet: basic demographic data; indication for CD; anaesthetic and operative details; duration of the surgery ('knife to skin' to 'last stich'); type of uterotonic drug used for prophylaxis; type of uterotonic drug used for treatment; estimated blood loss; operative and short term postoperative complications (Appendix A). The data collection was performed by the principal investigator who obtained the required data from the anaesthetic form which is completed by the anaesthetist during the operation, the operating notes completed by the surgeon and from the women's maternity care booklet. The maternity care booklet is a standard national document in which the events/interactions during the pregnancy are documented from booking to postnatal period and this remains in the hospital folder at women's discharge.

PPH for the purposes of this study was defined as bleeding at or after CD using the following indicators:

Blood loss more than 1000 ml as estimated by the operating team and/or:

a) Additional surgical measures such as uterine compression sutures or balloon tamponade are required to control bleeding;
b) Relook laparotomy with or without hysterectomy is required;
c) Blood/blood product transfusion are administered (excluding blood transfusion administered intra- or postoperatively because of chronic anaemia).

In order to evaluate the use of uterotonics at CD at MMH, the observed use was compared with the sequential steps for prevention and treatment of haemorrhage outlined in the national consensus recommendation in Table 2.1 of the literature review (Chapter 2).

## 4.5. Study sample size

The number of caesarean deliveries performed at MMH ranges from 300 to 400 per month as seen from previous studies (57,58). The sample size was calculated with the help of a free online sample size calculator for clinical audits (http://www.raosoft.com/samplesize.html accessed 27/07/2017 = 357) (59). A margin of error of 5% was accepted, confidence interval of 95%, population of 5000 being the number of caesarean deliveries per year at MMH, and a response distribution of 50%. For comparison purposes, different online calculators were used. www.wrha.mb.ca/ extranet/eipt/files/Sampcalcaudits.xls (60), www.uhbristol.nhs.uk/files/ nhs-ubht/sample size calculator.xls (61). Sample sizes were 303 and 304 respectively. A sample size of 310 was planned for and it was thought that this could be achieved in one month.

The medical records department at MMH was understaffed and had very limited personnel for the second half of June so the folders retrieved were for the first two weeks of June and the first two weeks of July.

## 4.6. Data analysis

This was done by the principal investigator with the co-supervisor. Data were entered onto Microsoft Excel and STATA (StataCorp) spreadsheets and the analyses were mostly descriptive with frequency calculations.

## 4.7. Ethics

Permission to conduct the study was obtained from the Department of Obstetrics and Gynaecology Research Committee and the facility (MMH). In addition, ethics approval was obtained from the University of Cape Town Human Research Ethics Committee (Appendix C). The women's data were anonymized, treated confidentially and held securely by the principal investigator in a password protected electronic device.

Patient information was held in confidence as per the 1964 World Medical Association Declaration of Helsinki as it pertains to biomedical research (62). This was a retrospective folder review thus individual woman consent was not required.

# Chapter 5: Results

## 5.1 Data analysis

A total of 319 folders were reviewed for this study. There were 404 CDs (both electives and emergencies) performed in MMH for the month of June 2017. The study sample was intended to be drawn from June 2017 only, however due to problems described above with clerical staff at MMH medical records, only 186 folders up to 15 June 2017 could be accessed. The number obtained did not meet the sample size required, so folders from CD performed in the first two weeks of July 2017 were accessed to make up the shortfall of 133.

## 5.2 Patient characteristics

The mean age (± SD) was 28 (±6.2) with a range of 14 to 46 years, median gravidity 2 (±1) (range 1 to 6) (IQR 2), median parity 1 (range 1 to 4) (IQR 2), see Table 5.1. The mean pre-operative haemoglobin (Hb) was 11.5 (±1.4) g/dl (Table 5.1).

Pre-existing medical or obstetric comorbidities were found in 227 (71.2%) women who had either one or more of the conditions tabulated in Table 5.2. Only one (0.3%) woman had severe anaemia of 7.3 g/dl preoperatively. A raised body mass index (BMI) in this study was taken as anything above 25 kg/m$^2$, and over half of the study population, 175 (54.9%), was overweight or obese.

There were 96 (30.1%) nulliparous women in the study while 223 (69.9%) women were parous. Among the parous women, 126 (56.5% of parous women and 39.4% of total study group) had had a previous CD, these being: 79 (25%); 45 (14%); and 2 (1%) with one, two or three previous CDs, respectively.

There were 67 (21%) women who were HIV positive and 65 (97%) of them were on antiretroviral therapy. There were no treatment records for the other two women. HIV viral load was suppressed (< 100 copies/ml) in only 49 (75%) of those of treatment.

**Table 5.1: Patient characteristics (n = 319)**

| | Median/Mean | Lowest | Highest |
|---|---|---|---|
| **mean Age (years)** | 28 | 14 | 46 |
| **median Gravidity** | 2 | 1 | 6 |
| **median Parity** | 1 | 0 | 4 |
| **mean Pre-op Hb* (g/dl)** | 11.5 | 7.3 | 15.9 |

*Hb: hemoglobin

**Table 5.2: Obstetric and medical co-morbidity (n = 319)**

| Condition | Number | % |
|---|---|---|
| **Previous CD** | 126 | 39.4% |
| **HIV positive** | 67 | 21% |
| **Hypertension (PET + CHPT)** | 47 | 14.7% |
| **Asthma** | 8 | 2.5% |
| **BMI > 25** | 175 | 54.9% |

Some women had more than one comorbidity.

## 5.3 Details of caesarean deliveries

There were 239 emergency CDs (75%) and 80 elective CDs (25%). Indications for CD were grouped into maternal (e.g. previous CD), fetal (e.g. pathological CTG) and placental (e.g. placenta previa) and specific indications for CD were then detailed (see Figures 5.1 and 5.2). There were 172 (54%) CDs performed for fetal reasons and 141 (44%) for maternal reasons. Fetal distress/pathological CTG was the most common specific indication for CD with 128 (40%). Previous CD was the second most common specific indication; this included patients with one previous CD who had an unsuccessful attempt at a vaginal delivery after CD (VBAC), those who declined to attempt a VBAC or had more than one prior CD. Infrequently occurring indications like retained second twin, previous obstetric anal sphincter injury, placenta previa, intrauterine growth restricted fetuses, placenta previa and eclampsia were grouped together as 'other' in Figure 5.2. This latter group accounted for 3% of all indications for CD.

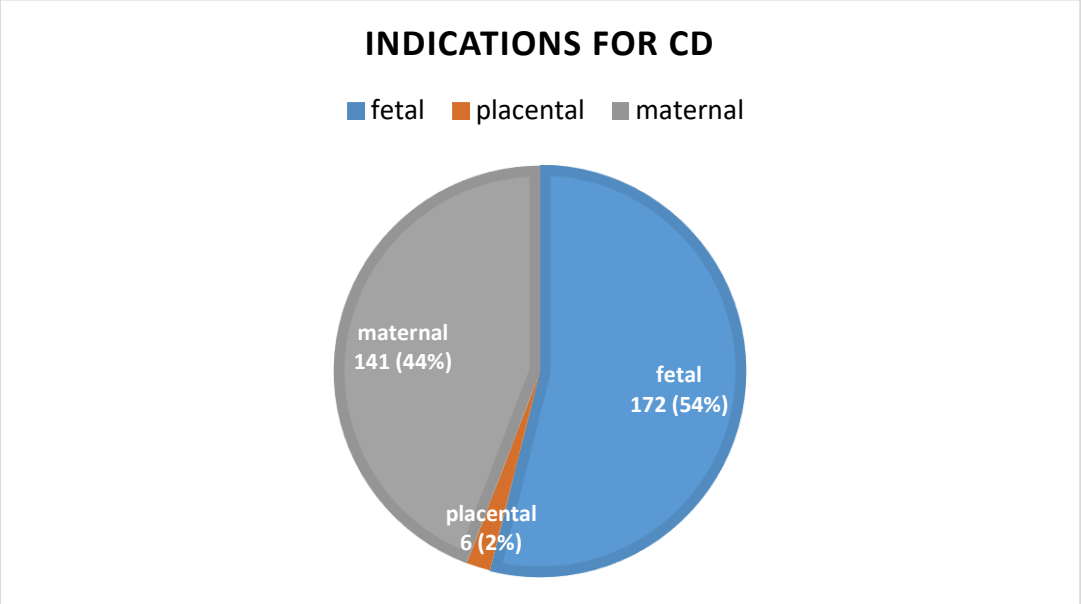


**Figure 5.1: Indications for caesarean delivery (n = 319)**

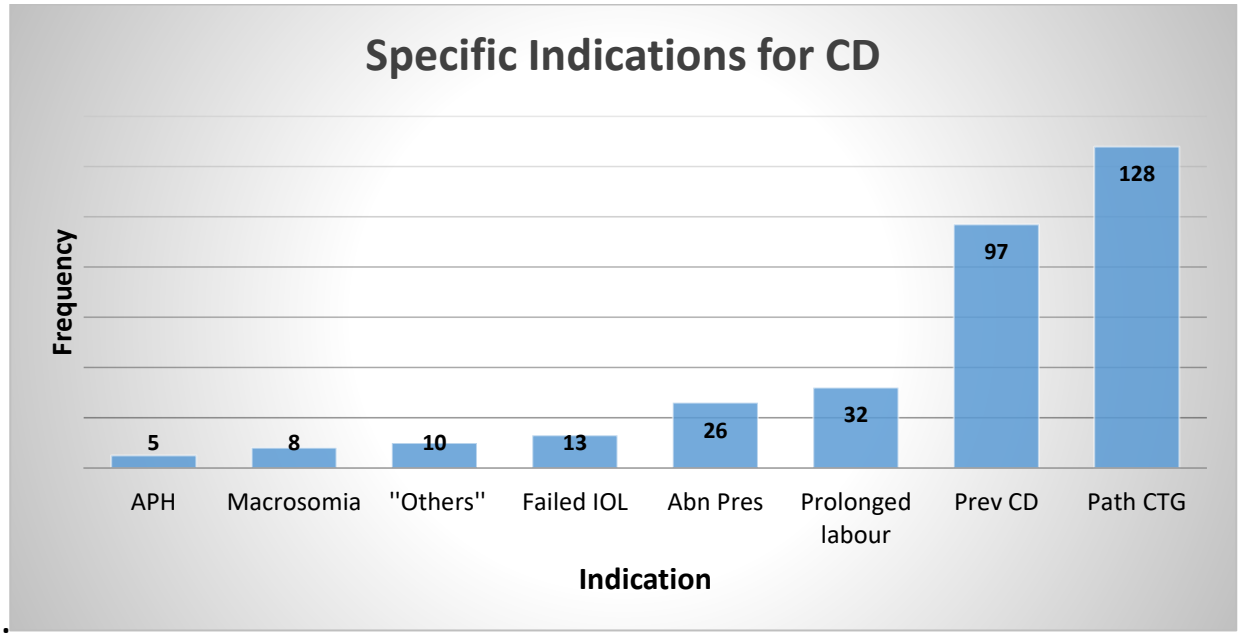


**Figure 5.2: Specific indications for caesarean delivery (n = 319)**

APH: antepartum haemorrhage, Abn Pres: abnormal presentation, IOL: Induction of labour, Prev CD: previous caesarean delivery, Path CTG: pathological cardiotocograph, 'Others': refers to a number of indications in this study that occurred twice or less (included previous third degree tears, retained second twin, eclampsia, fetal growth restriction, placenta praevia and cord prolapse).

There were 167 (52%) CDs performed during the day shift and 152 (48%) after 4 pm, when consultant staff were off site. (Note that there was no distinction between weekdays and weekends). The obstetric registrars did the majority of the operations 201 (63%) while medical officers did 118 (37%). None of the CDs were performed by consultant staff. The duration of surgery (incision to last suture) was 20 to 40 minutes in 210 (66%) operations, while 38 (12%) of the operations were performed in under 20 minutes and 71 (22%) over 40 mins.

## 5.4 Anaesthesia

Spinal anaesthesia was performed for 283 (89%) of the operations. This number rose to 92% if failed spinals (9 women, 2.8%) that were converted to general anaesthesia are included. General anaesthesia was used in 26 women (8%). There were no adverse complications or deaths related to anaesthesia. Only one woman had a 'high spinal' leading to maternal tachycardia.

## 5.5 Surgical problems documented at CD

The operative procedure was described by the surgeons in their operation notes to be easy/ uneventful in 256 (80.3%) women and a surgical problem was described in 63 (19.7%). The most commonly encountered surgical difficulties described by the surgeons were adhesions in 25 (7.8%) women due to previous CD, and uterine atony documented in 24 (7.5%) women. Uterine atony was diagnosed by uterine palpation for tone at CD. These difficulties were described or encountered by all ranks of surgeons and were dealt with either by the same surgeon (therefore longer operating time) or a senior doctor/consultant was called in to assist. Obesity/raised BMI was documented as a factor in operative difficulty in five cases (1.6%). Other reported difficulties were: difficult delivery of the fetus and uterine incision extending laterally, see Table 5.3. (N.B.: excessive blood loss is described separately in Table 5.4).

**Table 5.3: Surgical problems described at CD (n = 63, 19.7%)**

| | Frequency* | Percentage %** |
|---|---|---|
| **Adhesions** | 25 | 7.8 |
| **Uterine atony** | 24 | 7.5 |
| **Difficult fetal delivery** | 7 | 2.2 |
| **Uterine incision extended laterally** | 5 | 1.6 |
| **Obesity** | 5 | 1.6 |

*Three women had more than one factor responsible for surgical difficulty hence frequency > n.
**Percentages use 319 as the denominator.

Out of the 319 women operated on, three required additional surgical measures – one uterine compression suture (B-Lynch) and two had multiple haemostatic sutures secondary to uterine atony and uterine trauma/tears, respectively. None had balloon tamponade and none required a hysterectomy.

## 5.6 Estimated blood loss

Estimation of blood loss at MMH is done by the anaesthetist who visually inspects soaked abdominal swabs, blood (invariably mixed with liquor) in the suction bottle and any blood on the operating table linen. The average blood loss in this study was 487 ml (± 220) with a range of 100 to 2000 ml (see Table 5.4 and Figure 5.3). Estimated blood loss of ≥ 1000 ml occurred in 13 (4.1%) patients, while 218 (68%) had EBL of ≤ 500 ml. Haemodynamic status changes (hypotension and tachycardia) were documented in three women. One woman was transfused 2U packed red cells after an EBL of 1200 ml. She later developed an ileus for which she was

referred to a tertiary hospital. This resolved spontaneously while at GSH and she was referred back to MMH. There was only one patient with an EBL of 2000 ml.

**Table 5.4: Blood loss estimation (n = 319)**

| Est blood loss (ml) | ≤ 500 | 501 – 999 | 1000 – 1499 | 1500 - 1999 | >2000 |
|---|---|---|---|---|---|
| **Frequency** | 218 | 88 | 11 | 1 | 1 |
| **Percentage (%)** | 68 | 28 | 3 | 0.3 | 0.3 |

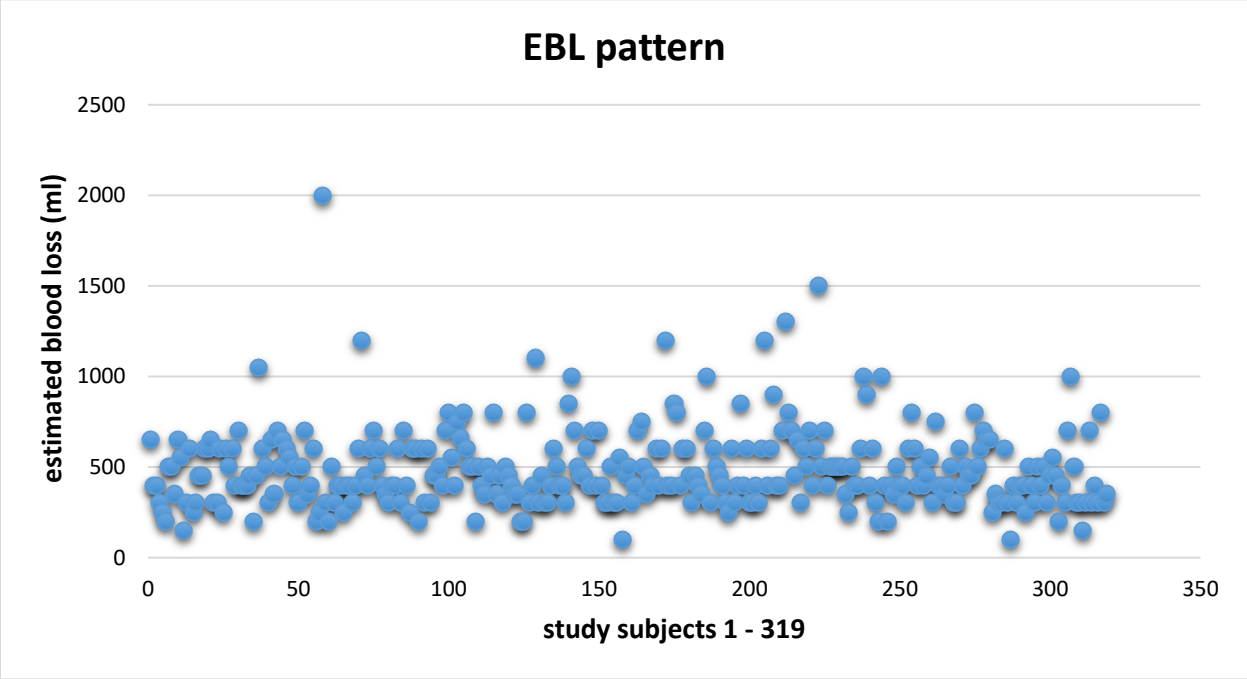


**Figure 5.3: Scatter diagram showing estimated blood loss in the study (n = 319)**
The most frequently occurring EBL was 400 ml. 13 patients had EBL > 1000 ml.

Of the 13 women with blood loss >1000 mls, there were five who had adhesions, four who had uterine atony, five with uterine tears, and one had difficult fetal delivery (she had two previous CDs, uterine atony, and adherent placenta and she subsequently required a uterine brace suture). (N.B.: Some women had more than one issue hence count exceeds 13). Eight of these 13 had a BMI > 25 kg/m$^2$ but their obesity was not documented as a factor in causing difficult surgery. Twelve women had an emergency CD, and three of the 13 women had general anesthesia. The duration of surgery was more than 40 minutes in 11 of the 13 women.

It was noted that 20 of the 24 women (83.3%) with documented uterine atony and 20 of the 25 (80%) with adhesions did not have PPH.

## 5.7 Uterotonic use

This will be described according to the steps in the recommended protocol for South Africa as described in Table 2.1, (page 8).

### 5.7.1 Step 1.1 (initial oxytocin 2.5 IU bolus)

75 (23.5%) of the 319 patients received 2.5 IU oxytocin IVI initial bolus as per protocol, while 227 (71.1%) got other doses (Figure 5.4). There were 17 (5.3%) women for whom there was no record of any initial bolus being given. There was no documentation of intramuscular prophylactic administration of oxytocin or syntometrine for any woman.

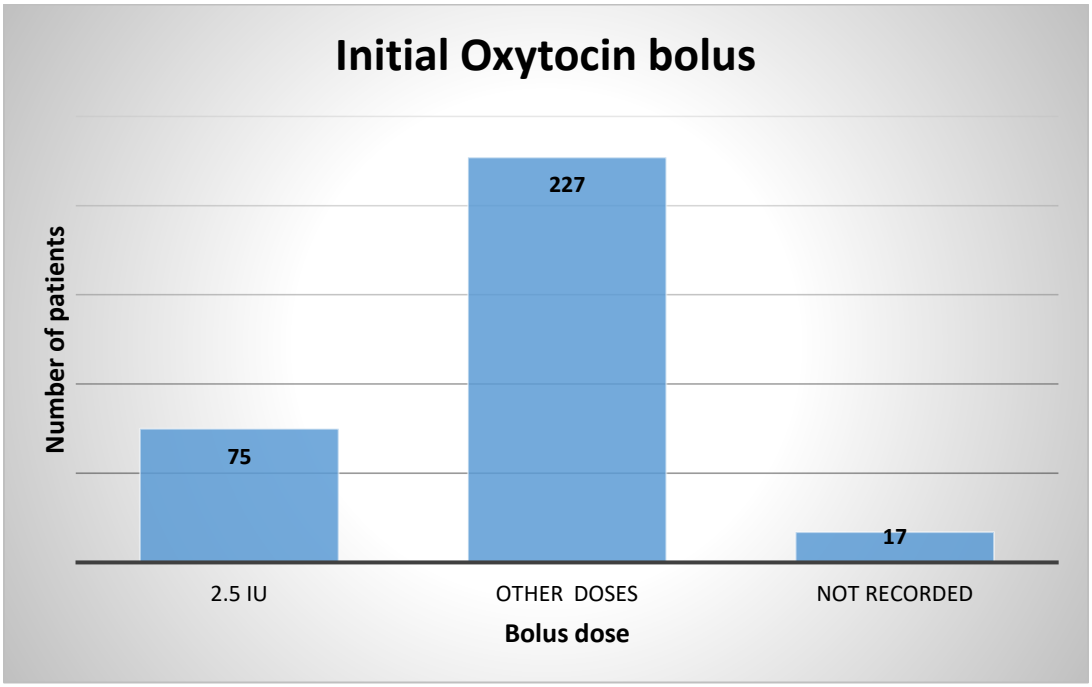


**Figure 5.4: Number of patients who received 2.5 IU oxytocin slow IVI bolus (n = 319)**
Only 23.5% of the study group received 2.5 IU.

The 2.5 IU bolus was more likely to be given during the working day than after hours 65% versus 35% ($p < 0.05$), see Figure 5.5.

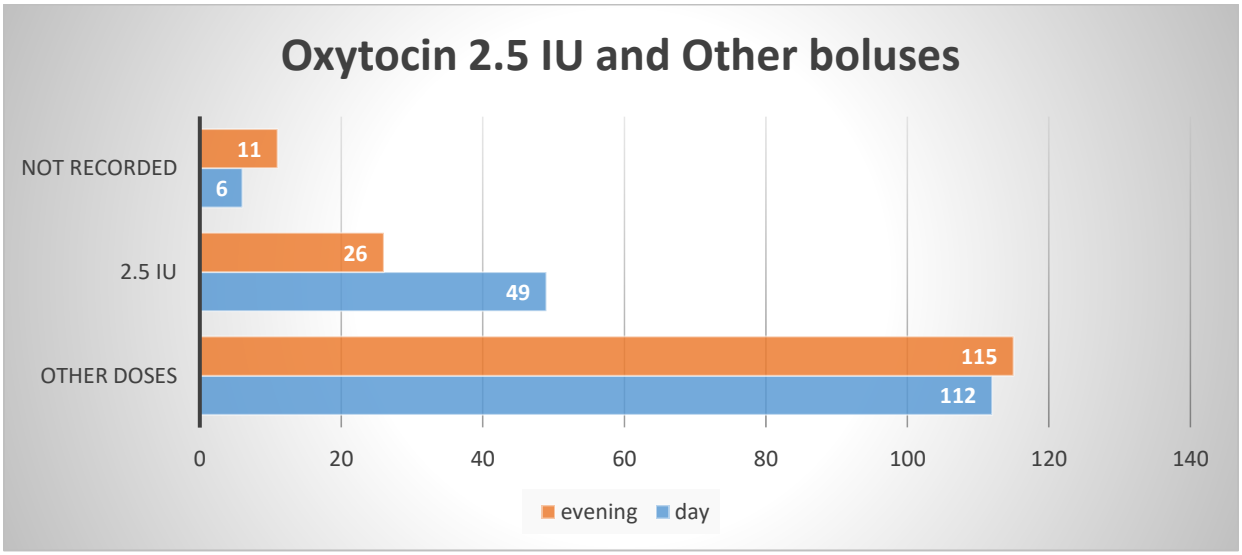


**Figure 5.5: Comparison of oxytocin bolus usage between day and night**

2.5 IU was more likely to be given during the day than in the evening. The time of the day did not influence how the other boluses were given.

The other different oxytocin boluses given in lieu of 2.5 IU ranged from 1 IU to 7.5 IU IVI and are shown in Table 5.5. Three (3) IU of oxytocin either as a single dose or in a variety of divided doses ('1+1+1' or '1.5+1.5') was the initial bolus that was most frequently given, 169 women (53%). It was noted that all initial IV boluses (except for one of 7.5 IU), were less than 5 IU.

**Table 5.5: Oxytocin prophylactic boluses administered (n = 319)**

| Oxytocin bolus (IU) | Frequency | Percentage (%) |
|---|---|---|
| **2.5** | 75 | 23.5 |
| **3** | 139 | 43.6 |
| **'1+1+1'** | 16 | 5 |
| **'1.5+1.5'** | 14 | 4.1 |
| **2** | 36 | 11.3 |
| **1** | 5 | 1.6 |
| **'1+1'** | 2 | 0.6 |
| **4** | 2 | 0.6 |
| **7.5** | 1 | 0.3 |
| **Nil** | 17 | 3.2 |

Nine unique oxytocin boluses were given in the study.

### 5.7.2 Estimated blood loss and initial oxytocin bolus

The mean EBL in the group (75) who got 2.5 IU was 488 (±158) ml while for 42 women who got < 2.5 IU the EBL was 535 (± 225) ml and 172 who were given > 2.5 IU the EBL was 469 (± 220) ml.

Among the 24 patients with documented atony, 7 (29.2%) were given initial 2.5 IU IVI, while 11 (45.8%) got alternative doses (2 IU for one patient; 3 IU for ten patients). Six (25%) did not get initial bolus oxytocin, or if given it was not documented.

5.7.3 Steps 1.2 and 1.3 (intraoperative and postoperative oxytocin infusion)

Step 1.2 refers to 7.5 IU infusion which is to be administered intraoperatively and Step 1.3 to the 20 IU prophylactic postoperative infusion. However, reading from the patient files it was not possible to determine whether the infusions were commenced intraoperatively or postoperatively; or for prophylaxis or treatment, so these steps have been combined.

Eighteen patients (5.6 %) received oxytocin 7.5 IU as an infusion in the remaining fluid as per protocol. Of the 75 patients who got the initial 2.5 IU bolus, 17 of them got 7.5 IU infusion. Other patients got different oxytocin doses for infusions as described below.

There were 212 patients (66.5%) who received 17 alternative doses of oxytocin infusion which ranged from 2.5 IU to 24 IU, see Table 5.6. Some of the other infusion doses not depicted in Table 5.6 were: 2.5, 4, 5, 8, 9, 15, 16 and “infusion”.

There was no documented evidence that 89 (26.6%) patients got any oxytocin infusion at all. The oxytocin for infusion, when given, was diluted in a variety of volumes of fluid – 500 ml to 1000 ml of modified ringers lactate (mRL). Twenty (20) IU of oxytocin in a litre of mRL was the most commonly prescribed infusion dose in 65 (20.4%) patients.

There was no documentation of volumetric pumps or dial flows being used to ensure an infusion rate of 125 ml/hr as per protocol.

**Table 5.6: Oxytocin infusion prophylactic doses used in the study (n = 319)**

| Oxytocin dose (IU) | Frequency | Percentage % |
|---|---|---|
| **20** | 65 | 20.4 |
| **22** | 11 | 3.4 |
| **18** | 13 | 4.1 |
| **17.5** | 24 | 7.5 |
| **17** | 14 | 4.4 |
| **12** | 11 | 3.4 |
| **10** | 33 | 10.3 |
| **7.5** | 18 | 5.6 |
| **7** | 10 | 3.1 |
| **0** | 89 | 27.9 |

31 (9.7%) women received other oxytocin doses with frequencies less than 10, see text.

### 5.7.4 Continued prophylactic oxytocin infusion in the ward

There was no instruction for the nursing staff by the obstetric doctor or anaesthetist to continue oxytocin prophylaxis in the ward in 270 (85%) of the patients' prescription charts. The order was documented in only 49 (15%) of women and the dose ordered was 20 IU in a litre to run over eight hours. There was documented evidence, however, as per nursing notes, of 103 (32%) women arriving in the ward with oxytocin infusion running. This means that, for these 103 women, an oxytocin infusion was commenced without any documentation or instruction in the prescription chart or anaesthetic record.

### 5.7.5 Step 2.1: Initial treatment of PPH/uterine atony by repeat IV bolus

Repeat bolus of oxytocin (to be given for ongoing uterine atony at three minutes) was given to 15 (5%) patients; however, in only three (3) women was the recommended 2.5 IU IVI repeat dose given. Other repeat doses were 2, 3 and 7.5 IU IVI bolus.

The reason for repeating the bolus dose was not documented in the anaesthetic charts. However, a perusal of surgical notes indicates that uterine atony was documented in only two patients where a repeat bolus was given. The mean blood loss in these patients was 650 ml (300 – 1500 ml).

### 5.7.6 Step 3: Further medical treatment of PPH/uterine atony

This step involves oxytocin infusions, IV or IMI administration of oxytocin or syntometrine, and other medications.

In terms of the oxytocin infusions, it was not always clear from the women's files whether they were given prophylactically or therapeutically.

***Thirteen (4.1%) women had EBL ≥ 1000 ml and 24 were reported to have uterine atony.***

**Table 5.7: Summary of the uterotonic management of the 13 patients with PPH and the 24 with uterine atony (N.B. four had PPH)**

| | Prophylaxis | | | Treatment | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 2.5 IU bolus IVI | Alt bolus dose | 7.5 IU Infusion | Repeat 2.5 IU bolus | Alt Repeat dose | 20 IU Infusion* | Ergo/ Synto | Miso | TXA |
| **PPH n=13** | 0 | 12 | 1 | 0 | 3 | 10 | 2 | 5 | 1 |
| **Uterine atony =24** | 7 | 11 | 0 | 1 | 1 | 15 | 3 | 13 | 1 |

Alt: alternate; Miso: misoprostol; TXA: tranexamic acid; Synto: syntometrine. None of the patients in the study got prostaglandin F2alpha.

*It was not possible to distinguish between prophylactic oxytocin infusion and treatment infusion.

In the PPH group (n=13), 12 got a low dose IV bolus and of these three had a repeat oxytocin bolus. There were ten who had a 20 IU oxytocin infusion, two who had syntometrine, five misoprostol and one tranexamic acid.

Considering the 24 women with uterine atony (of whom four had PPH), 18 got a low dose IV bolus and of these two had a repeat oxytocin bolus. There were six women who received no initial IV bolus. There were 15 who had a 20 IU oxytocin infusion, two who had syntometrine, 13 misoprostol and one tranexamic acid.

In addition to the additional treatments described above, a further 17 (5.3%) patients were given misoprostol while another seven (2.2%) got syntometrine yet they were not documented to have either PPH or uterine atony.

## 5.8 Additional surgical measures and further treatment

Three women required additional surgical measures. This included one woman who required uterine compression suture (B-Lynch) as a result of uterine atony and an adherent placenta following a difficult fetal extraction with blood loss estimated to be 1000 ml and two patients who had multiple haemostatic sutures secondary to uterine atony and uterine trauma/tears respectively. None had balloon tamponade and none required a hysterectomy.

In addition, no woman needed a re-look laparotomy, or died (at least in the first three or so days post operation). Two women were referred to Groote Schuur tertiary hospital for further management; one was for management of eclampsia while the second was for ileus (described above) and not for haemorrhage related complications.

# Chapter 6: Discussion

## 6.1 Introduction

This study of 319 patients having CD at a secondary level hospital showed that the majority (75%) of the CDs were done as emergencies by registrars and medical officers with a documented PPH rate of 4.1% and no major morbidity or mortality.

## 6.2 Prophylactic oxytocin bolus at CD

The recommended oxytocin protocol was not always adhered to in this study. Lack of, or poor documentation was noted in 5% of women.

Only 23.5% of the women were given the recommended 2.5 IU of intravenous slow bolus oxytocin after delivery of the fetus. The other 227 (71%) women who were not given 2.5 IU still received low dose oxytocin as a bolus (≤5 IU) which is lower than the recommendation of the RCOG and other workers in this area (34,40). This in effect means 301 (94%) of women in this study received bolus oxytocin less than 5 IU IV.

The rationale for giving doses of 2.5 IU in the national recommendation arose from studies showing it was the optimal dose that balanced safety with efficacy (39).

The most commonly administered oxytocin bolus in this study was 3 IU slowly IVI. The rationale for this is unclear, given that none of the national guidelines advocate for the use of this dose. Perhaps it all stems from the ease of drawing up 3 IU as opposed to 2.5 IU. An interesting finding arising from this study was that 2.5 IU was statistically significantly more likely to be given in daytime compared to afterhours, again perhaps due to the ease of drawing up the 3 IU dose. It is possible that the presence of more anaesthetic staff, including consultant anaesthetists, during the day could influence the adherence to protocol as opposed to at night time when a lone anaesthetist, sometimes a junior registrar just starting their rotation, runs the service alone. It is a shortcoming of this study that the rank of anaesthetic provider was not recorded as it was for obstetric doctors. This should be taken into consideration when the audit is repeated at other sites.

Some anaesthetists preferred to give the 3 IU in divided aliquots either ‘1+1+1’ or ‘1.5 + 1.5’, perhaps as a way of reducing the side effects of oxytocin, as evidenced by a few patients with hypotension in this study. The time interval between administering these could not be established from the anaesthetic chart. It was also difficult to tell if these ‘1+1+1’ could be characterised as repeat boluses. The ‘1+1+1’ regimen was given to 16 (5.2%) while the ‘1.5 + 1.5’ was given to 12 patients (3.9%).

Although this study showed that the 3 IU bolus was the most commonly given prophylaxis at CD which is a departure from the national recommendation, the difference is extremely small and the majority of dosages (94%) given were less than 5 IU and thus constitute low dose boluses.

The finding that a low PPH rate at CD with no severe morbidity or mortality can be achieved with low dose prophylactic oxytocin IV boluses is important. Moreover, it is in the context of the majority of CDs being emergencies and all being done by registrars or medical officers. The findings thus allay concerns that have been expressed by some constituencies in South Africa that the high levels of maternal mortality due the BLDACD in South Africa may be due to national recommendations for IV boluses at CD that are too low.

## 6.3 Comparison with other audits on oxytocin boluses

Despite MMH not fully adhering to protocol, the oxytocin doses used in this study are low compared to findings from a similar audit of 139 CD patients done by Tsima et al. (11) in Botswana who found very high doses of oxytocin boluses (10 to 20 IU IVI) being used. Tsima et al. indicate in their study that there were no local protocols governing the use of uterotonics in their setting and thus RCOG and WHO guidelines were the standards of care. However, compliance to those protocols was also poor, with only 30% of patients being given 5 IU IV bolus as per RCOG. There was no documented use of doses less than 5 IU in the Botswana study.

## 6.4 Oxytocin bolus dose and associated blood loss

There was no clear pattern that emerged from this study as to which bolus dose was associated with ongoing uterine atony and thus PPH (blood loss 1000 ml or more) because of the small number of patients with PPH in this study. Only three incidents of PPH occurred when the initial bolus was 3 IU compared to none when 2.5 IU and ‘1+1+1’ were given. It is evident from this study that PPH results from multiple factors. Of the patients who did not get the bolus oxytocin, none had PPH, only two had documented uterine atony which was managed with misoprostol.

## 6.5 Oxytocin infusion

A little over a quarter of patients in this study did not receive oxytocin infusion, or if given it was not documented. The current protocol of oxytocin use indicates that routine prophylactic oxytocin infusion be given to all women post-delivery of the fetus. Not giving prophylactic oxytocin by anaesthetists could be due to concerns about its side effects thus they would rather give it when indicated. This is in keeping with findings by Wedisinghe et al. (63), who did an oxytocin user survey in the UK and found that 78.7% of anaesthetists preferred selective use of oxytocin, while 21% preferred routine use. A follow up survey by the same group (25), now

extended to all countries of the UK and Ireland, also found that there was still wide variation in the oxytocin infusion use among obstetricians and anaesthetists; 38 different regimens were used to administer an oxytocin infusion. Obstetricians in that same survey also favoured selective oxytocin use. The commonest indications cited for infusion use were intraoperative haemorrhage, multiple pregnancy, placenta previa, previous PPH and prolonged labour. In South Africa, however, Saving Mothers Reports have described high rates of bleeding after CD being discovered in postnatal wards where monitoring may be poor (4,5). Thus routine postoperative uterotonic use is recommended. If IV infusions are difficult to maintain in understaffed postnatal wards, alternatives would be intramuscular syntometrine or oxytocin (9). The Canadian guidelines recommend postoperative carbetocin which is given as a single dose parenteral injection with a prolonged action. The introduction of a heat stable and cheaper form of carbetocin, could be more efficacious and cost saving in the public sector in South Africa (51). The CHAMPION trial has shown that heat stable carbetocin is just as efficacious as oxytocin (49).

## 6.6 Anaesthesia

This study showed that at MMH the anaesthetic of choice for CD is spinal anaesthetic. It was generally well tolerated by the patients with no adverse events associated with its use. This finding is dissimilar to Tsima et al. who found that general anaesthetic (GA) was used in 64% of patients in their study. GA is a known risk factor for uterine atony leading to PPH. Three women in this study with a blood loss ≥ 1000 ml had a GA and two of these had uterine atony.

## 6.7 Duration of surgical time

It is recommended that the ideal duration for performing a CD should be 45 to 60 minutes (64). Many junior doctors strive to perform shorter durations of the CD (≤ 10 minutes). Such short surgery duration is thought more likely to be associated with morbidity due to lack of care in ensuring good haemostasis. It is gratifying to note that despite MMH being an extremely busy hospital, the surgeons take time in performing surgery with all of the CDs taking more than 20 minutes.

## 6.8 Patient population

There were 67 (21%) HIV positive women; of these only two were not on antiretroviral therapy. This HIV prevalence is similar to the finding of a prevalence of 18.9% (2015 national data) (65) for the Western Cape among women attending antenatal care. Of those on treatment, 73% had a viral load less than 100 viral particles. Five of the women with blood loss ≥ 1000 ml were HIV positive.

Fifty-four percent of the women in this study had a BMI > 25. A raised BMI was a factor in contributing to operation difficulty and increased blood loss in this study. This is keeping with other studies that looked into the subject of obesity and its outcomes in pregnant women in South Africa (66).

## 6.9 Emergency caesarean deliveries

Three quarters (75%) of the CDs in this study were emergencies. This is not surprising for a regional level 2 hospital like MMH which has a large catchment area and serves as a referral centre for several MOUs. Emergency CD is well known to carry higher risk for maternal morbidity and mortality compared to elective CD. In this study 12 out of the 13 women with PPH had an emergency CD. There were no peripartum hysterectomies or other major morbidity that was seen in this study. This is due perhaps to the fact that the majority of women were operated on by senior staff (registrars) and experienced medical officers. It is important to note the finding that the numbers of women with PPH were less than the numbers with uterine atony which attests to prompt recognition and early treatment by surgeons and anaesthetists of the uterine atony. Poor surgical technique and inexperienced staff have been found to be factors in many confidential maternal mortality reviews, especially at level 1 hospitals in South Africa.

## 6.10 Patient outcomes

The majority of women in this study had an uneventful postpartum course (no adverse peri or post-operative complications). One woman was referred to GSH because of eclampsia, while another was referred for ileus.

## 6.11 Study limitations

Given that it was a retrospective folder review it was dependent on surgeons and anaesthetists documenting outcomes, surgical difficulty and uterotonic use. If it was not documented, it cannot be ascertained whether this was a recording error, or it did not occur. Also, the outcomes of uterine atony and PPH are subjective and may have been underestimated. Nevertheless, the observation of no relook laparotomies, and no severe morbidity or mortality support the finding of low reported complication rates.

Also, the sample size did not allow a correlation between PPH and oxytocin use to be performed. The PPH rate also was lower than expected.

# Chapter 7: Recommendations and Conclusion

## 7.1 Recommendations

The study results indicate a need for a more formal method for recording uterotonic use at CD and distinguishing whether it is for prophylaxis or treatment. This is particularly necessary for single bolus oxytocin doses as well as infusions. This could be incorporated as a checklist or text box into the standardised maternity case record which is currently in the process of revision.

Also, it would be important for the anaesthetic fraternity in South Africa to collectively re-discuss recommended dosages for oxytocin prophylaxis at CD. Although at a hospital such as MMH, there is consultant anaesthetic supervision, which could allow for some variation among specialists, this is not the case at district hospitals where the majority of CDs are performed in South Africa by non-specialist surgeons and anaesthetists. At this level there is the need for clear standardised protocols for uterotonic use at CD.

Repeating this study at peripheral district hospitals where there is high maternal morbidity and mortality from bleeding at CD is important to determine what is being practised, with the view to improving the quality of care.

## 7.2 Conclusion

The national recommended uterotonic protocol is not fully complied with at MMH; however alternative low dose oxytocin bolus and infusion regimes are used widely at CD. The finding that a low PPH rate at CD with no severe morbidity or mortality can be achieved with low dose prophylactic oxytocin IV boluses is important. Moreover, it is in the context of the majority of CDs being emergencies and all being done by registrars or medical officers.

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# Appendix A: Data Collection Sheet

**Data Collection Sheet**

| | |
|---|---|
| Patient Unique Study Number | |
| Hospital Folder number | |
| Age | |
| Gravidity | |
| Parity | |
| Indication for the CD 0=fetal 1=placental 2=maternal | |
| Specific indication 0=Path CTG 1=abnormal pres 2=macrosomia 3=APH 4=Prev CD 5=prolonged labour 6=prev myomectomy 7=failed IOL 8=other; specify ……. | |
| Elective v Emergency 0=Elective 1=Emergency | |
| Time of CD 0=8am-4pm 1=4pm-8am | |
| Rank of Surgeon 0=Reg 1= Senior MO 2=Junior MO 3=Intern 4=Consultant | |
| Duration of operation (minutes) 0=<20 1= 20-40 2=>40 | |
| Prev C/S 0=0, 1=1, 2=2, 3=3 or more | |
| Pre-op Hb (g/dl) | |
| Obstetric or Medical Comorbidity 0=No 1=Yes | |
| If Comorbidity exists specify: 1=HIV 2=Asthma 3=raised BMI 4=CHPT 5= IGT 6= Preeclampsia | |
| If HIV 0 = No ARV 1 = On ARV | |
| If HIV 0 = VL < 100 (suppressed) 1 = VL > 100 | |
| Type of anaesthesia 0=Spinal 1=GA 2= Spinal+GA | |
| Operative difficulty 0=Easy 1=Difficult | |
| If Operation difficult specify: 1=adhesions 2=diff delivery fetus 3=incision extended laterally 4=abnormal anatomy 5=obesity 6=other: specify……. | |
| PPH 0=No 1=Yes | |
| EBL (ml) | |
| Documented uterine atony 0=No 1=Yes | |
| Uterine trauma/tears 0=No 1=Yes | |
| Placenta previa 0=No 1=Yes | |
| Abruptio placentae 0=No 1=Yes | |

| | |
|---|---|
| Adherent placenta 0=No 1=Yes | |
| Additional surgical measures 0=No 1=Yes | |
| If additional surgical measures specify 0=brace sutures 1=uterine tamponade; 2=uterine artery ligation; 3 =other: specify……. | |
| Peripartum hysterectomy 0=No 1 =Yes | |
| Intraoperative hypotension * 0=No 1=Yes | |
| Intraoperative tachycardia ** 0=No 1=Yes | |

* Intraoperative hypotension: maternal systolic blood pressure less than 80 % of baseline readings or an absolute value of 100 mmHg or both(67)

** Intraoperative tachycardia: heart rate > 120 bpm

# Appendix B: Checklist re. Uterotonic Administration

Checklist re: Uterotonic administration

| | |
|---|---|
| PROPHYLAXIS (intraoperative) | |
| Oxytocin 2.5 mg IVI bolus 0=No 1=Yes 2=Not recorded (NR) | |
| Repeat Oxytocin 2.5 IU IVI given 0=No 1=Yes 2=Not recorded | |
| If repeat given was reason specified 0=No 1=Yes 2=Not recorded | |
| Alternative dose given 0=No 1=Yes 2=Not recorded. If 1=specify | |
| Alternative route used 0=No 1=Yes 2=Not recorded. If 1=specify | |
| | |
| Oxytocin Infusion | |
| Oxytocin 7,5 IU IVI in 1 liter 0=No 1=Yes 2=NR | |
| Alternative doses given 0=No 1=Yes 2=NR If 1 specify | |
| | |
| Other Uterotonics for prophylaxis | |
| Syntometrine/Ergometrine 0=No 1=Yes 2=NR<br>If 1 specify dose and route…… | |
| Misoprostol 0=No 1=Yes 2=NR<br>If 1 specify dose and route…… | |
| PROPHYLAXIS POST OPERATION | |
| Instructions on prescription chart for nursing to continue prophylaxis in postnatal ward? 0=No 1=Yes 2=NR | |
| | |
| Prophylaxis with uterotonics continued in the postnatal ward? 0=No 1=Yes 2=NR<br>If 1 specify agent, dose and route…… | |
| | |
| TREATMENT for PPH cases and suspected uterine atony | |
| Oxytocin infusion 20 IU in a liter 0=No 1=Yes 2=NR | |
| Alternative dose given 0=No 1=Yes 2=NR If 1 specify | |
| Other uterotonics for treatment: | |
| Syntometrine/Ergometrine 0=No 1=Yes 2=NR<br>If 1 specify dose and route | |
| Misoprostol 0=No 1=Yes 2=NR<br>If 1 specify dose and route | |
| Tranexamic acid 0=No 1=Yes 2=NR If 1 specify dose and route | |

| | |
|---|---|
| Prostaglandin F 2alpha 0=No 1=Yes 2=NR If 1 specify dose and route | |

# Appendix C: Letter of Approval for Study from Ethics Committee

**UNIVERSITY OF CAPE TOWN**
**Faculty of Health Sciences**
**Human Research Ethics Committee**

**Room E53-46 Old Main Building**
**Groote Schuur Hospital**
**Observatory 7925**
**Telephone** [021] 406 6492
**Email:** sumayah.ariefdien@uct.ac.za
**Website:** www.health.uct.ac.za/fhs/research/humanethics/forms

05 September 2017

**HREC REF: 613/2017**

**Prof S Fawcus**
Department of Obstetrics & Gynaecology
2nd floor
Mowbray Maternity Hospital

Dear Prof Fawcus

**PROJECT TITLE: AN AUDIT OF UTEROTONIC USE FOR THE PROPHYLAXIS AND TREATMENT OF HAEMORRHAGE AT CAESAREAN DELIVERY (MMeD-Candidate- Dr P Pheto)**

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

**Approval is granted for one year until the 30 September 2018.**

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

***We acknowledge that the student: Dr P Pheto will also be involved in this study.***

**Please quote the HREC REF in all your correspondence.**

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

pp **PROFESSOR M BLOCKMAN**
**CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE**

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938