

**A COMPARATIVE STUDY BETWEEN MISOPROSTOL COMBINED
WITH OXYTOCIN VERSUS OXYTOCIN ALONE IN REDUCING PPH**

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M.D. (PHARMACOLOGY)

BRANCH - VI



DEPARTMENT OF PHARMACOLOGY

COIMBATORE MEDICAL COLLEGE

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CERTIFICATE I

This is to certify that this dissertation entitled, **A COMPARATIVE STUDY BETWEEN MISOPROSTOL COMBINED WITH OXYTOCIN VERSUS OXYTOCIN ALONE IN REDUCING PPH** submitted by **Dr.ANANDHLS** in partial fulfilment for the award of the Degree of M.D.(Pharmacology) by The Tamilnadu Dr.M.G.R.Medical University, Chennai is a bonafide record of the research work done by her, under the guidance of **Dr.R.MANI M.D.**, Professor and Head, Department of Pharmacology, Coimbatore Medical College during the academic year 2017-20 in the Department of Pharmacology, Coimbatore Medical College, Coimbatore-641014. This dissertation is a record of fresh work done by the candidate **Dr.S.ANANDHI**, during the course of the study (2017-2020). This work was carried out by the candidate herself under my supervision.

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I solemnly declare that the dissertation entitled “**A COMPARATIVE STUDY BETWEEN MISOPROSTOL COMBINED WITH OXYTOCIN VERSUS OXYTOCIN ALONE IN REDUCING PPH**” is done by me at Coimbatore Medical College and Hospital, Coimbatore during the period of 2018-2019 under the guidance and supervision of **Dr.R.MANI M.D.**, Professor and HOD, Department of Pharmacology, Coimbatore Medical College. This dissertation is submitted to The Tamilnadu Dr.M.G.R.Medical University, Chennai towards the partial fulfilment of the requirements for the award of **M.D. DEGREE IN PHARMACOLOGY.**

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ACKNOWLEDGEMENT

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The Institutional Ethics Committee of Coimbatore Medical College, reviewed and discussed your application for approval of the proposal entitled "**A Comparative Study between Misoprostol Combined With Oxytocin Versus Oxytocin alone in reducing PPH.**" No.034/2017.

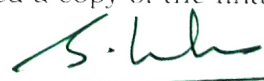
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LIST OF ABBREVIATIONS

PPH	- Post Partum Haemorrhage
APH	- Ante Partum Haemorrhage
WHO	- World Health Organisation
AMTSL	- Active Management of Third Stage of labour
MMR	- Maternal Mortality Rate
OXT	- Oxytocin Receptor
PLC-IP3-Ca	- Phospholipase-Inositol tri phosphate-Calcium
CNS	- Central Nervous system
PROM	- Premature Rupture Of Membranes
IU	- International Units
GIT	- Gastro Intestinal Tract
5HT2	- 5Hydroxytryptamine 2
PGE1	- Prostaglandin E1
AUC	- Area Under curve
Cmax	- Concentration maximum
RCOG	- Royal College of Obstetricians and Gynaecologists
PGF2	- Prostaglandin F2
RFT	- Renal Function Tests
LFT	- Liver Function Tests
NASG	- Non-Pneumatic Anti Shock Garment

INTRODUCTION

INTRODUCTION

Traditionally Obstetric Haemorrhage is classified as Ante partum (APH) and Postpartum (PPH) haemorrhage. APH is due to placental abruption and placenta praevia. Postpartum Haemorrhage (PPH) is the most common form of obstetric haemorrhage. It is one of the major causes of maternal mortality, accounting for nearly one quarter of all maternal deaths worldwide as per WHO. Postpartum Haemorrhage (PPH) is defined as blood loss of more than 500ml during normal vaginal delivery and loss of more than 1000ml following caesarean section⁽¹⁾. PPH can be classified as primary PPH or secondary PPH. PPH if it occurs within 24 hours of delivery is called as Primary PPH and PPH which occurs between 24hours and until 6 weeks postpartum is called as secondary PPH^{(2),(3)} or Late PPH⁽⁵³⁾. Definitions of PPH based on volume of blood loss vary in different countries. It is also defined as fall in haematocrit >10% postdelivery compared to predelivery haematocrit. Postpartum Haemorrhage is included in Priority diseases and reason for its inclusion list as item 6.16 by WHO considering its impact on community.

Causes of PPH is commonly classified as “Four Ts”

1. Tone: Uterine atony, distended bladder.
2. Trauma: lacerations of the genital tract during delivery-cervix, vagina, uterus and its appendages.
3. Tissue: retained placenta in whole or as bits or clots.
4. Thrombin: Pre-existing or acquired coagulopathy

PPH is one of the leading factor of maternal mortality worldwide with a reported incidence of 2–11%⁽²⁾. However the exact rate varies depending on data source, country and assessment methods with prevalence of 10.6% by objective assessment methods and 7.2% when measured by subjective assessment methods⁽²⁾.

Though it seems prevalence of PPH is low in developed countries when compared with developing nations, rates of PPH tend to raise in these developed countries as well ⁽²⁾.

India accounts for 19% of global burden of maternal deaths in 2016 with 56,000 maternal deaths⁽²⁾. PPH is not an infrequent complication of delivery. Its reported incidence in India is 2% - 4% after vaginal delivery and 6% after caesarean section with uterine atony being the most commonest cause (50%)⁽²⁾.

The five most common direct causes of pregnancy-related mortality in India are haemorrhage (38%), sepsis (11%), unsafe abortion (8%), hypertensive disorders (5%) and obstructed labour (5%) ⁽³⁵⁾. The remaining 34% of maternal deaths are due to unspecified indirect causes⁽²⁾.

In spite of vast and elaborate improvements and training in management of PPH, preventing and overcoming the complications of PPH remains a nightmare in developing countries⁽²⁾. This PPH induced morbidity and mortality can be prevented with early diagnosis and Active Management of Third Stage of Labour (AMTSL). It is the gold standard technique to prevent PPH. AMTSL constitutes 3 manoeuvres ⁽²⁾.

- a) Early clamping of cord.
- b) Uterotonic drug administration (Standard recommended drug- Oxytocin) soon after delivery of baby in both vaginal and caesarean deliveries
- c) Gentle cord traction with uterine counter traction (Brandt-Andrews manoeuvre).

An important component in AMTSL is administration of uterotonic agents. Commonly administered uterotonic agent in every hospital setting is Inj.Oxytocin. The dose being 10Units intramuscular, administered soon after the delivery of baby's anterior shoulder. This has been recommended by WHO as an essential component of AMTSL for all deliveries.

When this routine uterotonic agent fails and the patient has excessive bleeding, additional use of other uterotonic agents and transfusion of blood and blood products come into play. If patient still continues to have PPH, surgical interventions are done to rescue the patient.

Misoprostol is an uterotonic agent. It is a synthetic analogue of prostaglandin E1 analogue. It is commonly used for medical termination of first and second trimester conceptions. It is also used for induction of labour. It has strong uterotonic properties. It can be easily administered orally and sublingually. It is stable at ambient temperature when compared with oxytocin for which refrigeration is required and only parenteral route of administration is possible.

Because of its strong uterotonic properties, misoprostol can be used for PPH. It is said that misoprostol is less efficacious than oxytocin, and it has therefore been recommended only for prevention of PPH in settings where injectable conventional uterotonics are not available ⁽⁴⁾.

Misoprostol so far is not routinely used as an isolated regimen or as an add on treatment for prevention of postpartum haemorrhage. In spite of the promising results from various trials on misoprostol's therapeutic efficacy for the treatment of PPH, it is still used as an additional drug to standard oxytocics or as a last resort treatment option ⁽⁴⁾.

The aim of this study is to ascertain if 600µg of misoprostol given sublingually provides an add on benefit to standard oxytocin medication in prevention of PPH.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

‘TAJMAHAL’- One of the wonders of the world where people flock to admire the beauty and architecture is actually a monument built to mourn the death of Queen Mumtaz mahal, wife of Shahjahan, the Mughal Emperor. She died because of Postpartum haemorrhage during her 14th childbirth⁽⁵⁾.

Pregnancy and Childbirth are the two common processes which every woman will pass through in some phase of her life. Encountering complications during this phase is not infrequent. And some of the complications can turn life threatening. WHO estimates that in the world for every one minute a woman dies out of one of the complications of pregnancy and child birth.

HISTORY

The Early documentation done on Postpartum haemorrhage in the literature dates back to 18th century. Dr.W.P.Dewwes had published an essay on Uterine Haemorrhage in the year 1822. In this essay he has mentioned 5 reasons as cause of Uterine haemorrhage. The reasons being 1.A too short fundus 2.Mechanical violence 3.Emotions of mind 4.Atony 5.Spasm and inversion of uterus⁽⁶⁾.

Dr.Rockwell on Uterine Haemorrhage published an article in The New England Journal of Medicine and Surgery-Volume 11 in the year 1822 ⁽⁷⁾.He mentioned that applying irritants to uterus to promote its contraction,

administration of substances to promote coagulum in the mouth of blood vessels are the remedies to arrest haemorrhage. He mentions that the principle of initiating uterine contraction by mechanical irritation by hand of operator exists since the age of midwifery started. Though in that time period, administration of ergot alkaloids had emerged as new concept in controlling uterine haemorrhage, Dr.Rockwell doubts its usage in view of its side effects⁽⁷⁾. He said that side effects like nausea, vomiting are unusual which limit its usage.

Dr.Ingleby in the year 1832 in his book on “A practical treatise on Uterine haemorrhage and parturition” mentioned that placenta should not be forcefully removed unless natural separation of placenta from placental bed happens by spontaneous uterine contractions⁽⁸⁾.

Dr.Beatty's in the year 1834 published an article in Dublin J Med Sci- 1834 Volume-4 as “Dr.Beatty's contribution to Midwifery”. Here he had discussed a case of PPH where tight compression of uterus by holding the fundus over the abdomen and applying intravaginal compression controlled PPH⁽⁹⁾. It can be stated from then on importance on applying uterine compression by external abdominal pressure was laid which is a component of AMTSL criteria.

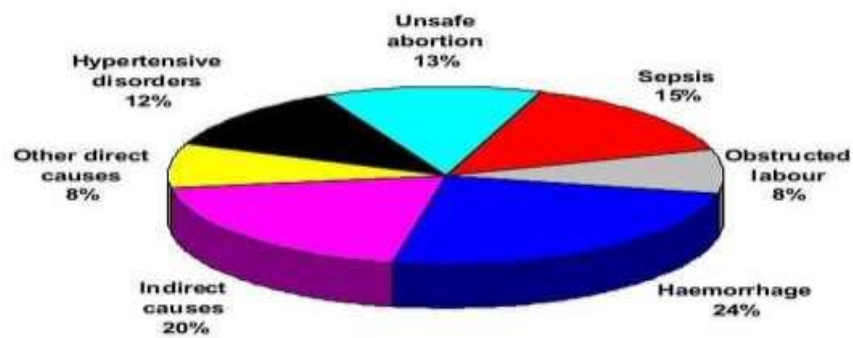
Dr.Brodhead in the year 1905 supporting on allowing spontaneous separation of placenta and then its removal, also insisted on manual removal of placenta when spontaneous removal does not happen. Also he recommended and practised oral and hypodermic administration of ergot

alkaloids for initiating and enhancing uterine contraction to prevent postpartum haemorrhage.

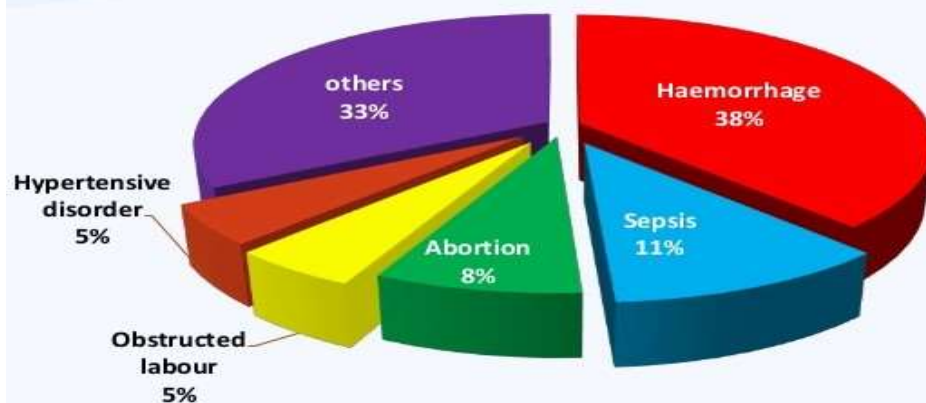
EPIDEMIOLOGY OF PPH

The major causes of maternal mortality all over the world include postpartum haemorrhage, sepsis, unsafe abortion, preeclampsia and eclampsia, obstructed labour and rupture uterus(10).

Causes of maternal mortality (Global)



Causes OF Maternal Death in India



Developed Countries

Incidence of PPH varies between developed and developing countries. In developed countries the prevalence of PPH with a blood loss around 500ml with expectant management of labour is 5% and with active management of third stage of labour is 13%. At the same time prevalence of blood loss around 1000ml is 1% with active management 3% with expectant management ⁽¹¹⁾.

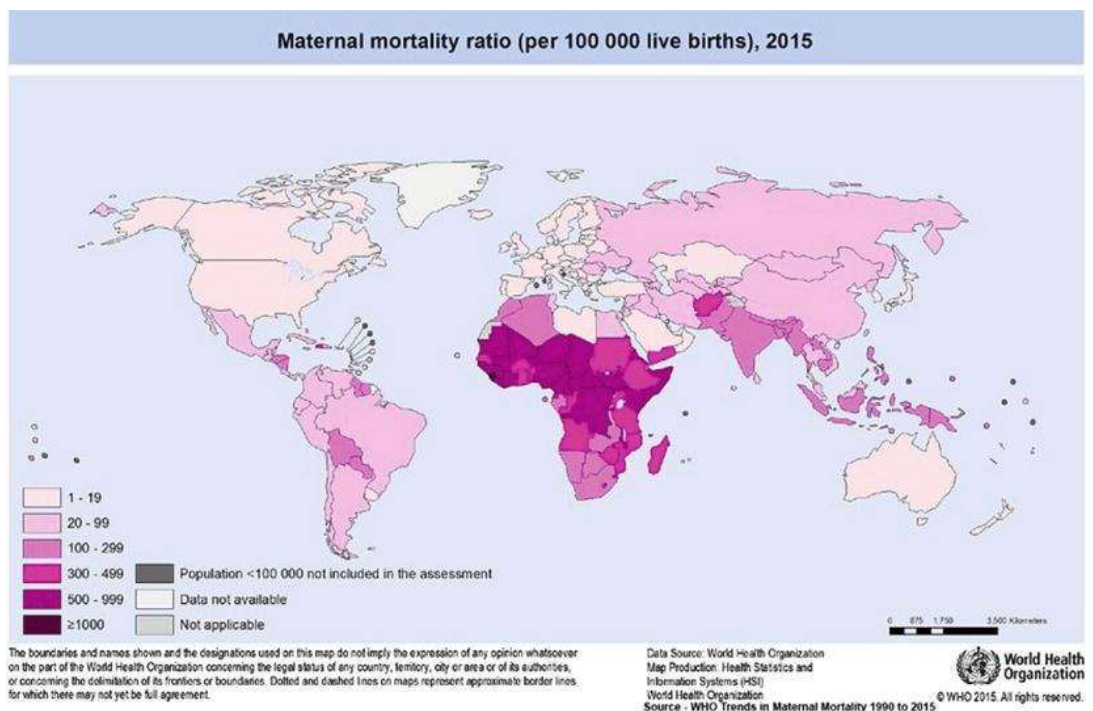
Developing Countries

Prevalence of PPH is high in developing countries. Prevalence of PPH for the blood loss of ≥ 500 ml was in the range from 2.55% in Asia to 10.45% in Africa. Prevalence of primary and secondary PPH is 6% and 1.86% of all deliveries, respectively⁽²⁾. The reasons for this high prevalence in developing countries being lack of quality centres for delivery, inadequate expertise care givers, inadequate blood transfusion and anaesthesia facilities.

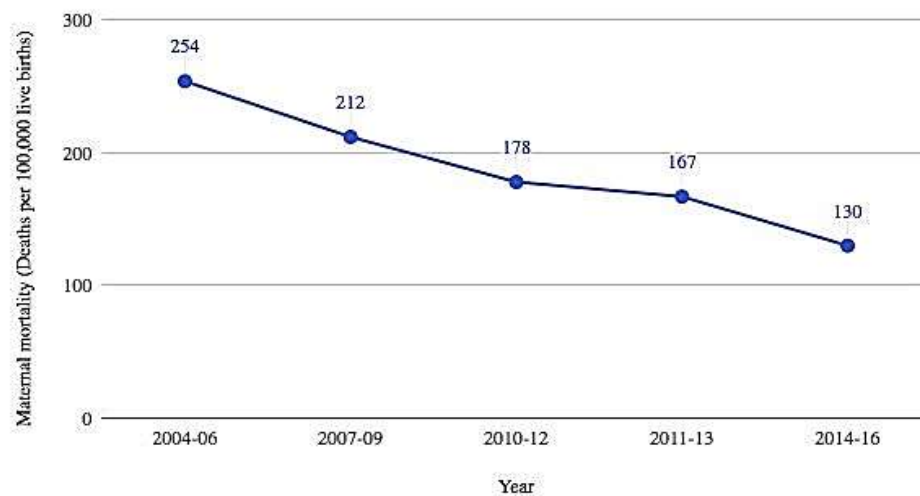
As per WHO around 830 women die every day worldwide out of preventable causes of pregnancy and child birth. Maternal death is 100times more in developing and underdeveloped countries when compared to developed countries. According to WHO, 14 million women suffer from PPH every year. Out of this, the risk of death by haemorrhage is 1 in 1000 deliveries⁽¹²⁾ and 99% of these deaths occur in low and middle income countries⁽²⁾.

Global Maternal Mortality Ratio (MMR) has dropped from 385/100000 live births in the year 1990 to 216/100000 live births in the year 2016.

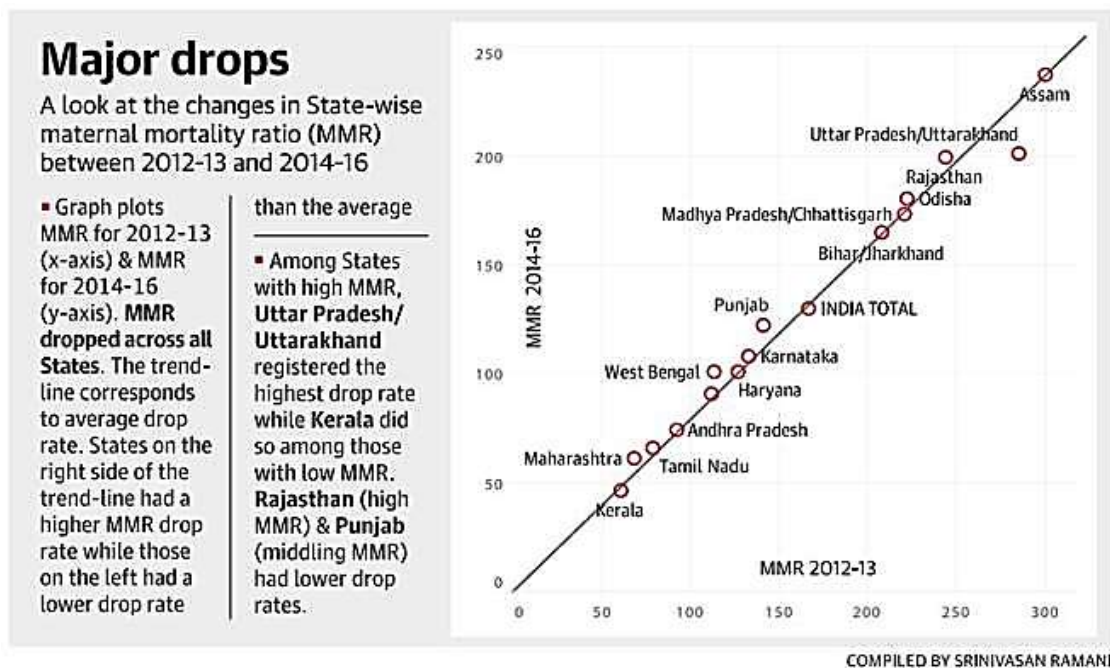
In India MMR has dropped from 167/100000 in the year 2013 to 130/100000 in the year 2016. Current MMR in Tamilnadu is 66/100000 live births and is the third best state in India with low MMR, first being kerala and second being Maharashtra as of data released by Registrar general of India. This has been appreciated by WHO as commendable performance in WHO's south east Asian Bulletin⁽¹³⁾.



India's Maternal Mortality Ratio



Decline in Maternal Mortality rate in India over years



State-wise comparison of Maternal Mortality Rate

Varied Definitions of PPH

PPH is one of the complications of Third stage of labour. Third stage of labour is defined as the time duration from birth of the baby to the delivery of placenta and its membranes. Third stage of labour is the shortest of all stages of labour. Normally it lasts for 5 to 30 minutes. This duration can be shortened by AMTSL in which administration of uterotonics is one of the component.

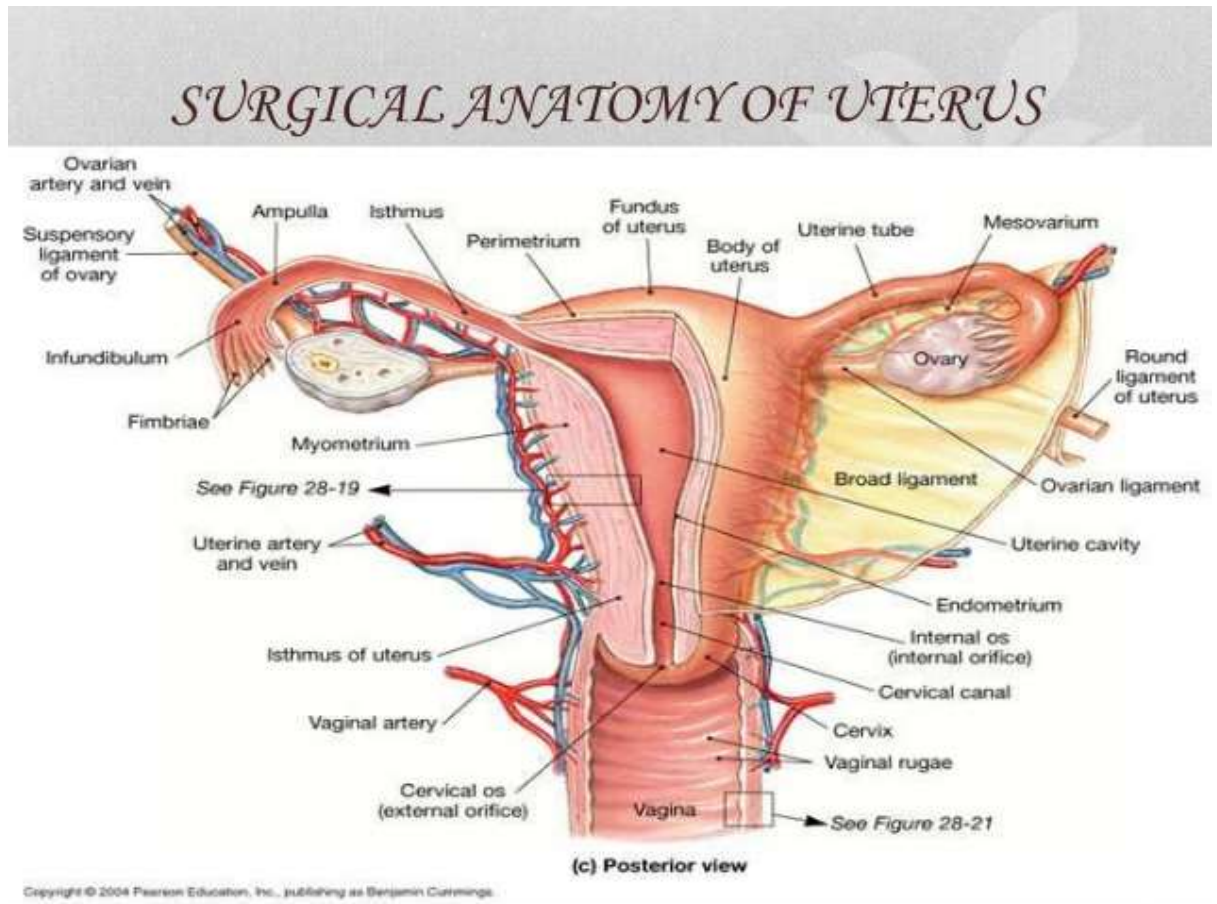
Postpartum haemorrhage (PPH) is commonly defined as loss of more than 500 ml of blood following vaginal delivery and more than 1000 ml after caesarean section in first 24 hours of delivery. Also there are various other definitions which include loss of more than 600ml of blood (Beischer 1986) and loss of more than 1000ml of blood (Burchell 1980) and to the extreme at loss of more than 1500ml of blood as mentioned by mousa et al⁽¹⁴⁾. Estimation

of blood loss is often inaccurate and subjected to errors due to observer or the methods used to quantify blood loss.

PPH also holds alternative definitions like a fall in >10% of predelivery haematocrit and volume of blood loss which requires blood transfusion as given in Cochrane database of systemic reviews-2009⁽¹⁵⁾.

Blood volume is dependent on body weight of an individual. It increases in pregnancy to approximately 100ml/kg, hence for a 70kg woman it will be around 7000ml. A loss of >40% of blood volume is considered life threatening which accounts for 2800ml of blood loss. In a healthy young pregnant woman, there will be estimated 30-50% increase in blood volume. These women will be more tolerant to blood loss when compared to pregnant woman with anaemia or other coexisting cardiac condition or volume depleted states like dehydration or preeclampsia. Hence a more rational definition of PPH would be any amount of blood loss which threatens hemodynamic stability of the woman.

ANATOMY OF UTERUS



Female Reproductive organ is classified as External genitalia and Internal genitalia. Internal genitalia include organs which lie within the true pelvis which are uterus, fallopian tubes, ovary, cervix and vagina.

Uterus is an inverted pear-shaped organ with dimensions of 7cm long, 5cm broad and 3cm thick. An adult non pregnant nulliparous uterus weighs around 50-70grams whereas multiparous uterus can weigh to the maximum of 110gms. Menopausal uterus becomes atrophic and small weighing less than 10-20gms. Uterus by itself is divided into fundus, body and cervix. A very indistinct shorter constriction is seen between body and cervix of uterus called

isthmus. Uterus can be positioned either anteverted or retroverted in respect to vagina, anteverted being the commonest. Uterus lies posterior to urinary bladder and anterior to rectum. The fallopian tubes enter into uterine cavity at the fundal region termed as cornua. The uterine cavity is triangular and flattened. Uterus is connected to surrounding structures by means of connective tissue and ligaments. They are broad ligament which has both anterior and posterior laminae into which uterine and vaginal vessels course through. Other ligaments are rectovaginal ligament, round ligament, uterosacral ligament, pubocervical ligament.

Blood supply to uterus is through uterine arteries and uterine veins. Uterine artery arises from anterior division of internal iliac artery. Uterine artery anastomoses with ovarian artery all along the fallopian tube. Lymphatic drainage of uterus is into lateral aortic, pelvic, and iliac nodes. Nerve supply of sympathetic nervous system is through hypogastric and ovarian plexuses and the parasympathetic nervous system is through the pelvic splanchnic nerves from the second, third and fourth sacral nerves.

ETIOLOGY:

Postpartum Haemorrhage is a final result of many other potential causes. The most common factor is uterine atony. The causes of PPH is commonly remembered as 4Ts which include

1. Tone
2. Tissue

3.Trauma

4.Thrombosis

Tone

Loss of uterine tone or uterine atony is due to failure of contraction and retraction of myometrial muscle fibres soon after delivery, consequently leading to flabby uterus that fails to arrest bleeding from blood vessels at placental implantation site.

Factors leading to uterine atony includes

- ✓ Overdistension of uterus- Multiple pregnancy, large foetus, Polyhydramnios, retained clots
- ✓ Anaesthesia mainly due to halogenated compounds causing relaxation of uterus which fails to contract soon after delivery
- ✓ Induction/Augmentation of Labour with drugs
- ✓ Other drugs like - Nitrates, magnesium sulphate used for preeclampsia, beta sympathomimetics and Nifedipine
- ✓ Abnormalities in progression of labour which can be rapid labour, prolonged labour, precipitate labour
- ✓ History of PPH in previous pregnancies.

Usually but not always the occurrence of uterine atony can be predicted prior delivery based on the presence of above said risk factors and therefore a need for vigilant watch. But the prediction of occurrence of PPH in women

undergoing caesarean section is only half the chance. Hence the identification of pregnant women who might encounter PPH is limited.

High parity is a definite risk factor for PPH. The incidence of PPH ranges from 0.3% in low parity to 1.9% in high parity of above 4 deliveries⁽⁵³⁾.

Tissue:

For uterus to contract and retract after delivery of baby, there should be complete detachment and expulsion of placenta in toto. Retention of placenta as a whole or partial will lead to PPH. Preterm deliveries tend to retain placenta rather than term deliveries.

Administration of vaginal misoprostol for second trimester pregnancy termination leads to marked reduction in retained placental bit rates when compared to intra amniotic instillation of prostaglandins.

Trauma

Injury to genital tract in a woman in labour can either be spontaneous or iatrogenic. Injury can range from simple extension of episiotomy which by itself can cause severe PPH to cervical tears and uterine rupture. a life-threatening event. Predisposing factors to trauma include exhausted uterus out of prolonged labour, induced labour, extra and intra uterine manipulation of foetus, removal of retained placenta, previous surgeries done on uterus and adnexa, cervical lacerations are common with assisted vaginal deliveries such as forceps and vacuum deliveries. Similarly, vaginal lacerations are associated

with assisted vaginal deliveries and manipulation done to resolve shoulder dystocia.

Thrombosis

The Uterine myometrial contraction and retraction is so efficient that usually patients with bleeding disorders does not encounter PPH. Fibrin formed at the mouth of blood vessels soon after delivery at placental site seals haemorrhage.

Patients often suffer from PPH with the following congenital and acquired bleeding disorders. This includes

Congenital:

- Von Willebrand s disease
- Idiopathic Thrombocytopenic purpura
- Haemophilia

Acquired:

- -HELLP Syndrome (Haemolysis, Elevated liver enzymes, Low platelet count) resulting out of Pre-eclampsia, Eclampsia, Abruptio placenta
- -DIC (Disseminated Intravascular Coagulation) occurring due to abruptio placenta, Amniotic fluid embolism, Sepsis, PIH, Intrauterine Foetal demise

Anticipation of PPH and exercising caution is a must in patients with history of menorrhagia since menarche, family history of bleeding disorders and history of GI bleed.

Though the factors mentioned above are the various risk factors for PPH, commonly it is due to prolonged and exhausted labour finally ending up in assisted vaginal deliveries.

PATHOPHYSIOLOGY OF PPH

Pregnant women during delivery maintains hemodynamic stability in spite of blood loss in labour when compared to the same amount of blood loss in nonpregnant individuals. This is because of plasma volume expansion. Plasma volume starts increasing from preconception and reaches 18% by 16 weeks, 27% by 20 weeks and 36% by 25 weeks gestation. Maximum mean plasma volume expansion increase is attained at 33-34 weeks of gestation which will be 52%, the range being 48%-59%. There after there will be a slight decline in plasma volume at term. Thus the plasma volume expands from 4Litres in pre pregnant state to 6Litres at term⁽¹⁶⁾.

Plasma volume expands more than the volume of total RBCs, result of which is fall in haemoglobin concentration and haematocrit value. This increase in plasma volume meets out the excessive perfusion demand of low resistant uteroplacental unit and to compensate the blood loss that happens during delivery.

Uterus gets contracted and retracted following delivery of the baby. Retraction is the maintenance of contracted state of the uterus following every successive contraction. This is because of unique arrangement of myometrial muscle fibres which run in crisscross pattern. The blood vessels are arranged

within the crisscross muscle fibres. On contraction and retraction of uterus, these crisscross fibres compress and occlude the vasculature to stop bleeding from placental bed. This is the reason why myometrial musculature are termed as “living ligatures”. This is facilitated along with the formation of fibrin and platelet plugs at the lumina of the bleeding vessels. Defect in any of the above steps will lead onto PPH.

CLINICAL PRESENTATION

Presentation is often dramatic with severe bleeding through vagina resulting in hypovolemic shock, with signs and symptoms of weak and rapid pulse, low blood pressure, pallor, restlessness, cold clammy skin, oliguria. This is true when PPH follows separation of placenta. When PPH occurs even before separation of placenta, bleeding will be mild and continuous with significant amount of blood retained in the uterus, retroplacental area, and within membranes.

In Atonic PPH vaginal bleeding is associated with large flabby uncontracted uterus on abdominal examination where as in PPH resulting out of lacerations of cervix and vagina, uterus will be firm and well contracted. This picture may vary in trauma to uterine adnexa where blood collects within broad ligament. retroperitoneum and within abdominal cavity as in uterine rupture.

ESTIMATION OF BLOOD LOSS:

Dating back to 18th century, from 1800s, physicians tried to quantify blood loss during delivery to prevent morbidity and mortality. Most of the blood loss during childbirth is during first one hour and the commonest cause being atonic uterus.

Different techniques of Blood loss estimation ⁽¹⁷⁾

- 1) Visual Estimation
- 2) Direct Measurement
- 3) Gravimetric method
- 4) Photometry
- 5) Miscellaneous

1. Visual Estimation

Blood loss is routinely estimated by visual methods by birth attendant from age old days. Main disadvantage being underestimation of the amount lost to as much as 50%. Since early and swift management is the ultimate necessity to prevent morbidity and mortality in PPH, underestimation of blood loss visually will delay management of PPH which is life threatening event. Sometimes there can be overestimation of blood loss as in operative deliveries. There was no difference in under estimating or over estimating blood loss between experienced surgeons or junior residents(17). Comparatively midwives were able to estimate blood loss accurately.

In Developing and underdeveloped countries where a fraction of deliveries are conducted by trained dhais, estimation of blood loss is an enigma.

In Tanzania, trained dhais estimate blood loss from a piece of pre-cut cloth soaked.

Two soaked pre-cut cloths roughly mentions >500ml of blood loss⁽¹⁷⁾.

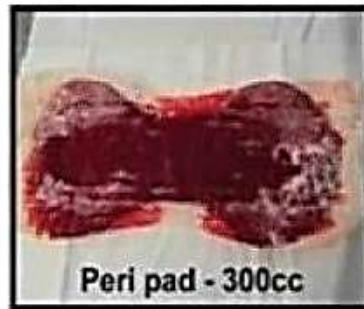
There is a tendency for clinical and para clinical personale to overestimate blood loss at lesser volumes and underestimate at larger volumes. Proper training sessions and drills improves their estimating skills.

Direct measurements:

Attempts to directly estimate blood loss started as early as 19th century. Dr .William's measured blood loss by placing a basin close to the genitals. Other methods used are quantifying blood loss by collecting in bed pan, drapes and sponges.

Graduated under buttock drapes (BRASS-V Drape) placed during delivery has a drape and a pouch⁽¹⁸⁾. Patient is allowed to lie down on the drape during delivery and the pouch collects blood and other fluids. They are finally quantified after subtracting the contaminants⁽¹²⁾. Disadvantage of these methods are contamination with foreign substances and its cumbersome separation of contaminants leading to erroneous results.

Estimation of Blood loss



THE BRASSS-V DRAPE
**A low cost calibrated plastic
blood collection drape.**



Gravimetric Methods:

Gravimetric method is weight by measurement method. It uses computerised scaling system to estimate weight of sponges and suction contents. Patients biometric parameters are entered and it alarms at loss of more than 10% of blood. This when combined with laboratory methods along with pre and post delivery haemoglobin concentration was able to quantify blood loss accurately.

Photometry:

In this method, photometric technique which converts blood pigment to alkaline haematin is used. Blood soaked sponges and towels are put in automatic extractor which extracts blood and this is blended with 5% sodium hydroxide solution. It is filtered and then either optical density or oxyhemoglobin is measured by colorimetric method⁽¹²⁾. Resulting haemoglobin concentration is compared with patient's pre op haemoglobin concentration to quantify blood loss. This is based on the theory that "If any unknown quantity of blood is added to a known volume of haemolysing solution the haemoglobin content of the resulting dilution will be proportional to the volume and original haemoglobin concentration of the blood added."

Other Methods⁽¹⁷⁾:

- 1) Comparing the size of Inferior vena cava by ultrasound. Significant reduction in venacaval diameter noted when blood loss is more than 450ml.
- 2) Radioactive tagged RBC method⁽¹²⁾

- 3) Comparing serum specific gravity before and soon after delivery
- 4) Drop in central venous blood saturation method
- 5) Pictorial methods

Comparison of Blood quantification methods

Visual estimation of blood loss is most common, practical and possible method though it is subjected to severe underestimation in vaginal deliveries.

With proper education and training sessions this defect can be rectified.

Direct measurements can be easily done. But it has the drawback of collecting contaminants other than blood. Failure can occur in collecting blood since women may deliver in different positions⁽¹²⁾

Gravimetric methods provide more or less correct quantification of blood loss. But has the disadvantage of weighing fluids other than blood origin if get absorbed. Also requires precise scaling methods.

Photometric methods is the accurate method. But it is expensive and needs experts and laboratory personnel to estimate blood loss. Errors can occur while collecting blood, extraction of blood, conversion of haemoglobin to alkaline haematin. Prior blood sample collection before delivery is a must.

In miscellaneous methods, most of them are impractical. Tagging RBCs with radioactive material in labouring mother is difficult. Specific gravity method is less reliable. Measuring diameter of Inferior vena cava is expensive and should have been done prior delivery⁽¹⁷⁾.

PREVENTION AND MANAGEMENT OF PPH

Early recognition of PPH and swift management is the ultimate necessity to prevent mortality and morbidity of delivering women. Various guidelines and protocols to manage PPH are in vogue. Most important of all is guidelines framed by WHO and RCOG (Royal College of Obstetricians and Gynaecologists) – Greentop Guidelines.

Protocol includes following measures

Identifying Risk factors and minimisation of PPH

Risk factors of PPH falls under 4 ‘T’ categories as mentioned earlier. As per Cochrane reviews of 2000, 2011 and 2018 it is AMTSL that reduces maternal blood loss and reduces the occurrence of PPH. As many a times PPH occurs in patients without even having any risk factors AMTSL can be offered to every woman who delivers.

AMTSL includes

- 1) Early cord clamping
- 2) Administration of Uterotonic agents
- 3) Controlled cord traction

Administration of uterotonic agent:

Use of uterotonic agents reduces risk of PPH by 60%⁽¹⁹⁾. This intervention is the main stay in active management of third stage of labour.

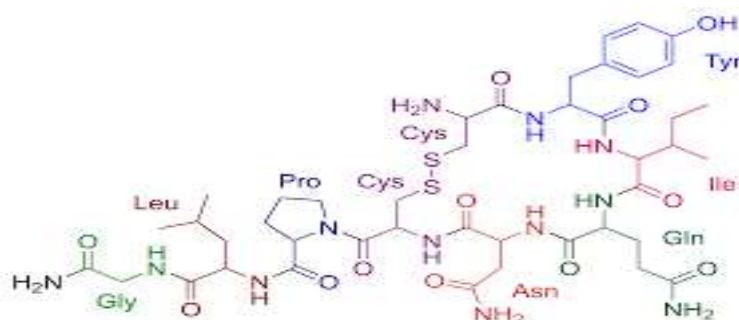
Drugs used under this category include;

- 1) **Oxytocin group**- Oxytocin, Carbetocin
- 2) **Ergot alkaloids**- Ergometrine, Methylergometrine
- 3) **Prostaglandin Analogues**-Misoprostol, Carboprost

Oxytocin

Oxytocin was discovered by British Pharmacologist Sir Henry Hallet dale in the year 1906. Its milk ejection property was enunciated by Ott and Scott in 1910. In 1920 oxytocin and vasopressin were isolated from pituitary extract. Oxytocin is derived from Greek word Oxytotic which means Quick birth.

Oxytocin Chemical Structure



Oxytocin

Oxytocin chemistry and Structure Activity Relationship:

It is a neuro nonapeptide. It is Arginine vasopressin. It is similar to ADH (Vasopressin). It consists of six amino acid ring (Cys1, Tyr2, Ile3, Gln4, Asn5, Cys6) with a tail of 3 amino acids (Pro7, Leu8, Gly9-NH2). It differs from vasopressin in 2 amino acids at position 3 and 8. Asn5 and Tyr2 are 2 amino acids required to elicit action at the level of uterus. Ile3, Gln4, Pro7 and Leu8 are the amino acids required to bind onto the receptors. Any changes

produced in this chemical structure either of chemical or physical instabilities can lead to loss of potency of oxytocin.

Synthesis of Oxytocin:

Oxytocin is produced as precursor in the neuronal cell bodies that lie in both the paraventricular and supraoptic nucleus of hypothalamus. It is transported to pituitary via and stored as granules in neurohypophysis.

Release of Oxytocin

Stimuli for release of oxytocin are dilatation of cervix and vagina, coitus, suckling reflex. It is released in pulsatile manner. Stimuli which secretes ADH also releases oxytocin like dehydration, haemorrhage, hypovolemia. This feature can lead on to water intoxication if given with large amounts of hypotonic fluid.

Mechanism of action

Oxytocin exerts its action through OXT receptor which is a G Protein Coupled Receptor. OXT couples to Gq /G11 to activate PLC-IP3-Ca pathway and activates voltage gated calcium channels. Also, it increases prostaglandin production which induces and enhances uterine contraction.

Effects of Oxytocin

Uterus:

It increases the force and frequency of uterine contractions especially in term uterus. Nonpregnant uterus is relatively resistant to oxytocin. It increases the tone of upper segment of uterus and relaxes the lower segment during labour. At low doses it causes intermittent relaxation between

contractions. Basal tone increases only with larger doses. Oestrogen increases sensitivity of uterus to oxytocin.

Breasts:

Oxytocin induces Milk ejection reflex by contraction of myoepithelial cells of mammary alveoli by suckling.

CVS:

Larger doses of oxytocin results in hypotension by causing vasodilatation. It causes flushing, tachycardia. Oxytocin constricts umbilical vessels soon after birth

Kidneys:

Oxytocin at higher doses elicit ADH like action, resulting in water intoxication and pulmonary edema when large volume of fluids administered with oxytocin.

Brain:

Oxytocin enhances parental bonding. Along with vasopressin it mediates socio emotional behaviour of fear and anxiety, processes sensory information in brain, modulates metabolism and food consumption. It is CNS regulator of trust.

Pharmacokinetics

Oxytocin gets inactivated when given orally hence not given by oral route. It is not bound to plasma proteins. It is metabolised by oxytocinase and excreted through kidneys. Has short half-life of 5-10 minutes.

Oxytocin antagonist

Atosiban is oxytocin antagonist to inhibit contractions of preterm labour

Therapeutic Uses of Oxytocin

1. Induction of labour

Oxytocin is administered for both induction and augmentation of labour in cases requiring early vaginal delivery as well as in conditions with uterine inertia.

Conditions requiring early vaginal delivery include toxemia of pregnancy, gestational diabetes mellitus, utero placental insufficiency, PROM

Dose

2.5 IU for primipara and 5 IU for multipara, infused slowly in 500ml of Dextrose normal saline infusion, stopped as soon as effective contractions are produced.

2. Milk Ejection reflex promotion

Oxytocin is used for promoting milk ejection before nursing. Administered as 25-30IU in each nostril as nasal spray. It does not increase milk production.

3. Prevention of Postpartum haemorrhage

WHO strongly recommends all women who deliver either vaginally or by caesarean should be given 10 IU of intramuscular oxytocin soon after delivery to prevent occurrence of PPH.

4.Treatment of PPH

First line drug for treatment of PPH is oxytocin. 5 IU is given by slow Intravenous injection or 40 IU in 500ml of hartmann solution is infused at the rate of 125ml/hour unless fluid restriction is mandatory. Maximum fluid infusion should not be more than 3 Litres to prevent water intoxication.

Adverse Effects:

Rupture of uterus, Foetal asphyxia, water intoxication

Contraindications:

Cephalopelvic disproportion, Placenta praevia and conditions requiring delivery by caesarean section

Formulations of Oxytocin:

Oxytocin is available in formulations for both intramuscular and intravenous administration. Also, des amino oxytocin is available in buccal formulation.

Oxytocin is available as 1ml ampule or 10ml vials. Each ml contains 10 IU of oxytocin along with chlorbutanol or ethanol. WHO approved product RH 053 contains glacial acetic acid, sodium acetate trihydrate, sodium chloride, sodium hydroxide, and water as excipients. pH ranges from 2-5⁽²⁰⁾.

Storage conditions

Oxytocin should be stored between 2C-8C. Hence refrigeration, cold chain maintenance, cold storage facility is a must. If stored in room temperature, formation of toxic products and loss of potency is encountered. Multiple degradation products of oxytocin are formed when exposed to room

temperature which are pH dependent. The optimal pH to be maintained for preserving the potency of oxytocin is 4.5⁽²⁰⁾. Toxic metabolite being a peptide, doesn't pose safety issue. It is acceptable to keep unrefrigerated oxytocin for short period of time - 1 month at 30C and 1 week at 40C⁽²⁰⁾.

Hence it can be seen that main disadvantage of oxytocin is its stringent storage conditions required and parenteral route of administration.

Carbetocin

Carbetocin is a long-acting synthetic analogue of oxytocin. It is 1-deamino-1-monocarbo oxytocin described first in 1987. It has half life of 40 minutes, 10 times longer than oxytocin. Dose is 100µg administered intramuscular. A single 100µg dose produces uterine contraction in less than 2 minutes and action prolongs for approximately 1 hour because of sustained uterine contractility of higher amplitude and frequency.

Mechanism of action

Carbetocin binds to oxytocin receptors and increases uterine tone by rhythmic uterine contractions.

Pharmacokinetics

Bioavailability is 80% following intramuscular injection. Half-life is 40 minutes

Uses

Carbetocin is used for prevention of postpartum haemorrhage in caesarean delivery under regional anaesthesia. Dose is 100µg intramuscular which is equivalent to 5 IU of oxytocin

Adverse effects

Nausea, vomiting, flushing, headache and hypotension

Ergot Alkaloids

Ergot alkaloids are obtained from fungus *claviceps purpurea* that grows on rye like grains. Literature on ergot poisoning is available in the middle ages where consumption of ergot contaminated grains resulted in gangrene of extremities.

Ergot alkaloid used as uterotonic agent is Ergometrine otherwise termed as ergonovine. Its synthetic analogues used clinically are methyl ergometrine and Dihydro ergometrine.

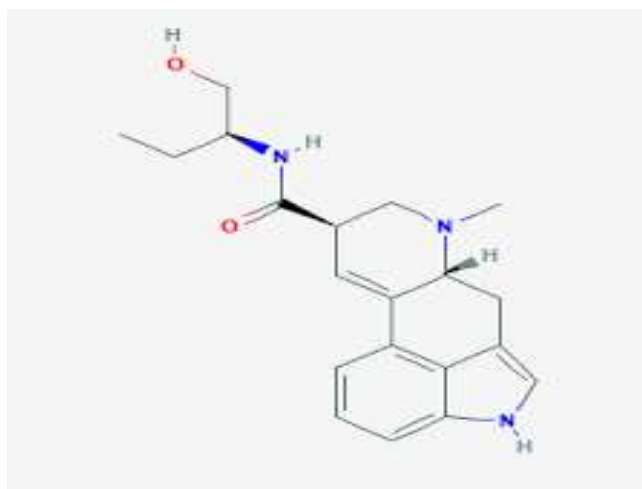
History

Pharmacological properties of ergometrine is known for centuries and are used by midwives since then for labour management. Ergometrine was discovered by C.moir and H.W.Dudley in 1920 and ergonovine was isolated in 1932.

Chemistry

Ergot alkaloids are subdivided into two families. Amine and peptide alkaloids. Both has tetracyclic ergoline nucleus. Naturally occurring alkaloid is d-lysergic acid. Semi synthetic derivatives are obtained by catalytic hydrogenation of natural alkaloid dihydroergotamine.

Chemical Structure



Ergometrine

Pharmacokinetics

Ergot alkaloids are variably absorbed from GIT. Can also be administered through intramuscular, buccal, rectal and aerosol routes. Absorption from intramuscular route is slow but reliable. Semi synthetic analogues are well absorbed orally. Speed of oral absorption can be accelerated by concomitant administration with caffeine. They are extensively metabolised in the body.

Pharmacodynamics

Ergot alkaloids act a partial agonist and antagonist at alpha adrenoceptors, serotonin receptors, dopamine receptors. They have affinity on both presynaptic and post synaptic receptors. Ergometrine and methyl ergometrine used for management of PPH acts as agonist on alpha adrenoceptor, serotonin receptors and exert motor activity on uterine smooth muscle.

Effects on organ systems:

Central Nervous System:

Acts as agonist at 5HT₂ receptor. By acting on dopamine receptors in central nervous system and pituitary they control extrapyramidal symptoms and prolactin release.

Vascular smooth muscle:

Ergotamine and similar compounds produce sustained vasoconstriction by partial agonistic action on alpha adrenoceptors and serotonin receptors. Overdosage cause severe and prolonged vasospasm.

Uterine smooth muscle:

Ergot alkaloids exert uterine stimulant action and vascular smooth muscle action by its agonistic action on alpha adrenergic receptors and serotonergic receptors. Alpha adrenergic receptors in uterus increase in number on reaching term in pregnant women. Hence the sensitivity of uterus to ergometrine increases at term. At lowest doses ergometrine evoke rhythmic contraction and relaxation of uterus whereas at higher doses it results in powerful and prolonged uterine contraction.

Other smooth muscle organs:

In GIT ergot alkaloids lead to nausea, vomiting and diarrhoea.

Uses of Ergot alkaloids

Migraine:

Ergotamine tartarate is highly specific for migraine when given during acute attacks. It is combined with caffeine to facilitate quick absorption. It is

available in oral, sublingual, rectal and inhaler routes. Dose should not exceed 6mg for each attack and not more than 10mg per week, since ergotamine produced vasoconstriction is long lasting and cumulative.

Hyperprolactinemia:

Pituitary tumours and Dopamine₂ receptor blocking antipsychotic drugs cause hyperprolactinemia resulting in galactorrhoea and amenorrhoea. This can be treated with dopamine agonists like bromocriptine at the dose of 2.5mg twice or thrice daily. Cabergoline is more potent than bromocriptine in reducing galactorrhoea.

Cabergoline is used to treat cardiac failure occurring at the end of term pregnancy due to prolactin surge.

Postpartum haemorrhage:

Because of powerful and sustained contraction produced even by minimal doses of ergometrine, it is used for management of PPH only and not for inducing delivery. It is given at the dose of 0.2mg intramuscular soon after delivery. But Oxytocin is the preferred agent.

Ergometrine is contraindicated in patients with hypertensive disorders, preeclampsia and eclampsia, cardiac disorders.

Variant Angina diagnosis:

Ergonovine given intravenously produces instant vasoconstriction during coronary angioplasty to diagnose variant angina.

Senile Cerebral insufficiency:

Dihydroergotoxine is used for reversal of senility and Alzheimer's dementia.

Toxicity

Gastrointestinal side effects –nausea, vomiting, diarrhoea due to stimulation of medullary vomiting centre and activation of Gastrointestinal serotonin receptors.

Ergometrine produces prolonged vasospasm leading to gangrene requiring amputation. Bowel infarction can occur. Vasospasm produced by ergot is irreversible by most vasodilators except infusion of large doses of nitroprusside.

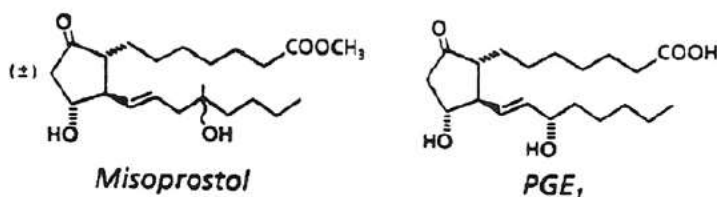
Misoprostol

Misoprostol is synthetic analogue of prostaglandin E1. It is 15-deoxy-16-hydroxy-16 methyl PGE1. Naturally occurring prostaglandin E was discovered in 1967 by Robert et al. It is further developed in the year 1973. It is included in the WHO's essential medicine drug list. Initially its use was limited to prevention and treatment of peptic ulcer owing to its gastric acid anti secretory and gastric mucosal protective properties. It is used in obstetric practice for uterotonic and cervical ripening properties.

Chemistry

Molecular formula for misoprostol is $C_{22}H_{38}O_5$. Its chemical names are isprelor, misoprostolum.

Naturally occurring prostaglandin E has the disadvantage of being rapidly metabolised on oral administration and short duration of action on parenteral administration(21). Also they are chemically unstable and has more adverse effect profile. Hence, synthetic prostaglandin E analogue, misoprostol is produced to overcome the drawbacks.



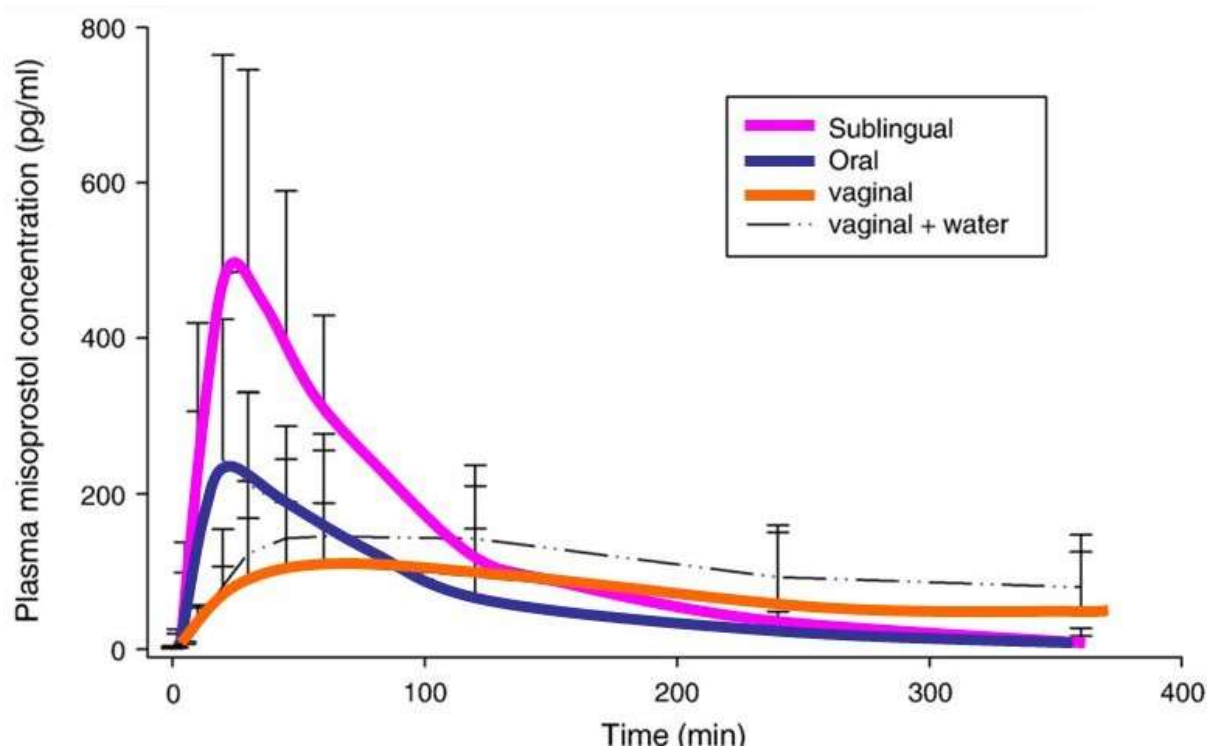
Structure Activity Relationship of Misoprostol and naturally occurring Prostaglandin E

Misoprostol differs from natural prostaglandin E by possessing methyl ester at C₁, methyl group at C₁₆ and a hydroxyl group at C₁₆. These modifications in the structure gives misoprostol improved oral activity, increased duration of action, improved safety profile and potent decrease in gastric acid anti secretory effect.

Pharmacokinetic profile:

Misoprostol can be given through various routes, oral, sublingual, rectal and vaginal. Pharmacokinetic parameters vary for different routes of administration⁽²²⁾.

Plasma concentration of different routes of misoprostol administration



On oral administration, misoprostol gets rapidly absorbed and gets de-esterified to form misoprostol acid, which is the principal and active metabolite of the drug. Food and antacids decrease the rate of absorption. The free acid is excreted in the urine. Elimination half-life is 20-40minutes. With 400 μ g of misoprostol administration, peak plasma concentration reaches at 30 minutes and declines at 120minutes⁽²²⁾.

On vaginal administration, misoprostol absorption is inconsistent because of variation in the amount and pH of vaginal discharge. Attains peak plasma concentration in 70-80 minutes and concentration declines slowly with drug levels detectable even after 6 hours of administration⁽¹¹⁾. Though peak plasma concentration attained during vaginal administration is low, Area Under Curve (AUC) is large, which explains increased efficacy of vaginal misoprostol in medical abortion and cervical priming in labour induction.

On sublingual administration, peak plasma concentration is achieved within 30 minutes as of oral administration, this is because of rapid absorption due to abundant blood supply and neutral pH and bypassing first pass metabolism. AUC is larger for sublingual misoprostol within first 6 hours than for any other routes. This property of sublingual misoprostol having shortest T_{max} facilitates its usage in emergency situation of PPH.

On buccal administration (placing the drug between cheek and teeth) misoprostol has pharmacokinetic profile similar to that of vaginal administration. This route is less often used for cervical priming in labour and for medical abortion. AUC is 4 times less than that of sublingual administration.

Rectal route is preferred for PPH management. T_{max} is achieved within 40-65 minutes but can be as early as 20 minutes. Absorption curve is similar to that of vaginal administration but AUC is 1/3 rd of vaginal administration.

The pharmacokinetic knowledge on different routes of misoprostol administration guides in choosing the route for various clinical applications. Side effects are more with sublingual route because of its greater C_{max}.

Also, there are few studies done with intrauterine misoprostol administration for treatment of atonic PPH⁽²³⁾.

Pharmacokinetics of Misoprostol in breastmilk

Misoprostol is sometimes administered to breast feeding mothers when they encounter PPH. On oral administration, misoprostol becomes detectable

in breast milk at 30 minutes and reaches peak at 1 hour and becomes undetectable after 4-5 hours. Misoprostol acid concentration is 1/3 rd on comparing with plasma concentration for the same dose of misoprostol administration⁽²²⁾.

Misoprostol is extensively absorbed. It is 85% protein bound. It is de esterified to misoprostic acid and undergoes beta and omega oxidation. It then undergoes reduction of ketone to yield prostaglandin F analogues.

Effects on Uterus and cervix:

When misoprostol was initially used for peptic ulcer, its uterotonic and cervical softening properties were considered as side effects. But these are the properties which facilitates its broad usage in obstetrics and gynaecology. When administered vaginally uterus starts to contract and regular uterine contractions start after 1 hour and lasts for 4-5 hours.

Mean time to attain maximum tonus is 8 minutes after oral administration and 11 minutes for sublingual administration compared to 20 minutes for vaginal administration. Misoprostol activity ends at 1-2 hours for oral, 3 hours for sublingual and 4 hours for vaginal routes of administration. Rather than high serum levels, low and sustained serum levels of misoprostol is required for regular uterine contraction for inducing medical abortion and labour. Hence vaginal route is often preferred.

Effect on Uterine cervix:

Misoprostol when administered to pregnant women, produces cervical priming, a process in which cervix becomes soft and yielding and so minimum

mechanical pressure is all needed for its dilatation. This is due to misoprostol action on connective tissue stroma evidenced by disintegration and dissolution of collagen.

Effect on Gastric acid secretion

Misoprostol decreases volume and pH of gastric acid secretion by various mechanisms. It acts by binding to prostaglandin receptors in parietal cells. These receptors are G protein coupled receptors.

Gastric mucosal cytoprotective actions are elicited by following mechanisms

1. Secretion of bicarbonate is increased
2. Volume and pepsin content of the gastric secretions is decreased
3. By tightening of epithelial junctions thereby preventing gastric mucosal injury by back diffusion of H⁺ ions into gastric mucosa
4. Increased secretion of mucus
5. By increased mucosal blood flow due to direct vasodilatation
6. Stabilization of tissue lysozymes
7. Increased mucosal regeneration capacity.

Uses of Misoprostol

Prevention and treatment of Gastric ulcer:

Primary indication of misoprostol is prevention and treatment of NSAID induced gastrointestinal injury. But proton pump inhibitors are more effective and cheaper than misoprostol. Multiple doses of 200µg is required for the treatment.

Medical abortion along with Mifepristone:

Terminating pregnancy of less than 7 weeks duration can be achieved with high success rate by administering 2 tablets of 200µg of misoprostol vaginally after 600mg of mifepristone administered 48 hours prior. Uterine cramps followed by expulsion of products of conception occur in next few hours. Misoprostol is also used for terminating second trimester abortions, molar gestation and intrauterine deaths.

Misoprostol converts oxytocin resistant midterm uterus to oxytocin responsive one.

Induction of labour

In certain places misoprostol is used for induction of labour. It is administered vaginally. Dose being 50µg for primipara and 25µg for multipara.

Postpartum Haemorrhage:

Prevention

Misoprostol is not as much effective as oxytocin in preventing PPH⁽¹⁹⁾. It has minor adverse effects, which are dose related. The dose is 600µg orally or sublingually. In settings where skilled birth attendants are not present, in low resource settings and where oxytocin is unavailable, misoprostol 600µg per orally can be administered by community health care workers and lay health workers for the prevention of PPH^{(10),(24)}.

Treatment of PPH

Misoprostol is used if intravenous oxytocin is unavailable, or if the bleeding does not stop with oxytocin. Misoprostol 800µg is given sublingually or 1000µg is administered rectally for management of PPH as per RCOG guidelines and as per Dr.Arulkumaran in his book on comprehensive management of PPH ⁽²⁵⁾.

Adverse effects

Common adverse effects that occur soon after administration of misoprostol are diarrhoea, nausea, vomiting, flatulence, shivering and pyrexia. Shivering and pyrexia persists for 6 hours following delivery and are self limiting. 5% of women develop diarrhoea 1 hour later which will persist for 12 hours⁽²⁶⁾.

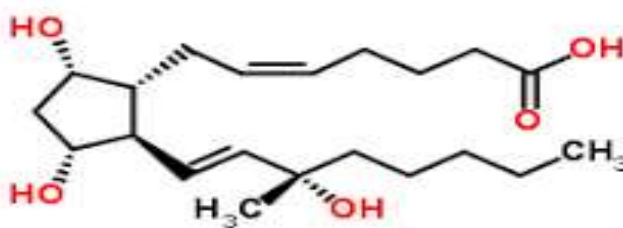
Carboprost

Carboprost is 15 methyl analogue of naturally occurring 15-methyl Prostaglandin F₂α (PGF₂ α) which possess oxytocic properties.

Chemistry

Molecular formula for carboprost is C₂₁H₃₆O₅. Its chemical name is carboprostum.

Chemical Structure



Carboprost

Pharmacokinetics

Carboprost is administered through intramuscular route. It gets rapidly absorbed. Plasma levels peak after 20 minutes and decline from then on. In amniotic fluid half life of carboprost is between 31-37 hours. Metabolised to many metabolites by ω oxidation. Excreted mainly through urine.

Pharmacodynamics

On Intramuscular administration, carboprost stimulates uterine myometrial contraction, resulting in evacuation of products of evacuation. This property of uterine contraction is used in the treatment of PPH. Similar contraction produced in gastric smooth muscle produces diarrhoea and vomiting. Normal therapeutic doses produce transient rise in temperature due to its action on central thermoregulatory centre. Higher doses can elevate blood pressure and may cause transient bronchoconstriction.

Mechanism of Action

Carboprost binds to Prostaglandin E2 receptors in the myometrium to produce myometrial contraction. These receptors are G protein coupled receptors.

Uses of carboprost

1. Postpartum Haemorrhage

Carboprost is used in the treatment of PPH when oxytocin is not available or if the bleeding does not get arrested with other uterotonic agents. 0.25mg of carboprost is given intramuscularly, dose repeated every 15-30 minutes for a maximum dose of 2mg.

2.Abortion

- Carboprost is used for aborting pregnancies of
- 13th to 20th weeks of gestation
- Failure of expulsion of foetus by other methods
- In cases requiring repeated intrauterine instillation of drugs

Dose

0.25mg once by deep intramuscular injection. Subsequent doses of 0.25mg can be administered at 2-4-hour intervals depending on uterine response. Dose can be increased to 0.5mg if uterine contractility is judged to be inadequate with several doses of 0.25mg. Maximum total dose allowed is 12mg. Duration of therapy should not be more than 2 days.

Contraindications

- Bronchial asthma
- Hypersensitivity reaction
- Patients with active cardiac, pulmonary, liver and renal diseases

Adverse effects

Adverse drug reactions are because of smooth muscle contractile effect which includes nausea, vomiting, diarrhoea, transient rise in temperature, flushing.

GUIDELINES ON MANAGEMENT OF PPH

RCOG Green top guidelines for management of PPH⁽¹⁰⁾

Management of PPH - measures include

1. Proper communication

2. Resuscitation
3. Monitoring
4. To arrest Bleeding

1. Proper Communication

Call for experienced obstetrician, anaesthetist and mid wifery should be done. Blood bank should be alerted for need of compatible blood

2. Resuscitation

Assessment of airway, breathing and evaluation of circulation should be done. Oxygen at the rate 10-15 lts/min can be administered. 3.5 litres of crystalloids/colloids can be infused until compatible blood is available for blood transfusion.

3. Monitoring and investigation

Two peripheral cannulas of size 14-16 gauge are secured. Venous blood samples withdrawn for crossmatch, blood counts, coagulation screening including fibrinogen, RFT and LFT.

Temperature, pulse, Blood Pressure, saturation and urine output through Foley's catheter insertion to be monitored at regular intervals.

4. Arresting the Bleeding

Atonicity of uterus is the most common cause of PPH. Careful examination should be done to rule out any other causes of PPH like cervical and other lacerations. Measures to arrest bleeding includes the following

1. Mechanical and Physiological measures
2. Non-Pharmacological measures

3. Pharmacological measures
4. Surgical measures

Mechanical and physiological measures

- Uterine massage, that is rubbing the fundus of uterus should be done until uterus gets contracted.
- Bimanual compression of uterus can be done
- Bladder should be kept empty by insertion of foley's catheter
- Vaginal and Uterine packing is contraindicated

Pharmacological measures

Uterotonic agents as mentioned above oxytocin, methyl ergometrine, misoprostol, carboprost are used to arrest bleeding.

Oxytocin

Prevention of Postpartum haemorrhage

For women without risk factors of PPH who deliver either vaginally or by caesarean section are administered with 10 IU of intramuscular oxytocin.

Treatment of PPH

First line drug for treatment of PPH is oxytocin. 5IU is given by slow Intravenous injection or 40IU in 500ml of hartmann solution is infused at the rate of 125ml/hour unless fluid restriction is mandatory. Maximum fluid infusion should not be more than 3 litres.

Methyl Ergometrine

Because of powerful and sustained contraction produced even by minimal doses of ergometrine, it is used for management of PPH, at the dose of 0.5mg slow intravenous or intramuscular soon after delivery.

Misoprostol

Prevention of PPH

So far misoprostol is not as an isolated agent in preventing PPH. If it is used the dose is 600µg orally or sublingually. In settings where skilled birth attendants are not present, in low resource settings and where oxytocin is unavailable, misoprostol 600µg per orally can be administered by community health care workers and lay health workers for the prevention of PPH⁽¹⁰⁾.

Treatment of PPH

Misoprostol is used if intravenous oxytocin is unavailable, or if the bleeding does not stop with oxytocin. 800µg is given sublingually or 1000µg is administered rectally as per RCOG guidelines for treatment of PPH⁽⁹⁾.

Carboprost

Carboprost is used in the treatment of PPH when oxytocin is not available or if the bleeding does not get arrested with routine uterotonic agents. 0.25mg of carboprost is given intramuscularly, dose repeated every 15 - 30 minutes for a maximum dose of 2mg.

Other drugs that can be used are tranexamic acid. But Cochrane meta-analysis doesn't support the usage of tranexamic acid⁽¹⁰⁾

Non-Pharmacological measures

Non Pneumatic Anti Shock Garment (NASG): NASG reverses the shock by compressing the lower body vessels and so shifting blood from peripheral to central pool. Circulating blood is directed mainly to the core organs heart, lungs, brains, adrenals.

This device with its pneumatic action effectively prevents obstetric haemorrhage, maternal mortality and morbidity by impeding the blood flow to the uterus through its vascular compression. This device should be considered for the first line management to combat hypovolemia due to PPH⁽²⁷⁾



NASG-Non Pneumatic Anti Shock Garment



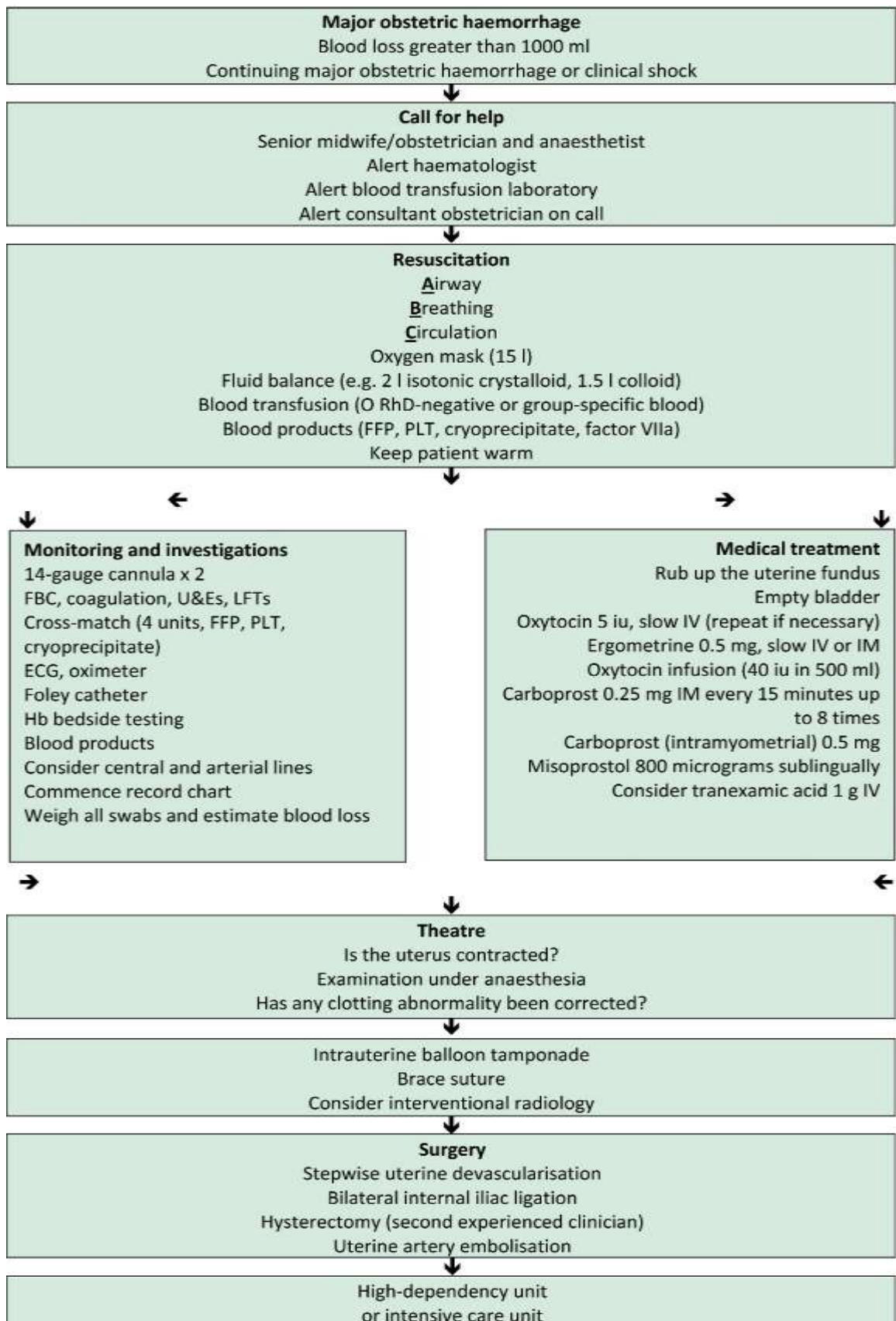
NASG Suit applied to a patient

Surgical measures

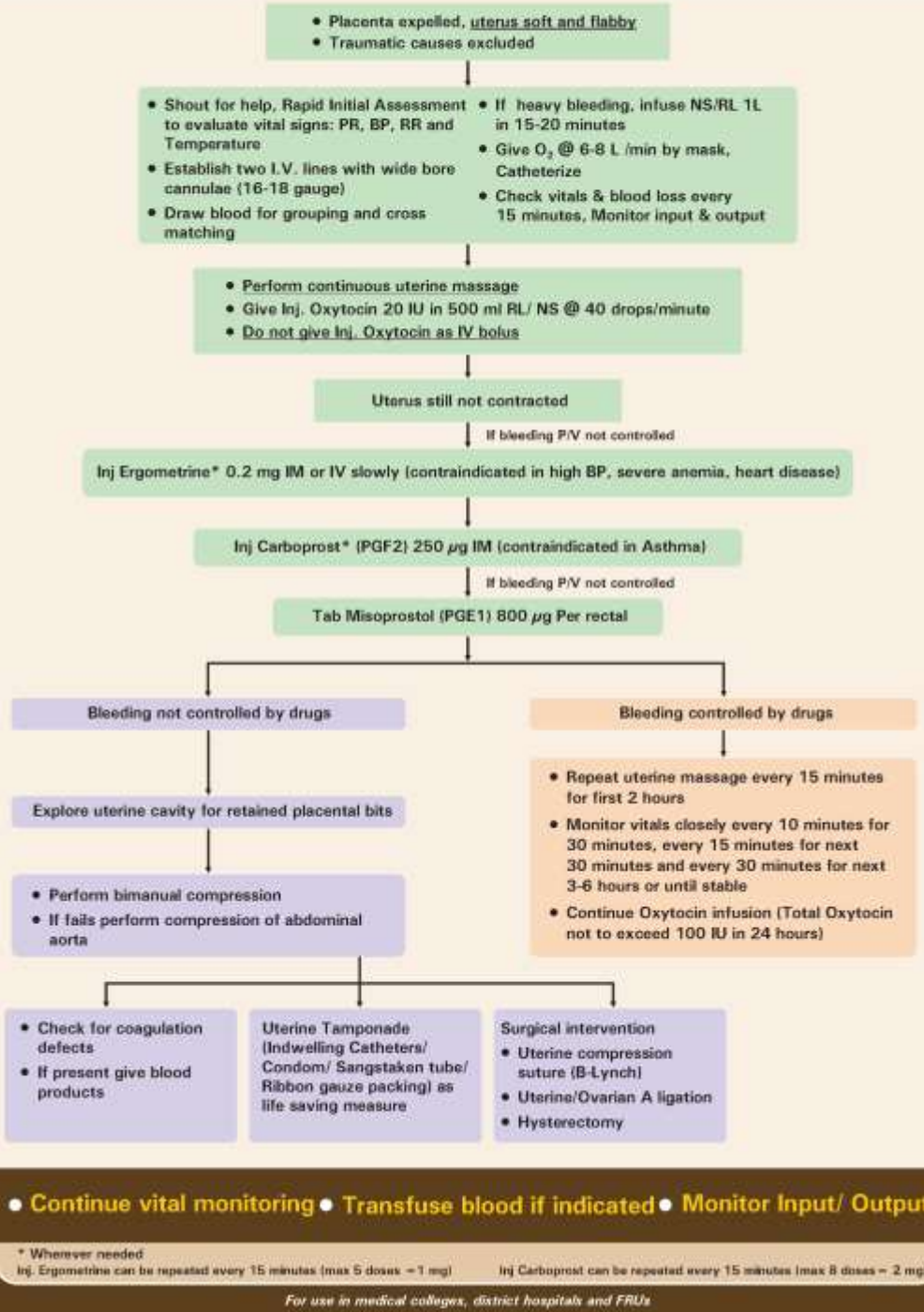
If bleeding does not get arrested by pharmacological measures, surgical measures. It includes either conservative surgical measures or invasive procedures if bleeding persists.

- ❖ Balloon Tamponade- Inflation with Foley catheter, Bakri balloon, sengstaken-Blakemore oesophageal catheter, condom catheter can be done within the uterine cavity to arrest bleeding. 4-6 hours of tamponade is required to arrest bleeding⁽²⁵⁾
- ❖ Haemostatic suturing techniques-These are the techniques which arrests severe PPH and evades hysterectomy. This includes B-Lynch suturing, Hayman's suturing method. Complications like pyometra and uterine necrosis can occur⁽²⁵⁾.
- ❖ Internal iliac artery ligation- It is a conservative surgical method. It preserves menstruation and fertility
- ❖ Uterine artery embolization-Has similar efficacy as balloon tamponade but needs expertise
- ❖ Sub-total Hysterectomy-It is the final invasive surgical procedure if bleeding does not get arrested by any of the above methods. Menstruation and fertility can't be preserved with this method⁽¹⁰⁾.

Management of PPH-Green Top Guidelines-Issued by RCOG



Management of Atonic PPH



Guidelines issued by Ministry of Health and Family Welfare for management of PPH at primary and secondary level health care system

AIM & OBJECTIVES

AIM AND OBJECTIVES

AIM

The aim of this study is to compare the efficacy and safety of misoprostol combined with oxytocin versus oxytocin alone when given during Active Management of Third Stage of Labour (AMTSL) in reducing Postpartum blood loss.

OBJECTIVES

PRIMARY OBJECTIVE

To study the efficacy of sublingual misoprostol when combined with oxytocin in reducing blood loss when administered during third stage of labour.

SECONDARY OBJECTIVE

- To elucidate the safety and tolerability of misoprostol administered with oxytocin.
- To study the need for additional uterotonic agents in both groups
- To observe the need for number of blood transfusions in both groups

MATERIALS & METHODS

METHODOLOGY

STUDY TYPE

Interventional study

STUDY DESIGN

Prospective, Open labelled, Interventional, Comparative, Randomised study

STUDY POPULATION

Women undergoing uncomplicated normal vaginal deliveries in the labour ward of Coimbatore medical college hospital

STUDY CENTRE

Labour ward, Department of Obstetrics and Gynaecology, Coimbatore Medical College Hospital, Coimbatore-18

STUDY PERIOD - One year

January-2018 to December-2018

SAMPLE SIZE

160 patients. (80 patients in each group)

STUDY DURATION

Day of Delivery and 24 hours after delivery

ELIGIBILITY CRITERIA

INCLUSION CRITERIA

- ✓ Patients willing to participate and give informed consent in written
- ✓ Age group-20 -30 years
- ✓ Term Primipara/multipara with normal antenatal record with no other high risk factors undergoing uncomplicated normal vaginal delivery

EXCLUSION CRITERIA

Any high-risk pregnancy which includes

- Gestational hypertension/Pre-eclampsia/Eclampsia
- Gestational Diabetes
- Antepartum Haemorrhage
 - Abruptio placenta
 - Placenta praevia
- Elderly primipara
- Short primipara
- Precious baby
- Long period of primary and secondary infertility
- Multiple Pregnancy
- Polyhydramnios
- Oligohydramnios
- Anaemia complicating pregnancy
- Heart disease complicating pregnancy
- Malpresentations
- Patients undergoing Assisted Vaginal Deliveries
- Patients undergoing caesarean section
- Patients under trial vaginal delivery
- Vaginal birth after Caesarean section patients
- Associated with any medical or surgical disorder

STUDY PROCEDURE

This study was conducted after obtaining Institutional Human Ethical Committee, Coimbatore Medical College, Coimbatore. Ethical committee number dated 21.11.2017. This study was done in adherence to Good Clinical Practices (GCP) and declaration of Helsinki.

Term Pregnant women without any risk factors undergoing uncomplicated normal vaginal deliveries are included in this study. Patients were recruited from labour ward, Department of Obstetrics and Gynaecology, Coimbatore Medical College Hospital.

Patients and their relatives who stay as birth companion are explained on the nature of study procedure, benefits and side effects. Written Informed consent obtained from patients who gave willingness to participate in the trial in the prescribed format in the regional language (Tamil) prior to the performance of any procedure related to the study. In patients who are illiterate left thumb impression was obtained after explaining the study in detail with the birth companion nearby who serve as an impartial witness.

The demographic details of the patients were collected. History recorded from patients, particularly menstrual, marital and obstetric history. Vitals were recorded, General, Systemic and obstetric and vaginal examination were done. Foetal heart rate monitored regularly. Laboratory investigations performed. Patients who fulfil the inclusion and exclusion criteria were enrolled and randomized by simple randomisation to either test group or control group.

Vitals recorded

Height and Weight of antenatal mother

Pulse rate

Respiratory rate

Blood Pressure

Axillary Temperature

Investigations done during antenatal visits

- Complete Hemogram
- Blood grouping and typing
- Fasting and Postprandial blood sugar
- VDRL
- HIV-ELISA
- HBsAg
- Liver Function Test
- Renal Function Test
- Urine Routine

Investigations done on the day of delivery

- Complete Hemogram
- Urine Routine
- Random Blood Sugar

Investigations done 24hours after delivery

- Complete hemogram

RECRUITMENT

200 patients were screened. 160 patients fulfilled eligibility criteria. 80 patients enrolled in each group. 3 patients lost after randomisation in each group due to non-progression of labour ending in assisted vaginal delivery or caesarean section.

RANDOMISATION

Block randomisation by random allocation numbers of the enrolled patients was done to allot them into control and study groups.

TREATMENT

CONTROL GROUP (n=77)

During active management of third stage of labour, standard drug treatment of 10 IU of oxytocin is administered through intramuscular route along with other components of AMTSL criteria exercised.

STUDY GROUP (n=77)

During active management of third stage of labour, standard drug treatment of 10 IU of oxytocin is administered through intramuscular route along with 600µg of misoprostol administered orally with other components of AMTSL criteria exercised.

STUDY PROCEDURE

When patients enter into active labour pains, patients are closely monitored for vitals and foetal heart rate monitored. Patients were allowed to lie on labour couch with **calibrated blood collecting drape** spread under her back. For each patient one drape is used. The drape is disposable. When

patient enters into second stage of labour, on delivery of anterior shoulder of the baby, to patients randomised to control group, standard treatment of 10units of oxytocin is administered intramuscularly. To patients randomised to test group, along with standard treatment of 10units of intramuscular oxytocin, 600µg of misoprostol is administered sublingually.

Measurement of blood loss was done soon after delivery of the baby. Collecting drape (BRASS-V Drape) was tied to the waist of the patient while funnel shaped collecting portion of the drape is suspended down between patient legs. Blood loss was measured till one hour after delivery or if in case bleeding continued after one hour, was measured till active bleeding stopped. When active bleeding had stopped, calibrated blood collecting portion of the drape examined to quantify the volume of blood loss. Vitals-pulse rate, respiratory rate, blood pressure, temperature were measured soon after delivery and after one hour.

During this procedure, following parameters were observed

1. Number of patients who needed blood transfusions in each group
2. Number of patients who needed additional uterotonic agents in each group
3. Number of patients who developed shivering in each group
4. Number of patients who developed pyrexia in each group

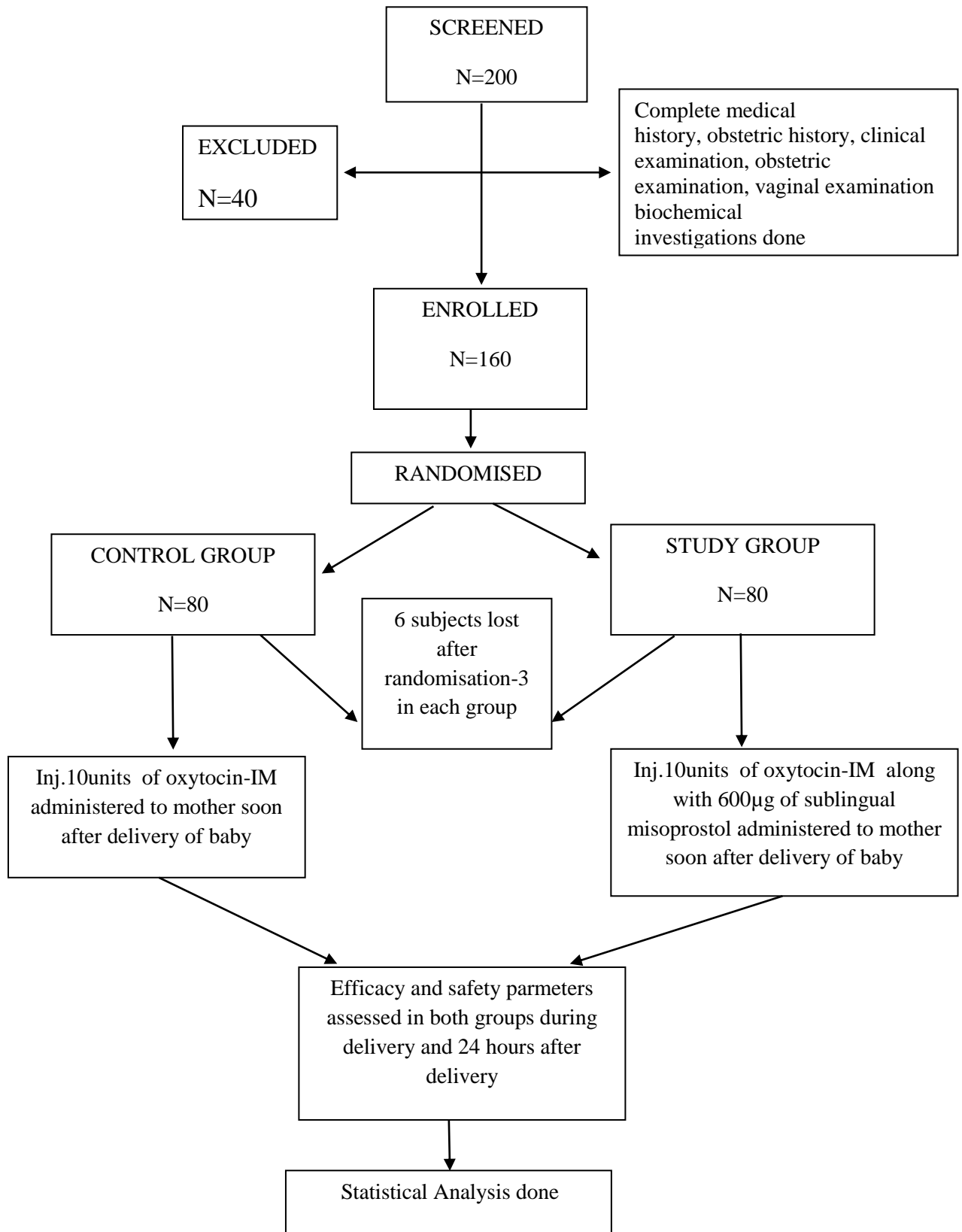
24 hours after delivery, patients were monitored. General examination, systemic examination, abdominal examination and per-vaginal examination

done. Vitals-pulse rate, respiratory rate, blood pressure, temperature were recorded.

Haemoglobin gram percent and haematocrit percent were taken prior active labour and approximately 24 hours post-delivery. Haemoglobin and haematocrit were measured using standard automated flow cytometric method.

Data collected were entered in case record form and in excel sheet.

METHODOLOGY FLOW CHART



ASSESSMENT

Patients are assessed for

1. Efficacy parameters
2. Safety parameters

Parameters evaluated soon after delivery

Efficacy parameters

1. Volume of blood loss

Volume of blood collected in the blood collecting drape is measured against the calibrated markings in the drape for each group. Data compared and analysed between each group. The drape is disposed as per biomedical waste management.

2. Need for additional uterotonic agents

In both groups apart from allotted uterotonic drugs, data on need for additional uterotonic agent is noted. Also, the usage of misoprostol in control group is considered in this category.

3. Number of units of blood transfused

Need for blood transfusions and the number of units of blood transfused owing to excessive blood loss despite the use of additional uterotonic agents in both groups are calculated.

Safety parameters

Misoprostol is known to cause shivering and pyrexia as side effects

1.Number of patients developing postpartum shivering

Subjects who developed postpartum, shivering in both groups after intervention were assessed

2.Number of patients developing pyrexia

Subjects who developed temperature above 38 degree Celsius measured by digital thermometer, post-delivery were assessed

Parameters measured 24 hours after delivery

1.Comparison of Haemoglobin

Haemoglobin as gram percent is measured by standard automated flow cytometer when patient had active labour pains and compared with haemoglobin measured 24 hours post-delivery evaluated by the same flow cytometer method. Drop in haemoglobin percent between these two values are statistically compared between both control and study groups

2.Comparison of Haematocrit value

Haematocrit as percentage is measured by standard automated flow cytometer when patient had active labour pains and compared with haematocrit measured 24 hours post-delivery evaluated by the same flow cytometer method. Drop in haematocrit percentage between these two values are statistically compared between both control and study groups

Adverse events:

Any other adverse events reported by the patient or observed by the obstetrician during the study were recorded. The time of onset of the adverse events, causal relationship to the study drug and action taken was recorded. Appropriate medical care was provided.

Withdrawal:

At the discretion of the investigator the subjects were withdrawn from the study if any adverse event was observed by the physician or reported by the patients.

During the study period the subject was also allowed to withdraw her voluntary consent and opt out of stud

STATISTICAL ANALYSIS

Data entry was made in Microsoft excel sheet software in codes analysis was done with SPSS-20 software version. Categorical variables are expressed as percentages whereas continuous variables are expressed as mean \pm standard deviation. Association between categorical variable was found by chi-square test and relationship between continuous variable was assessed by Student's t-test. The difference in parameters were assessed using paired t-test. P value <0.05 was considered as statistically significant.

RESULTS

RESULTS AND ANALYSIS

The data collected from the study were statistically analysed using SPSS software 21 version according to per protocol analysis. Hence the data of 154 patients, 77 patients in control group and 77 patients in test group who completed the study were analysed.

- Mean age distribution, mean body weight, mean birth weight of delivered babies of all participants in both groups were analysed by Student independent t test.
- Parity comparison between both groups was done by chi square test of independence.
- Volume of blood loss between both control and test groups analysed by independent 2 sample t test and within the sub groups compared by trend chi square test.
- Need of blood transfusions, need of additional uterotonic agents, postpartum shivering and postpartum pyrexia were analysed by chi square test.
- Comparison of haemoglobin percentage and haematocrit before and after delivery in both control and test groups were analysed by paired t test.
- Incidence of adverse events were analysed by paired t test.

Probability of <0.05 was considered to be statistically significant.

*p value ≤ 0.05 was considered significant.

*p value ≤ 0.01 was considered highly significant.

*p value ≤ 0.001 was considered very highly significant.

In this study, out of 160 patients randomised, 6 patients were lost in randomisation, 3 in control group and 3 in study group. Hence 77 patients in control group and 77 patients in study group completed the study and their results were analysed.

TABLE 1 -DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

<i>Demographic Characteristics</i>	Control Group	Study Group
Age (in years)	22.90 ± 03.70	23.10 ± 03.60
Mother's weight (in kg)	66.20 ± 12.60	69.50 ± 12.00
Birth Weight (in Kg)	02.80 ± 00.40	02.90 ± 00.40
<i>Contraceptive Usage</i>		
Used (Multi)	16 (20.5%)/35	15 (19.5%)/35
Not used	61 (79.2%)	62 (80.5%)
<i>Parity</i>		
Primiparous	43 (55.1%)	42 (54.5%)
Multiparous	35 (44.9%)	37 (45.5%)
<i>Clinical Parameters</i>		
Pulse rate	80.43 ± 5.22	80.36 ± 6.10
Blood sugar level	78.60 ± 5.64	77.86 ± 5.58

Table 1 shows Demographic and clinical characteristics of both control and study groups which are comparable.

TABLE 2-MEAN AGE DISTRIBUTION OF PARTICIPANTS

Group	No. of Patients	Mean age (in years)	Standard Deviation	P value
Control group	77	22.9	3.7	0.707
Study group	77	23.1	3.6	

(By Student Independent t-test)

Table 2. shows mean age in years of both study and control group.

Mean age in control group was 22.9 years and mean age in study group was 23.1 years. The mean age was comparable in both the groups with no significant statistical difference between control and study groups. Using student independent t-test p value is found to be 0.707 illustrating there is no statistically significant difference in both groups.

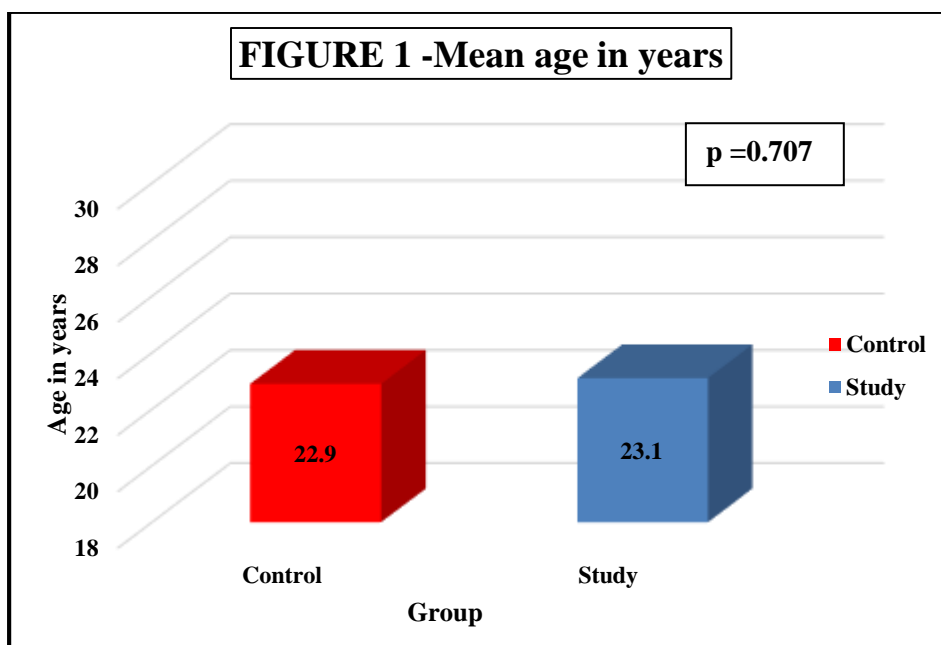


Figure 1 -Mean Age in years

TABLE 3-MEAN BODY WEIGHT DISTRIBUTION OF PARTICIPANTS

Group	No. of Patients	Mean weight (in kgs)	Standard Deviation	P value
Control Group	77	66.0	12.4	0.068
Study Group	77	69.5	12.0	

(By Student independent t-test)

Table 3 shows mean body weight of participant’s in kilograms in both control and study groups. Mean body weight in control group was 66kg and in study group was 69.5 kg. Mean body weight in study group was 3.5kg higher than control group. Intergroup analysis showed p value of 0.068 using student independent t-test illustrating there is no statistically significant difference in both groups.

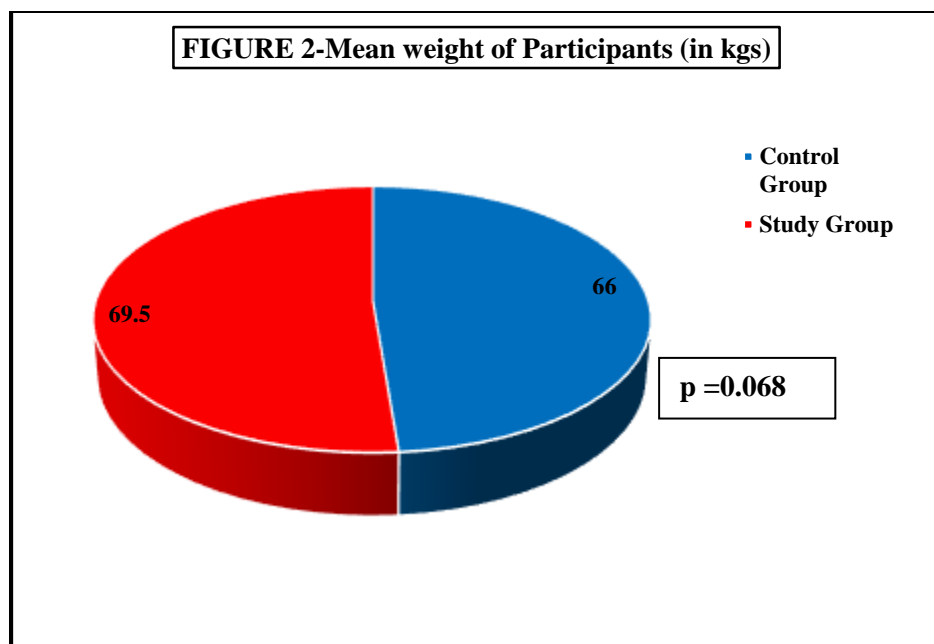


Figure 2 -Mean weight of participants in Kgs

TABLE 4-MEAN BIRTH WEIGHT OF DELIVERED BABIES

Group	No. of Patients	Mean weight (in kgs)	Standard Deviation	P value
Control group	77	2.8	0.4	0.428
Study group	77	2.9	0.4	

(By Student independent t-test)

Table 4 shows Mean body weight of delivered babies in kilograms in both groups. In control group mean body weight was 2.8kgs and mean body weight in study group was 2.9kgs. Intergroup analysis show p value of 0.428 by using student independent t-test which illustrates no statistical difference in between both groups.

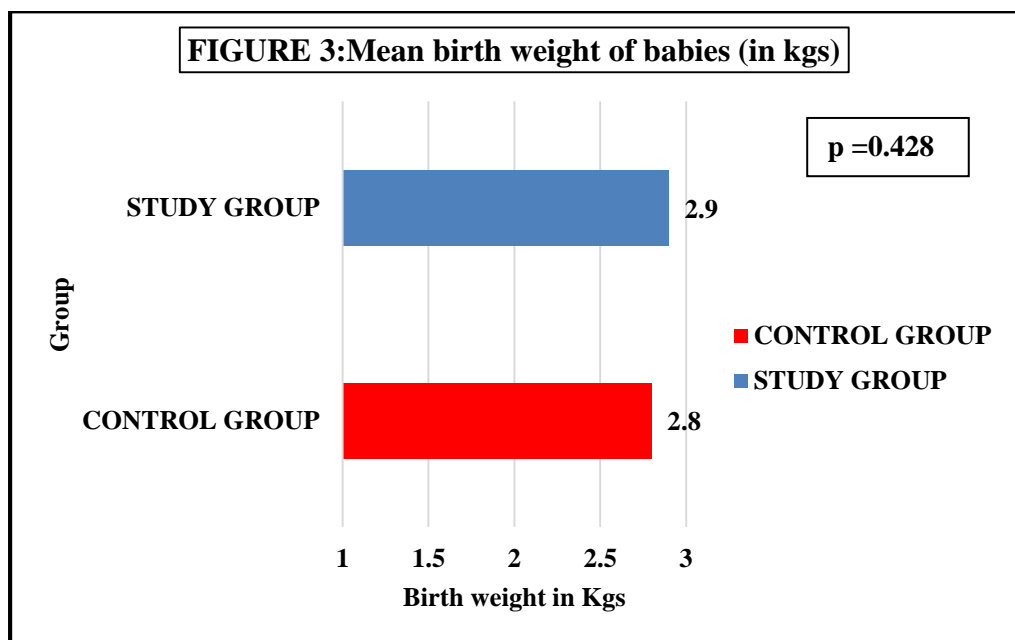


Figure 3 Mean birth weight of babies in Kgs

TABLE 5-CONTRACEPTIVE HISTORY

Usage of contraceptive	Used N=77 (%)	Not Used N=77 (%)	P value
Control Group	16 (20.5%)	61 (79.2%)	0.711
Study Group	15 (19.5%)	62 (80.5%)	

Table 5 shows contraceptive usage in both control group and study group which are comparable with p value of 0.711 which illustrates statistically no significant difference in between both groups.

FIGURE 4-CONTRACEPTIVE USAGE

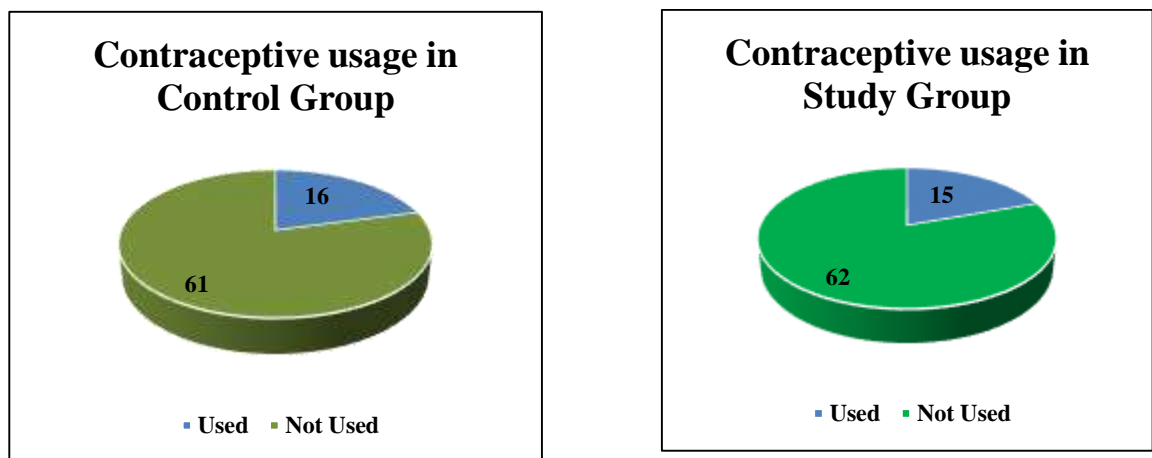


Figure 4 Contraceptive usage in control and study groups

TABLE 6-PARITY COMPARISON IN BOTH GROUPS

Parity	Control Group N=77 (%)	Study Group N=77 (%)	P value
Primipara	43 (55.1%)	42 (54.5%)	0.192
Multipara	34 (44.9%)	35 (45.5%)	

(By Chi-square test of Independence)

Table 6 shows parity comparison between control and study groups expressed in %. Number of primipara and multipara in control group was 43(55.1%) and 34(44.9%) respectively whereas number of primipara and multipara in study group was 42(54.5%) and 35(45.5%) respectively. Intergroup analysis showed p value of 0.192 using chi square test of independence which illustrates no significant statistical difference between both groups and are comparable.

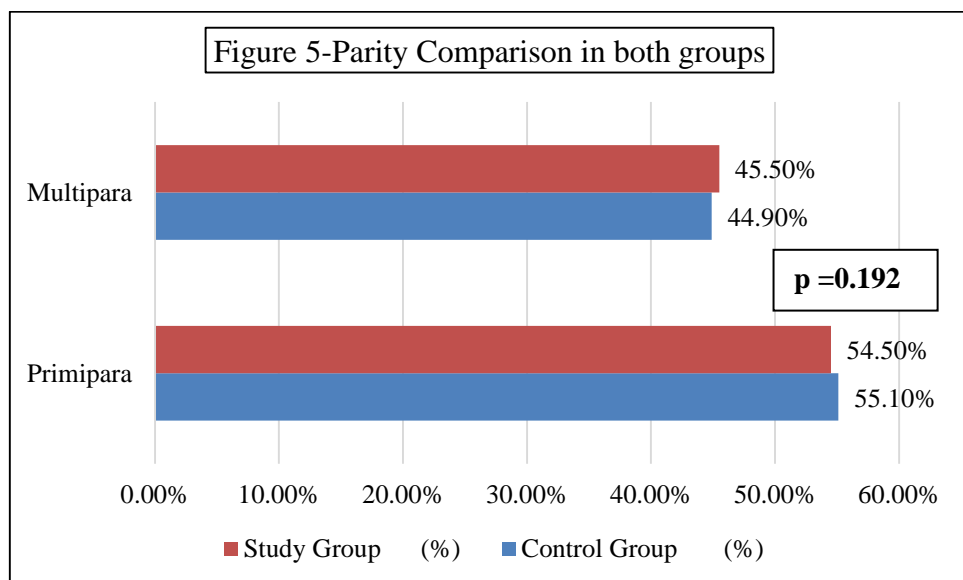


Figure 5 -Parity comparison in both groups

ANALYSIS

ANALYSIS OF EFFICACY PARAMETERS

TABLE 7-VOLUME OF BLOOD LOSS

Postpartum blood loss	Control Group (n=77)	Study Group (n=77)	P value
Total Average blood loss	237.4 ml ± 138.3 ml	187.5ml ± 102.4ml	<0.001 ⁽¹⁾
<200ml	14 (18.1%)	29 (37.6%)	<0.001 ⁽²⁾
200-500ml	41 (53.2%)	41 (53.2%)	
500-1000ml	17 (22.1%)	04 (05.2%)	
>1000ml	05 (06.5%)	03 (03.9%)	

(1.By Independent 2 sample t-Test)

(2.By Trend Chi square test)

Table 7 shows volume of blood loss in both control group and study group. Blood loss was categorised into 4 subgroups - <200ml, 200-500ml, 500-1000ml, >1000ml in each group.

Total average blood loss represented in ml in terms of mean ± Standard deviation in control group was **237.4 ml ± 138.3 ml** and in study group was **187.5ml ± 102.4ml**. Intergroup analysis by Independent 2 sample t-Test between control and study groups and by Trend chi square test of all subgroups show significant reduction in blood loss in study group when compared to control group with p value of <0.001 which illustrates statistically highly significant difference. (Figure 6a and Figure 6b)

Figure 6a shows Categorisation of post partum blood loss in sub-groups of both the control and study groups

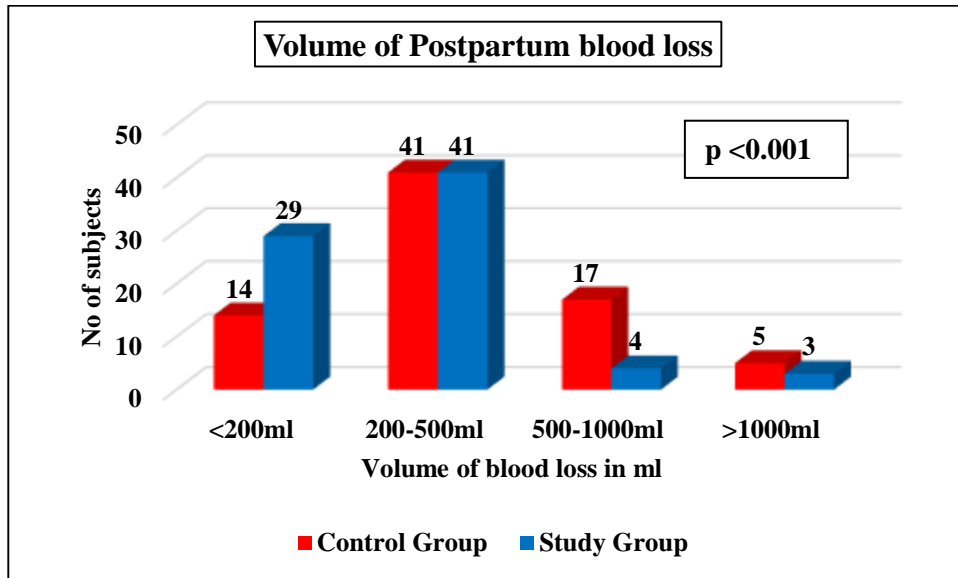
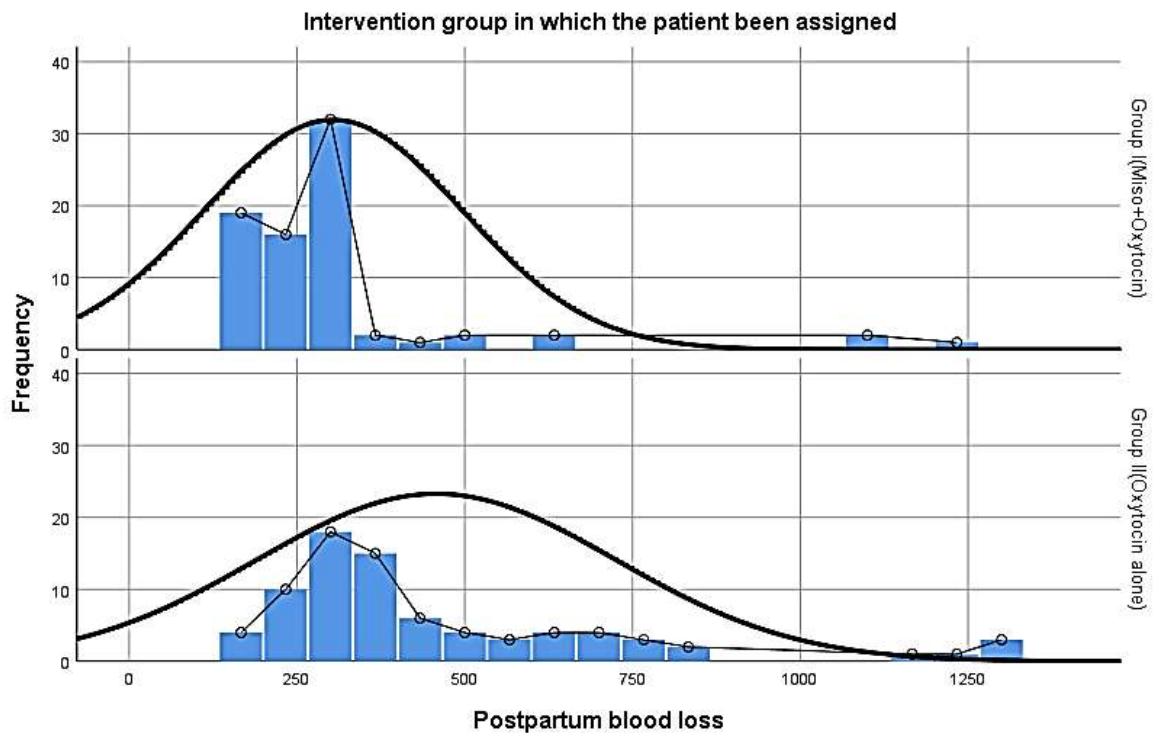
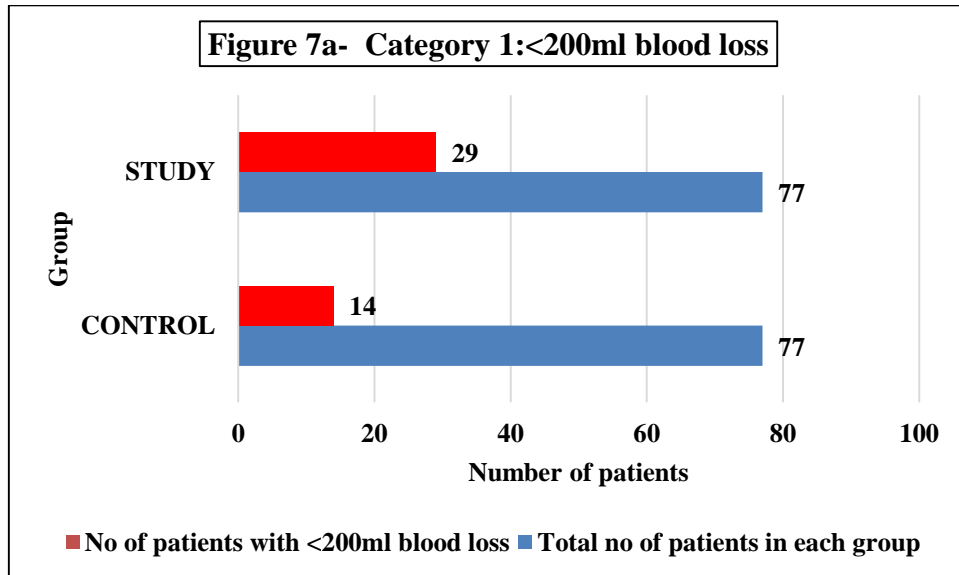


Figure 6b shows Frequency distribution of post partum blood loss in sub-groups of both the control and study groups



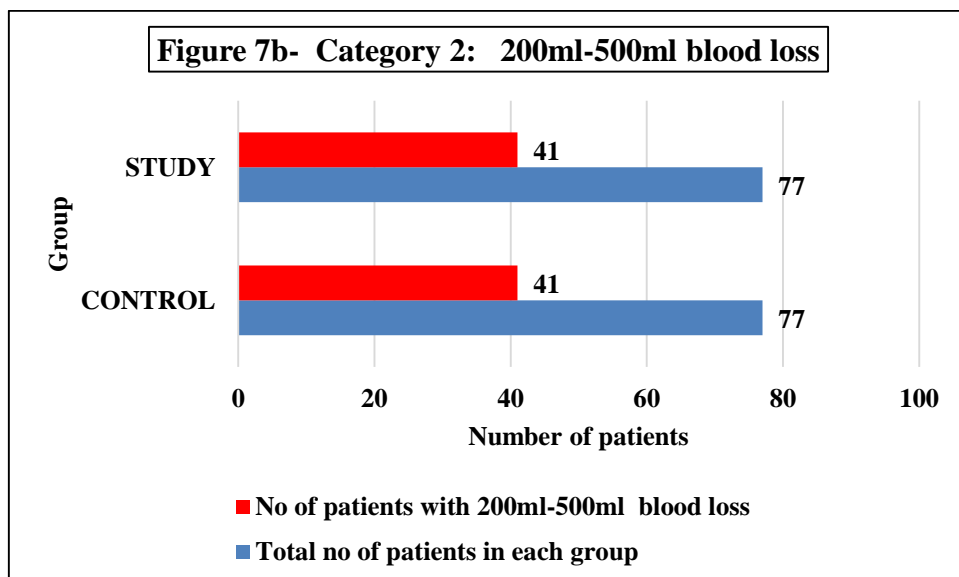
Category 1: <200ml blood loss (Figure 7a)

In category 1, out of 77 patients in each group, 14 (18.1%) patients had <200ml of blood loss in control group whereas 29 (37.6%) patients in study group had less than 200ml blood loss which was statistically significant.



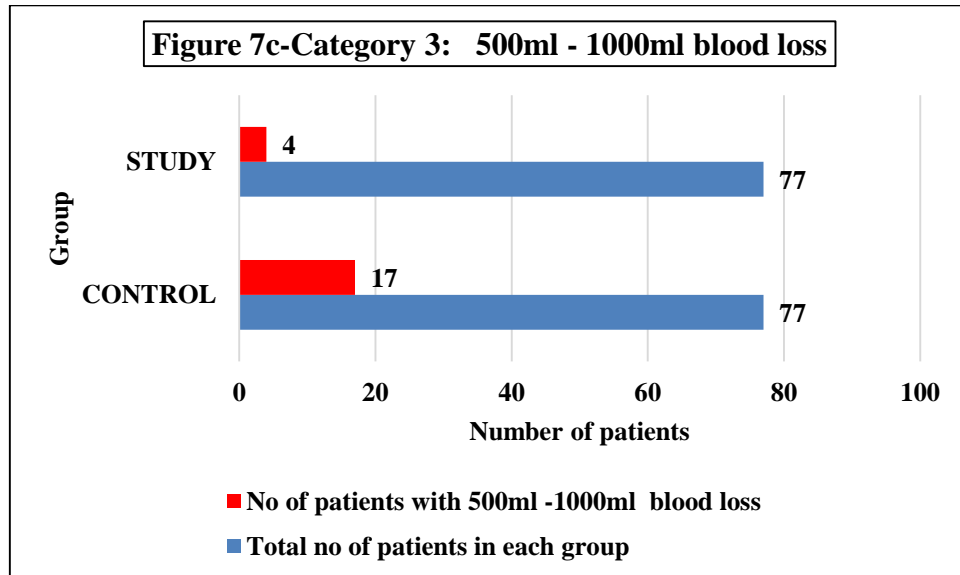
Category 2: 200ml-500ml blood loss (Figure 7b)

In category 2, out of 77 patients in each control and study groups group, equal number of patients 41 (53.2%) in each group had 200ml -500ml of blood loss



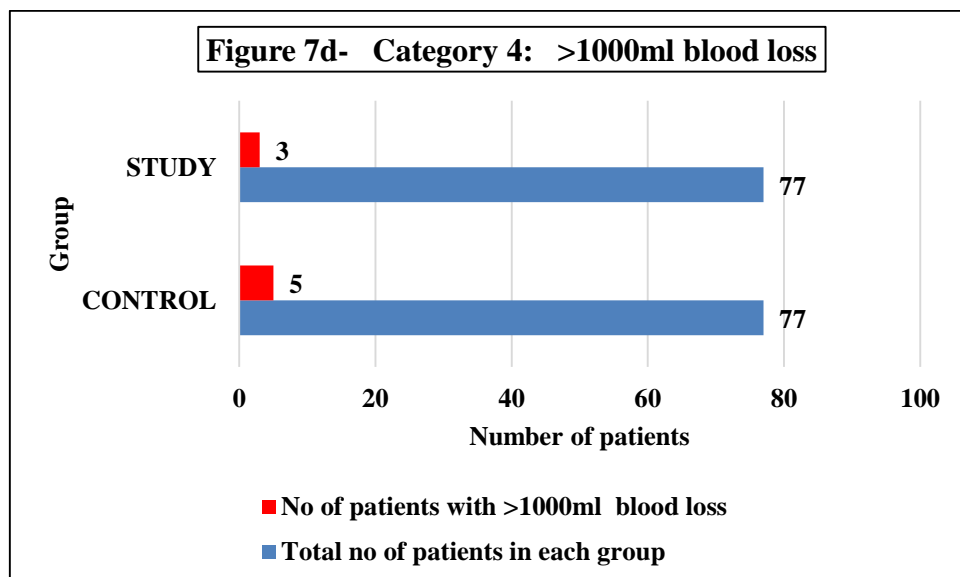
Category 3: 500ml-1000ml blood loss (Figure 7c)

In category 3 patients, out of 77 patients in each group, 17 patients (22.1%) in control group and 4 patients (5.2%) in study group had blood loss between 500ml -1000ml.



Category 4: >1000ml blood loss (Figure 7d)

In category 4 patients, out of 77 patients in each group, 5 patients (6.5%) in control group and 3 patients (3.9%) in study group had blood loss >1000ml.



When overall comparison is done statistically for all the four categories of blood loss by Trend Chi square test, intergroup analysis shows significant reduction in blood loss in study group with p value <0.001 which is statistically highly significant.

Table 8: NEED FOR BLOOD TRANSFUSION IN BOTH GROUPS

Need for Blood transfusion	Control group No of Units (% of Patients)	Study group No of Units (% of patients)	P value
Yes	29 (37.1%)	07 (09.1%)	<0.001
No	48 (62.3%)	70 (90.9%)	

(By Chi square test)

Table 8 shows number of units of blood transfused in both control and study groups. In control group 29 units (37.1% of Patients) of blood were transfused. In study group 7 units (9.1% of patients) of blood were transfused. Intergroup analysis by chi square test show there is significant increase in the number of units of blood transfused in control group when compared with study group. p value (<0.001) which is statistically highly significant.

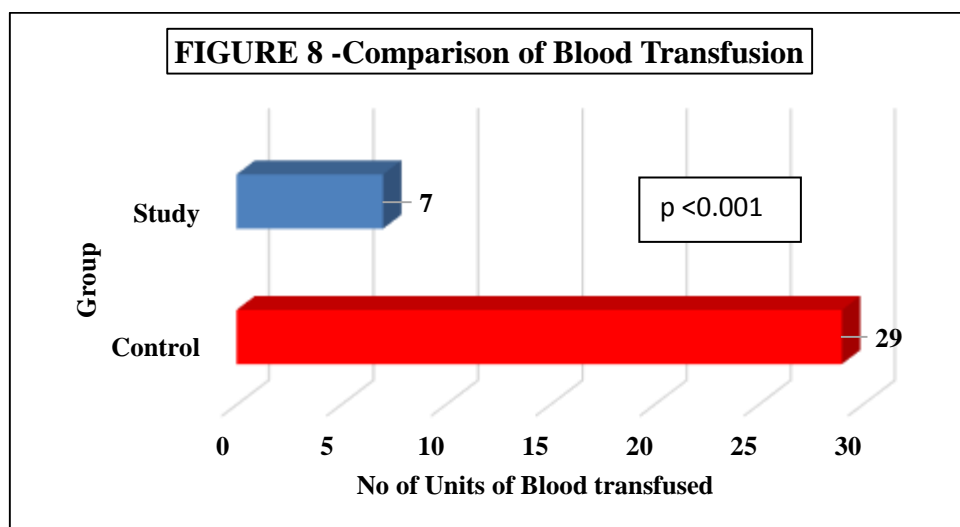


Figure 8 -Comparison of Blood Transfusion in both groups

Table 9: NEED FOR ADDITIONAL UTEROTONIC AGENTS

Group	No of Patients who needed additional Uterotonics (%) N=77	No of Patients who didn't need additional Uterotonics (%) N=77	P value
Control	28 (36.36%)	49(63.63%)	<0.001
Study	9 (11.68%)	68 (88.32%)	

(By Chi square test)

Table 9 shows need for additional uterotonic agents in both control and study groups. 28 patients (36.36%) out of 77 patients needed additional uterotonic agents in control group whereas only 9 patients (11.68%) needed additional uterotonic agents in study group. Intergroup analysis by chi square test between control and study group shows significant decrease in the need of additional uterotonic agents in study group. p value is less than 0.001 which is statistically highly significant.

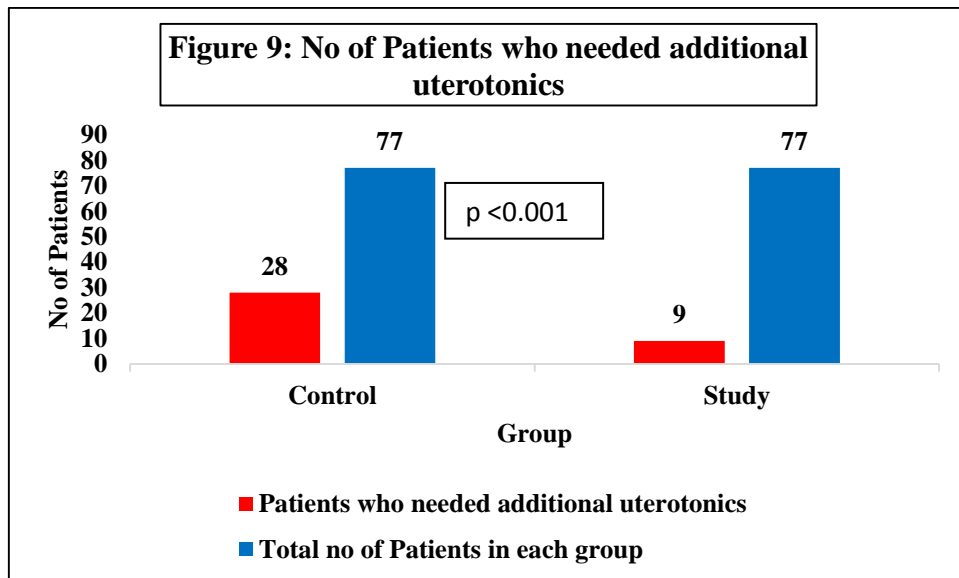


Figure 9- Number of patients in need of additional uterotonic agents in both groups

Table 10: POSTPARTUM SHIVERING

Postpartum Shivering	Control Group N=77 (%)	Study Group N=77 (%)	P value
No of patients who developed shivering	3 (3.9%)	26 (33.7%)	<0.001
No of patients who did not develop shivering	74 (96.1%)	51 (66.23%)	

(By chi square test)

Table 10 shows number of patients who developed postpartum shivering in both control and study groups. In control group, 3 patients (3.9%) out of 77 patients developed shivering and in study group, 26 (33.7%) patients out of 77 patients developed shivering. Intergroup analysis by chi square test between control and study group shows significant increase in the incidence of postpartum shivering as side effect in study group. p value is less than 0.001 which is statistically highly significant

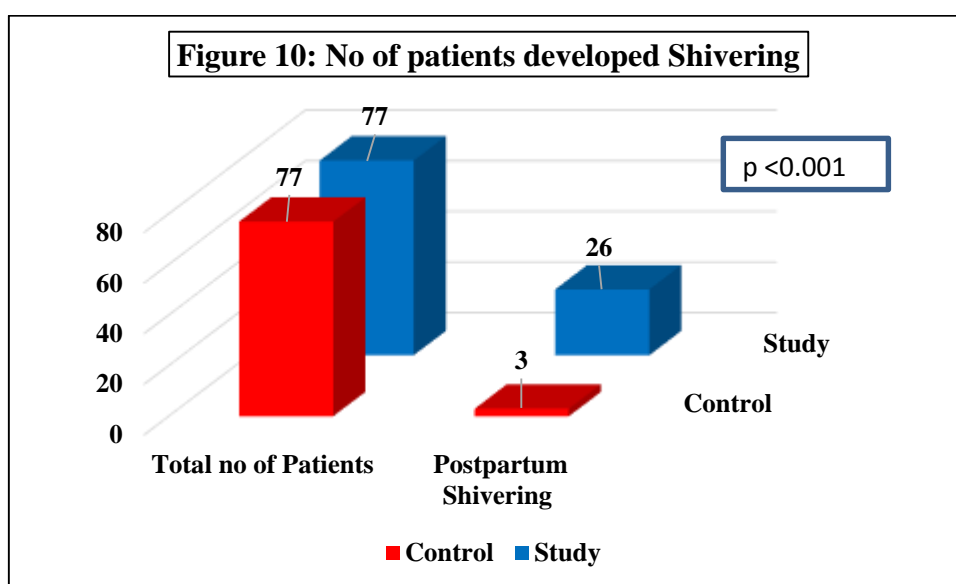


Figure 10- Number of patients who developed shivering in both groups

Table 11 POSTPARTUM PYREXIA (Temperature between 38°C and 40°C)

Pyrexia	Control Group N=77 (%)	Study Group N=77 (%)	P value
No of patients who developed Pyrexia	2 (2.6%)	24 (31.16%)	<0.001
No of patients who didn't develop Pyrexia	75 (97.4%)	53 (68.83%)	

(By Chi square test)

Table 11 shows number of patients who developed postpartum pyrexia in both control and study groups. In Control group, 2 out of 77 patients (2.6%) developed pyrexia whereas 24 out of 77 patients (31.16%) developed pyrexia in study group. Intergroup analysis by chi square test between control and study group shows significant increase in the incidence of postpartum pyrexia as side effect in study group. p value is less than 0.001 which is statistically significant

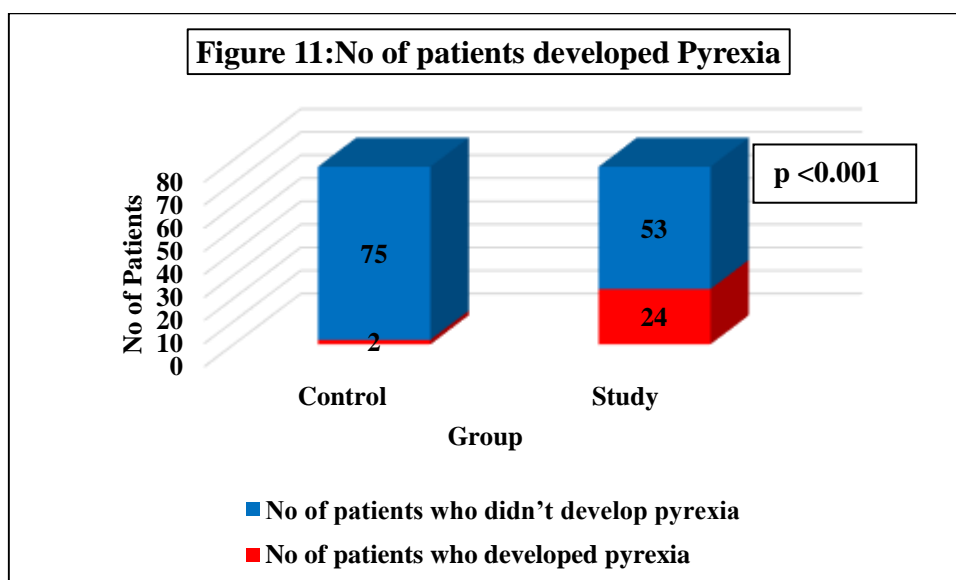


Figure 11 - Number of Patients who developed pyrexia in both groups

TABLE 12: HEMOGLOBIN IN GM% PRE AND POST DELIVERY

Group	Pre-delivery hemoglobin in gm% Mean \pm SD	Post-delivery hemoglobin in gm% Mean \pm SD	P value
Control Group	11.5 \pm 1.0	9.2 \pm 1.8	<0.05
Study Group	11.6 \pm 0.7	10.6 \pm 1.0	

(By Paired t-test)

Table 12 shows pre delivery haemoglobin and post-delivery haemoglobin expressed in gram% in both control and study groups. Pre delivery haemoglobin in control group was 11.5 \pm 1.0 which dropped to 9.2 \pm 1.8 post-delivery in control group. Pre delivery haemoglobin in study group was 11.6 \pm 0.7 which dropped to 10.6 \pm 1.0 post-delivery. Intergroup analysis by paired t test between post-delivery haemoglobin of control and study groups show p value <0.05 which implies statistically significant difference.

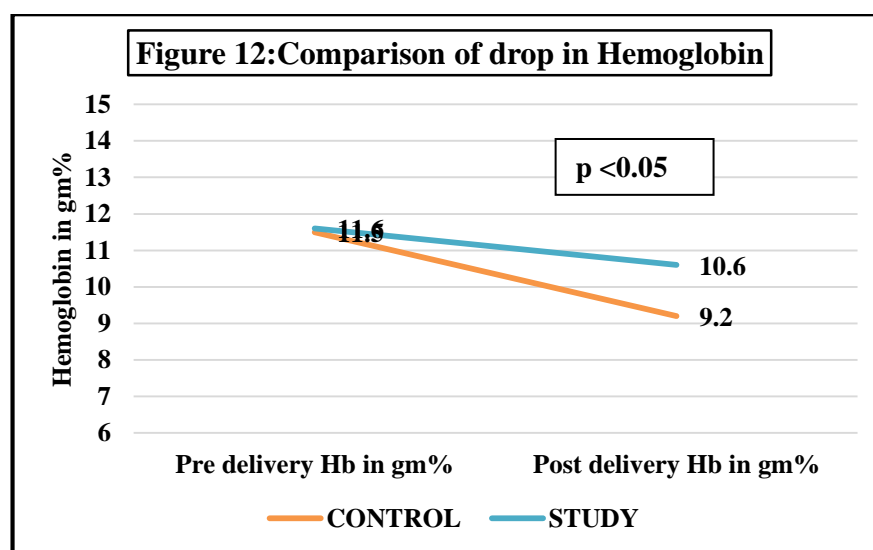


Figure 12 – Comparison of drop in haemoglobin in both groups

TABLE 13: HEMATOCRIT IN % PRE AND POST DELIVERY

Group	Pre-delivery hematocrit (%) Mean \pm SD	Post-delivery hematocrit (%) Mean \pm SD	P value
Control Group	34.7 \pm 3.1	29.3 \pm 4.2	<0.05
Study Group	35 \pm 2.3	31.7 \pm 3.1	

(By Paired t-test)

Table 13 show Pre delivery hematocrit and postdelivery hematocrit in both control and study groups. In control group predelivery hematocrit was 34.7 \pm 3.1 which dropped to 29.3 \pm 4.2 post-delivery. In study group predelivery haematocrit was 35 \pm 2.3 which dropped to 31.7 \pm 3.1 postdelivery. Intergroup analysis by paired t test between post-delivery haematocrit of control and study groups show p value <0.05 which implies statistically significant difference.

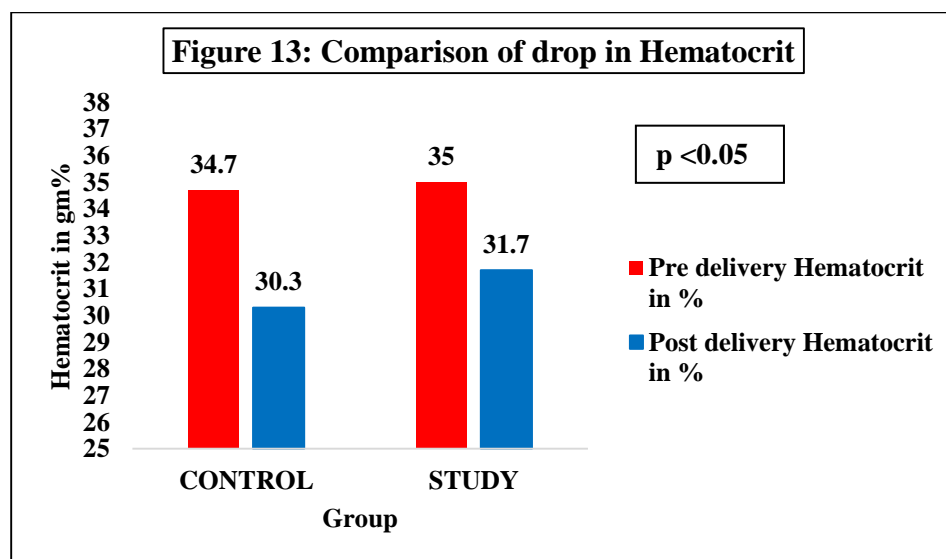


Figure 13- Comparison of drop in hematocrit

TABLE-14. OTHER ADVERSE EVENTS

Adverse event	Control group N=77 Expressed in %	Study group N=77 Expressed in %	P value
Nausea	12 (15.58%)	23 (29.87%)	<0.001
Vomiting	2 (2.59)	17 (22.07)	<0.001
Diarrhoea	0	9 (11.68)	0.003

Table 14 shows other adverse events observed in both control and study groups. In control group number of patients who developed nausea were 12 (15.58%) and in study group were 23(29.87). Intergroup analysis shows p value of 0.001 which is statistically highly significant.

Number of patients who developed vomiting in control group were 2 (2.59) in control group and in study group were 17 (22.07%), Intergroup analysis shows p value of 0.001 which is statistically highly significant.

Number of patients who developed diarrhoea in control group were nil and in study group were 9 (11.68%). Intergroup analysis show p value of 0.003 which is statistically significant.

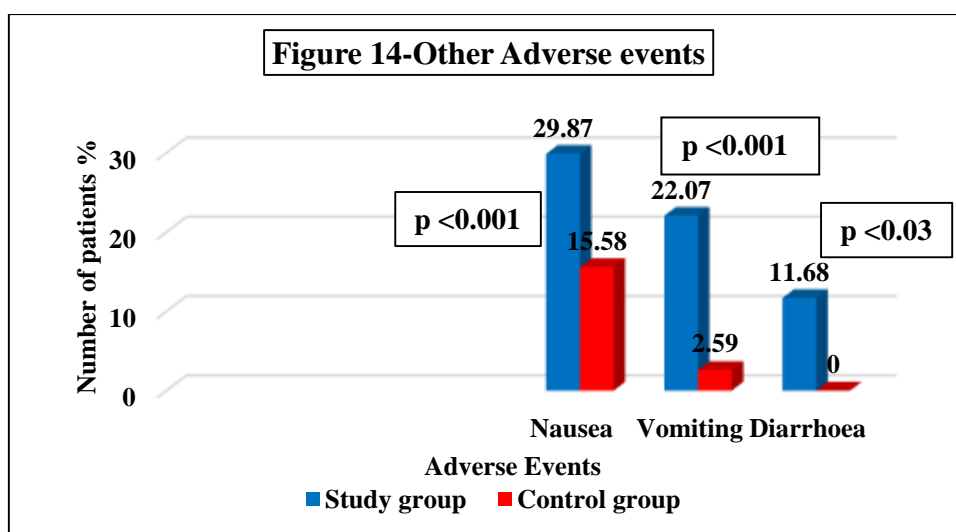


Figure 14 - Other adverse events

DISCUSSION

DISCUSSION

Postpartum Haemorrhage (PPH) is defined as blood loss of more than 500ml during normal vaginal delivery and loss of more than 1000ml following caesarean section⁽¹⁾. PPH is the most common and serious obstetric risk factor resulting in increased morbidity and mortality among women in developing and under developed countries. Though many protocols and guidelines were framed for prevention of PPH, the incidence of PPH remains on the raise.

Standard treatment guidelines (Green top Guidelines) framed by RCOG (Royal college of Obstetricians and Gynaecology) and WHO Recommendations for prevention of Post-Partum Haemorrhage strongly recommends to follow AMTSL criteria- Active Management of Third stage of Labour to reduce incidence of PPH. AMTSL includes usage of uterotonic agents as one of its criteria along with early cord clamping and uterine massage.

In most clinical settings, Oxytocin is commonly recommended first line uterotonic agent in prevention as well as treatment of PPH. Also, it has lesser side effects. Oxytocin is formulated for intramuscular and intravenous administrations which requires skilled personnel for its administration. Oxytocin is unstable at room temperature and requires special storage conditions, temperature of 2^oC-8^oC and cold chain maintenance till administration, to maintain its potency which ultimately depends on changes in pH of its formulation on exposure to heat. Des amino oxytocin is available as buccal preparation which is relatively costly.

On the other hand, misoprostol which is prostaglandin analogue is available for multiple routes of administration which include oral, sublingual, rectal, vaginal, buccal where no expertise needed for administration. Misoprostol is cheap, easily available, no refrigeration needed, can be stored in ambient temperature. On exposure to moisture it becomes hydrated and gets wet which is its disadvantage.

200 patients were screened for this study. 40 patients who didn't meet selection criteria were excluded .160 patients were enrolled in the study. 6 patients, 3 in each group were lost after randomisation. 77 subjects in control group received 10 units of intramuscular oxytocin during active management of third stage of labour and 77 subjects received 600µg of misoprostol along with 10units of intramuscular oxytocin during active management if third stage of labour and they were assessed during delivery for volume of blood loss, usage of additional uterotonic agents, number of units of blood transfused, number of patients who developed pyrexia and post-partum shivering and for the other adverse events. After 24hours of delivery, subjects were assessed for drop in haemoglobin and haematocrit percent.

The mean age distribution was similar in both groups. Among 77 patients in each group, mean age in control group was 22.9 years and in study group was 23.1 years showing no significant difference between the control and study groups.

The mean subject's body weight was 66.2 kg in control group and 69.5 kg in study group. The mean body weight distribution was similar in both

groups showing no significant difference between the control and study groups.

The mean birth weight of delivered babies in control group was 2.8kg and 2.9kg in study group. Thus the mean birth weight distribution was similar in both groups showing no significant difference between the control and study groups.

The mean contraceptive usage among 35 multipara subjects in control group were 16 in control group and 15 in study group. The mean contraceptive usage distribution in both groups shows no significant difference.

The mean primipara and multipara age distribution in both groups showed no significant difference on inter group comparison. The mean primipara and multipara in control group were 43 and 34 respectively. The mean primipara and multipara in study group were 42 and 35 respectively.

The average volume of blood loss in control group was 237ml and in study group it was 187ml. The difference in volume of blood loss was 50ml. The mean blood loss distribution in both groups shows statistically significant difference between the control and study groups with p value of <0.001 which is similar to the study done by Chaudhuri et al, Majumdar et al⁽²⁸⁾ where high risk patients alone were the participants of the trial and these findings are also consistent with the study done by Gallos et al⁽¹⁹⁾ and consistent with findings of study done by Derman et al⁽²⁹⁾ which is a placebo controlled study. The findings are also similar to a review article published in research gate by

author Joy Chindinma Agom et al⁽³⁰⁾. This article, a review of many studies concluded that misoprostol effectively decreases blood loss during delivery and it should be used to reduce incidence of PPH. Similarly a trial done in Uganda comparing misoprostol versus oxytocin done by Esther CA Tukunda et al yielded similar results⁽³¹⁾. Findings similar to this study is seen with study done by Bellad et al⁽³²⁾. Here only 400µg of oral misoprostol was compared with 10 units of oxytocin in reducing blood loss. Only modest reduction in blood loss was achieved in a similar study done by Adineran and Fawole et al⁽³³⁾.

Number of subjects who had less than 200ml blood loss subcategory is 14 subjects in control group and 29 in study group. This finding implies that when misoprostol is administered along with standard oxytocin regimen, it substantially reduces volume of blood loss. This finding is consistent with the study done by Chaudhuri et al⁽³⁴⁾ and study conducted by Priya et al⁽³⁵⁾ and study done by Gunjan singh et al⁽³⁶⁾

Number of subjects who had blood loss between 200ml-500ml were 41 subjects in both control and study groups. This finding implies that addition of sublingual misoprostol to oxytocin substantially reduces blood loss of mild severity and blood loss >500ml and not in moderate blood loss between 200ml - 500ml category. This study finding is consistent with the findings of study done by Widmer et al⁽³⁷⁾ and Hofmeyr et al⁽³⁷⁾.

Number of subjects who had blood loss between 500ml -1000ml sub category were 17 in control group and 4 in study group. This finding implies addition of misoprostol along with standard oxytocin decreases blood loss of more than 500ml and therefore reduces the incidence of postpartum haemorrhage. This study finding is consistent with the study done by Nadeem Zuferi et al⁽⁴⁾ where blood loss >500ml is controlled by addition of misoprostol to standard oxytocin. Also, they reported a decreased need of interventional procedures to control excessive blood loss in misoprostol added group⁽⁴⁾.

Number of subjects who had blood loss >1000ml were 5 in control group and 3 in study group. This finding is consistent with the study done by Chaudhuri et al⁽³⁴⁾

Decreased incidence of >500ml blood loss in study group implies that when sublingual misoprostol is used along with 10 units of intramuscular oxytocin, number of subjects suffering from postpartum haemorrhage can be reduced.

Intergroup analysis done for all sub categories of blood loss by trend chi square test yielded a p value <0.001 which states statistically that the difference in volume of blood loss distribution is highly significant.

Two systematic reviews, which includes the 2018 Cochrane review, focused on misoprostol to treat PPH and examined the optimal route and dosage, and its efficacy⁽¹⁹⁾ ⁽³⁰⁾. As per this systematic review, the three most effective drugs for prevention of PPH \geq 500 mL were ergometrine plus

oxytocin combination, carbetocin, and misoprostol plus oxytocin combination(19). These three options were more effective at preventing PPH \geq 500 mL compared with oxytocin, the drug currently recommended by the WHO. The outcomes and rankings for the outcome of PPH \geq 1000 mL were similar to those of PPH \geq 500 ml. with the evidence for ergometrine plus oxytocin combination being more effective than oxytocin ⁽¹⁹⁾.

Similarly studies showed that when misoprostol used as an adjunct with oxytocin in caesarean section, volume of blood loss decreased significantly as study done by Shalom et al and Shaddy et al⁽³⁸⁾.

Largest number of clinical data supports the safety and efficacy of a 600 μ g oral dose for prevention and an 800 μ g sublingual dose for treatment of PPH⁽³⁹⁾

Number of units of blood transfused in control group was 29 units and in study group was 7 units. This finding suggests that volume of blood loss is minimal in study group and hence the requirement of blood transfusion was less in this group. This finding is similar to study done by Picklu Chaudhuri et al⁽²⁸⁾ and Widmer et al⁽³⁷⁾, though the difference is not statistically significant but there is considerable difference in misoprostol added group. Also, this finding is consistent with meta-analysis report done by Gallos in 2018⁽¹⁹⁾.

Number of patients who needed additional uterotonics in control group was 28 and in study group was 9 with p value <0.001 on intergroup analysis which is statistically significant. This finding is in contradiction to the study done by Anjuman alam et al where need of uterotonics was greater in

misoprostol group⁽⁴⁰⁾. But in this study, 600µg of sublingual misoprostol was used alone in management of AMTSL and compared with 10 units of intramuscular oxytocin in control group. Also, this finding is consistent with meta-analysis report done by Gallos in 2018⁽¹⁹⁾. This is supported by evidence of second largest SUCRA (SUrface underneath this Cumulative RAnking line) scoring which indicates the need for lesser additional uterotonic agents for misoprostol with oxytocin combination next to carbetocin which has the first largest SUCRA score in this meta analysis. Also, based on statistical analysis this meta analysis concludes that though injectable uterotonics are effective in management of AMTSL, misoprostol is effective in low socio economic settings and in places lacking trained personnel and lack of drug storage facility⁽⁴⁰⁾. Similar finding of decreased need of uterotonic agent is seen in the study done by Widmer et al⁽³⁷⁾, though in this study the difference is not statistically significant, there is considerable difference in misoprostol added group.

Number of patients who developed postpartum shivering in control group were 3 and 26 patients in study group. Statistically the difference between both groups is highly significant with p value <0.001. This side effect of misoprostol is common but self-limiting. Postpartum shivering will subside within 6 hours of its onset⁽²⁶⁾ and pose no threat to patient's health apart from causing discomfort. Shivering caused by misoprostol is due to lowered threshold for physiological shivering or effect on central thermoregulatory mechanisms by prostaglandin E1⁽⁴¹⁾. Misoprostol does not produce any side

effects in the newborn ⁽⁴¹⁾. Only 28% of women who developed shivering following misoprostol administration required treatment as per the study done by Shobana patted et al⁽⁴¹⁾. In our study 26 out of 77 patients developed shivering and out of this 26, 6 patients were treated for shivering which is 23% of total patients which is similar to the study done by Shobana patted et al. The findings of current study are similar to metaanalysis report by Gallos et al⁽¹⁹⁾ and Leon et al ⁽⁴²⁾

Number of patients who developed postpartum pyrexia in control group were 2 and 24 in study group with intergroup statistical analysis showing p value of <0.001, the difference being significant. This indicates misoprostol is the reason for pyrexia. Misoprostol being a prostaglandin E1 analogue acts on central thermoregulatory centre causing fever^{(43), (44)} . Numerous randomised controlled trials and systematic reviews have mentioned pyrexia as the common side effect of misoprostol but are self-limiting^{(19), (44)}. Usually patients who develop moderate to severe shivering develop pyrexia which peaks within first 1-2 hours and subsides after 3 hours of onset⁽⁴⁴⁾. A study was done by Durocher et al (Ecuador study) where findings showed 35% of people treated with misoprostol experienced temperature above 40⁰C and the peak was within 1-2 hours and subsided after 3hours⁽⁴⁴⁾.Also the author reported there was no difference in outcome in discharge of patients who had pyrexia from patients who did not experience pyrexia. Similarly, a study done by Pisaki Lumbiganon et al showed 17% of patients treated with 600µg of oral misoprostol developed pyrexia which subsided 6 hours after its

administration. The findings of current study are similar to metaanalysis report by Gallos et al⁽¹⁹⁾ and Leon et al⁽⁴²⁾

In this study, 24 patients in study group and 2 patients in control group who developed pyrexia were treated with antipyretics and tepid sponging to avoid discomfort.

Other adverse events observed in this current study are nausea, vomiting and diarrhoea which are predominant in misoprostol added group than the isolated oxytocin group. This is because of the propulsive action of misoprostol on the intestines.

In control group number of patients who developed nausea were 12 (15.58%) and in study group were 23(29.87%). Intergroup analysis showed p value of 0.001 which is statistically highly significant. This finding is consistent with meta-analysis report done by Gallos et al⁽¹⁹⁾

Number of patients who developed vomiting in control group were 2 (2.59%) in control group and in study group were 17 (22.07%), Intergroup analysis shows p value of 0.001 which is statistically highly significant. This finding is consistent with meta-analysis report done by Gallos et al⁽¹⁹⁾ . Patients who had nausea and vomiting were treated with anti emetics.

Number of patients who developed diarrhoea in control group were nil and in study group were 9 (11.68%). Intergroup analysis show p value of 0.003 which is statistically significant. This finding is consistent with meta-analysis report done by Gallos et al⁽¹⁹⁾ .

These findings on adverse effects are also similar with study findings of Patted et al⁽⁴¹⁾, Lumbiganon et al⁽²⁶⁾, Durmen et al⁽²⁹⁾ and Chong et al⁽⁴⁵⁾.

Side effects of misoprostol are dose dependent and also depends on route of administration⁽⁴⁴⁾. Doses of misoprostol more than 400µg when administered sublingually or vaginally which produces earlier peak plasma concentrations causes more side effects than doses less than 400µg and through other routes of administration.

Mean predelivery haemoglobin in gram percent (Taken prior active stage of labour) in both the groups were comparable with control group value of 11.5g% and study group value of 11.6g%.

Postdelivery haemoglobin in control group was 9.2g%. The drop in haemoglobin in control group being 2.3g%. Postdelivery haemoglobin in study group was 10.6g%. The drop-in haemoglobin in study group being 1g%. Intergroup analysis between control and study group shows significant difference in drop in haemoglobin of 1.3g% with p value less than 0.001 which is statistically highly significant.

This finding is controversial to studies done by Widmer et al where no statistical difference was found in drop in haemoglobin in both groups⁽³⁷⁾. In a study done by Blum et al⁽⁴⁶⁾, the drop-in haemoglobin in both groups had no statistically significant difference. But in this study, misoprostol was used as a stand-alone drug in management of AMTSL and not as an add on drug along with oxytocin. And the study concluded that misoprostol is non inferior to oxytocin in AMTSL in all aspects⁽⁴⁶⁾.

In a study done by Nadeem F Zuberi et al also showed similar results of decreased drop in haemoglobin percent in misoprostol added group and concluded that misoprostol given sublingually showed promising result as an adjunct treatment for PPH and should be used for women with PPH⁽⁴⁾.

Similarly drop in haematocrit was less in study group when compared with control group, from 34% of predelivery haematocrit to 29% of postdelivery haematocrit. The fall being 5%. And in study group from 35% of predelivery haematocrit to 31% of postdelivery haematocrit. The fall being 4% which shows statistically significant difference on intergroup analysis with p value of 0.05. These findings are consistent with study findings of Badejoko et al⁽⁴⁷⁾.

In this current study irrespective of the treatment with additional uterotonics and blood transfusions for atonic PPH, 5 women underwent subtotal hysterectomy in control group and 3 women underwent subtotal Hysterectomy in study group for uncontrolled PPH.

In developing countries and underdeveloped countries, anaemia in pregnant women is very much common. Even a mild to moderate blood loss during delivery endangers women's life by causing decompensation. Hence by adding misoprostol as an adjunct drug along with standard management of 10 units of intramuscular oxytocin, a greater volume of blood loss will be prevented in both vaginal and caesarean deliveries ⁽⁴⁸⁾ and hence fall in haemoglobin can be prevented and so its untoward effect. This is supported by study done by Walraven et al⁽⁴⁹⁾ and by study done by O brien et al⁽⁵⁰⁾.

Evidence supports usage of sublingual misoprostol for treatment of PPH whenever oxytocin is unavailable. It can be recommended as the first-choice treatment for PPH occurring in women who received oxytocin as prophylaxis. Misoprostol is an important drug to combat PPH in places where oxytocin usage face logistical challenges for its IV use, non-availability, absence of skilled personnel for parenteral administration, unavailability of refrigeration facility ⁽²⁵⁾.

Many studies have concluded that misoprostol alone can be used for management of third stage of labour to reduce blood loss and is equally efficacious to standard drug oxytocin, Derman et al ⁽²⁹⁾, Winikoff et al⁽⁵¹⁾, and study by Alfirevic et al⁽⁵²⁾

Hence a single dose of 600µg of sublingual misoprostol as an adjunct to standard 10 units of intramuscular oxytocin will be more effective in reducing blood loss than oxytocin alone when administered during Active Management of Third Stage of Labour.

LIMITATIONS OF THE STUDY

- Smaller sample size
- Study is open labelled
- Only patients without risk factors are chosen for this study, hence results cannot be generalised
- Objective assessment of patient's adverse effects in misoprostol group is not done and their tolerability towards these adverse effects was not estimated
- In very few patients, minimal collection of amniotic fluid and patient's urine was unavoidable during postpartum collection of blood loss, volume of which is to be subtracted.

CONCLUSION

CONCLUSION

Diagnosis, prevention and management of PPH still remains an enigma in medicine which keeps the maternal mortality in developing as well as developed countries on the rise. Hence exploration for newer drugs and framing of clinical guidelines and updating treatment protocols with available drugs is essential for betterment of health.

From this current study, it is seen that misoprostol when added as an adjunct drug with oxytocin reduces volume of blood loss in third stage labour.

Misoprostol has the advantages of cost effectiveness, ease of administration and easy to store which makes it the drug of choice for prevention of PPH in low resource settings. Also, these properties make it user friendly drug even for traditional birth attendants and community health care workers in under developed and developing countries where still a percentage of deliveries are conducted by them.

Though side effects with misoprostol are more common, they are self-limiting and dose related. Benefits outweighs risk with additional usage of misoprostol with oxytocin.

This study suggests that misoprostol is not only useful in community-based settings but also has a role to play in hospital based settings, when used as an adjunct with oxytocin it reduces the incidence of PPH and therefore averts the necessity of invasive procedures and thus reducing maternal mortality.

To conclude, a single dose of 600µg of sublingual misoprostol as an adjunct to standard 10 units of intramuscular oxytocin will be more effective in reducing blood loss than using 10 units of intramuscular oxytocin alone in Active Management of Third Stage of Labour.

SCOPE FOR FURTHER RESEARCH

Further researches are needed in larger population group including high risk patients.

Studies on different doses and different routes of administration of misoprostol, which raises its efficacy and limits its side effects are needed.

Also, researches are needed after introduction of misoprostol in primary, secondary and tertiary health care centres to demonstrate its effectiveness in reducing incidence of PPH.

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ANNEXURES

ANNEXURE I
DATA COLLECTION TOOL

Name :

IP NO :

Age :

Date of examination :

Address :

H/O Amenorrhea : Months days

Any complaints :

Menstrual History:

LMP:

EDD:

Obstetric History :

Contraceptive History:

Past History:

Family History:

GPE:

Weight:

Pallor:

Pulse:

Oedema:

BP:

Jaundice:

RR:

Breast:

Temp:

Nipple:

Systemic Ex:

CVS:

RS:

P/A: Fundal Ht:

Lie:

Presentation:

FHS:

Previous scar:

Vaginal Ex : if necessary

Diagnosis:

Investigation:

HB: USG:

Blood grouping and Typing:

URE:

HBs Ag: VDRL:

DELIVERY DETAILS

Mode of delivery:

Intervention in third stage of labour: Control Group (Oxytocin alone) / Study Group II(Oxytocin and Misoprostol)

Volume of blood loss: ml

Need for other Uterotonics: Yes/ No

Drug used:

Need for blood transfusion: Yes/No

No of units transfused :

Post delivery vitals:

PR: BP Temp: RR:

Investigations: HB : HCT:

(24hrs hrs after delivery)

ANNEXURE - II
INFORMATION SHEET

We are conducting a study on “A COMPARATIVE STUDY BETWEEN MISOPROSTOL COMBINED WITH OXYTOCIN VERSUS OXYTOCIN ALONE IN REDUCING PPH.” in our Institution, Coimbatore Medical College Hospital, Coimbatore.

- Your participation may be of immense value for the study.
- We are selecting patients who satisfy our inclusion criteria and they are included in the study.
- The privacy of the patients will be maintained throughout the study, in the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.
- Participation depends on patients own voluntary decision. Their decision will not result in any loss of benefits to which they are otherwise entitled.
- The results of the study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator Signature of the Participant

Dr. S.ANANDHI

Date :

Place :

ANNEXURE - III
INFORMED CONSENT FORM

Title of the study : “A COMPARATIVE STUDY BETWEEN MISOPROSTOL COMBINED WITH OXYTOCIN VERSUS OXYTOCIN ALONE IN REDUCING PPH.”

Name of the participant :

Name of the Investigator : Dr.S.ANANDHI

Name of the Institution : Coimbatore Medical College Hospital

Documentation of the informed consent.

I _____ have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in “A COMPARATIVE STUDY BETWEEN MISOPROSTOL COMBINED WITH OXYTOCIN VERSUS OXYTOCIN ALONE IN REDUCING PPH”

1. I have read and understand this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. I have been explained about my rights and responsibilities by the investigator.
5. I have been informed the investigator of all the treatments I am taking.

6. I have been advised about the risks associated with my participation in this study.

7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.

8. I have not participated in any research study within the past_____.

9. I have not donated blood within the past_____ - Add if the study involves extensive blood sampling.

10. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.

11. I am also aware that the investigator may withdraw my participation in the study at any time for any reason, without my consent.

12. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the sponsors, regulatory authorities, Govt.Agencies, and IEC. I understand that they are publicly presented.

13. I have understood that my identity will be kept confidential if my data are publicly presented.

14. I have had my questions answered to my satisfaction.

15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the Investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

For adult participants:

Name and signature/thumb impression of the participant (or legal representative if participant incompetent)

Name _____ signature _____ Date _____

Name and signature of impartial witness (require for illiterate patients)

Name _____ signature _____ Date _____

Address and contact number of the impartial witness:

Name and signature of the investigator or his representative obtaining consent:

Name _____ signature _____ Date _____

Name and signature of the investigator or his representative obtaining consent:

Name _____ signature _____ Date _____

ஒப்புதல் படிவம்

மரு.

அவர்கள்,

கோவை மருத்துவக்கல்லூரி, பரிசோதனை நடத்த சம்மதம் அளிக்கிறேன். இந்த ஆய்வின் செய்முறை மற்றும் இது தொடர்பான அனைத்து விளக்கங்களையும் கேட்டுக்கொண்டு, எனது சந்தேகங்களையும் தெளிவுபடுத்திக்கொண்டேன் என்பதையும் தெரிவித்துக்கொள்கிறேன். இந்த ஆய்வில் என் விவரங்கள் பாதுகாக்கப்படுவதுடன் இதன் முடிவுகள் ஆய்விதழில் வெளியிடப்படுவதில் ஆட்சேபனை இல்லை என்பதையும் தெரிவித்துக்கொள்கிறேன்.

கையொப்பம்

MASTER CHART

Name	Age	Address	IP No	Part History	Cycles	Obs His	Contractive History	General Examination	System Examination	Per Abdomen Examination	
Bhavayathi	24	Sevayapuram,Coimbatore	202149	Nil significant	Regular cycles	Primi	Nil	WT 90 Edema No Jaundice Not Pp 74 Bp 110/80	Normal	Normal	Uterus term,acting,head engaged,FH good
Annapoorani	22	Aarampalayam,Coimbatore	199124	Nil significant	Regular cycles	G3P1L1	Copper T	78 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Bhuvaneshwari	21	Sundakkemthur	201938	Nil significant	Regular cycles	G3P1L1	Nil	79 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Latha	24	Kanaranthapuram	201904	Nil significant	Regular cycles	Primi	Nil	68 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Dhanalakshmi	21	Vellore	2021113	Nil significant	Regular cycles	Primi	Nil	72 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Dhiva	25	Sevayapuram,Coimbatore	201850	Nil significant	Regular cycles	G3P1L1	Cu T	56 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Anandhi	21	High phase colony,Velichy road	201733	Nil significant	Regular cycles	Primi	Nil	85 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Ilavazai	23	Umapalayam	200523	Nil significant	Regular cycles	G3P1L1	Nil	45 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Ranganayaki	18	Manjunnary,udumalpet	201164	Nil significant	Regular cycles	Primi	Nil	67 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Naradhi	19	ST vinayapuram	202151	Nil significant	Regular cycles	G3P1L1	Cu T	87 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Jeevathi	21	Bulathur,Karamahdi	200844	Nil significant	Regular cycles	Primi	Nil	46 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Srinaya	25	Vellore	201406	Nil significant	Regular cycles	Primi	Nil	57 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Nandhini	25	Thadagam road,Kanvai	201186	Nil significant	Regular cycles	Primi	Nil	78 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Pavitra	25	Thadagam road,SS Puram	201100	Nil significant	Regular cycles	G3P1L2	Nil	86 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Bhuvanai	19	Thudiyalur,Coimbatore	201486	Nil significant	Regular cycles	G3P1L1	Nil	56 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Kasthuri	18	Kumarasamy colony,BS puram	201481	Nil significant	Regular cycles	Primi	Nil	78 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Kalarasi	21	Sannurthy station,Karur	100936	Nil significant	Regular cycles	Primi	Nil	89 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Eshwar	19	Madraraman kovil street,Karuvampahay	200813	Nil significant	Regular cycles	Primi	Nil	97 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Gokula	19	Ravayalavayam,Sulur	201553	Nil significant	Regular cycles	G3P1L1	Cu T	67 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Muthulakshmi	20	Thadagam street,Coimbatore	201110	Nil significant	Regular cycles	G3P1L1	Nil	56 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Yasodha	22	UC nagar,Pethanam	201748	Nil significant	Regular cycles	G3P1L1	Nil	55 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Shankaravathi	23	V.Veerapandi,Coimbatore	201881	Nil significant	Regular cycles	G3P1L1	Nil	87 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Anilabharathi	18	East street,Coimbatore	200102	Nil significant	Regular cycles	Primi	Nil	78 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Rohy	23	Chinnampalayam,Coimbatore	200353	Nil significant	Regular cycles	Primi	Nil	67 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Latha	18	Mylkal,Marudurai	200299	Nil significant	Regular cycles	Primi	Nil	46 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Kalashwini	21	Thirudhuvanam,Sivagangai	200328	Nil significant	Regular cycles	G3P1L1	Cu T	76 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Dhiva	19	Ayazhagar,Chennai	200348	Nil significant	Regular cycles	Primi	Nil	86 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Dhavalakshmi	21	Kedambadi,Coimbatore	200099	Nil significant	Regular cycles	G3P1L1	Nil	76 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Dhanrajwari	19	New housing unit,Puliyakkulam	200343	Nil significant	Regular cycles	Primi	Nil	47 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Bharathi	19	Pachayappan,Coimbatore	198042	Nil significant	Regular cycles	Primi	Nil	85 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Asha	19	AD colony,Preethan	199607	Nil significant	Regular cycles	G3P1L1	OCp	65 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Jamshreea	18	Newtopes road,gudalur	196142	Nil significant	Regular cycles	G3P1L1	OCp	65 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Lakshmi	20	Rathnapur,Coimbatore	199243	Nil significant	Regular cycles	G3P1L1	Cu T	56 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Jayapradha	22	Nandudapuram,Coimbatore	196650	Nil significant	Regular cycles	Primi	Nil	67 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Chinnamma	20	Peyyakkul,Coimbatore	196650	Nil significant	Regular cycles	Primi	Nil	66 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Nagamani	22	PN palayam,Coimbatore	199153	Nil significant	Regular cycles	Primi	Nil	87 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Krotiiga	18	Thudiyalur,Coimbatore	182253	Nil significant	Regular cycles	Primi	Nil	52 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Nandhini	24	Idayarpalayam,Coimbatore	187326	Nil significant	Regular cycles	G3P1L1	OCp	61 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Nagamal	18	Metu palayam,Coimbatore	187435	Nil significant	Regular cycles	Primi	Nil	71 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Veeramani	22	Vellathottam,Ganapathy	187539	Nil significant	Regular cycles	Primi	Nil	83 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Nandhya	28	Iruvar,Coimbatore	187609	Nil significant	Regular cycles	G3P1L1	Cu T	74 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Prernaatha	24	Sankaran,kharthakaduru	187597	Nil significant	Regular cycles	Primi	Nil	58 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Menaka	20	Kondamangalam,Coimbatore	187653	Nil significant	Regular cycles	Primi	Nil	62 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Deepa	19	Ginnadi,adalgam,Coimbatore	187284	Nil significant	Regular cycles	G3P1L1	Cu T	50 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Srinaya	26	Kanurathampatty,Phudur	187642	Nil significant	Regular cycles	G3P1L1	Nil	58 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Ashtwarya	18	Sigayapuram,pillayarpalayam	187781	Nil significant	Regular cycles	Primi	Nil	60 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Meena	19	Pollath,Coimbatore	187886	Nil significant	Regular cycles	Primi	Nil	67 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Bharathi	21	Karamnadi,Coimbatore	187572	Nil significant	Regular cycles	Primi	Nil	82 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Ashvaya	18	Mettupalayam,Coimbatore	187291	Nil significant	Regular cycles	Primi	Nil	78 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Kashiba	20	Kanarpasa, Tirchi	188915	Nil significant	Regular cycles	Primi	Nil	72 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Reemuthakuma	23	Mandur,Nilgiris	188624	Nil significant	Regular cycles	G3P1L1	Cu T	75 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Sambhi	23	Keelkambalavaram	188439	Nil significant	Regular cycles	G3P1L1	Nil	64 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Shobana	23	Sundarapuram,Coimbatore	188513	Nil significant	Regular cycles	G3P1L1	Cu T	45 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Remya	19	Maddur,Coimbatore	188628	Nil significant	Regular cycles	G3P1L1	Nil	62 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Kaaleshwari	22	Orindudhur,Coimbatore	188630	Nil significant	Regular cycles	G3P1L2	Cu T	50 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Vanaraja	23	Chinnampalayam,Coimbatore	188438	Nil significant	Regular cycles	G3P1L1	Nil	48 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Anitha	18	Swarandha colony,Coimbatore	188748	Nil significant	Regular cycles	G3P1L2	Nil	58 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Muthuramgan	23	Sulur,Coimbatore	189576	Nil significant	Regular cycles	G3P1L1	Nil	87 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Kovvala	19	Thondanathur,Coimbatore	189412	Nil significant	Regular cycles	Primi	Nil	47 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Aashiba	20	Regalath street,Coimbatore	189651	Nil significant	Regular cycles	Primi	Nil	54 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Sangeethapriya	21	Nagarajapuram,Coimbatore	189780	Nil significant	Regular cycles	Primi	Nil	74 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good
Rabhatubaiysy	33	Kemunkkadai,Coimbatore	183628	Nil significant	Regular cycles	G3P1L1	Cu T	86 Not anemic No Edema Not jaundiced	Normal	Normal	Uterus term,acting,head engaged,FH good

Durgaree	21	Ganapathy,Coimbatore	17254	Nil,significant	Regular cycles	Primi	Nil	67	Not anemic	No Edema	Not jaundiced	80	120/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Aruna rani	24	Gandhi,ma nagar	17276	Nil,significant	Regular cycles	Primi	Nil	72	Not anemic	No Edema	Not jaundiced	70	110/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Sudha	27	Chelakeralal,Truipur	17298	Nil,significant	Regular cycles	G2P1L1	Nil	64	Not anemic	No Edema	Not jaundiced	84	120/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Shanthini	32	Thalwaady,Erode	17834	Nil,significant	Regular cycles	G2P1L1	Cu T	73	Not anemic	No Edema	Not jaundiced	87	110/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Renuga devi	31	Prelamadu,Coimbatore	17845	Nil,significant	Regular cycles	G2P1L1	Nil	65	Not anemic	No Edema	Not jaundiced	76	120/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Swaithi	24	AD Colony,Coimbatore	17867	Nil,significant	Regular cycles	Primi	Nil	55	Not anemic	No Edema	Not jaundiced	90	110/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Laxmibiva	22	FCI Road,Coimbatore	17873	Nil,significant	Regular cycles	Primi	Nil	72	Not anemic	No Edema	Not jaundiced	78	120/70	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Archana	23	Chinnampalayam,Coimbatore	17865	Nil,significant	Regular cycles	Primi	Nil	76	Not anemic	No Edema	Not jaundiced	80	120/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Padmavati	27	Palaasadi,Truipur	17887	Nil,significant	Regular cycles	G2P1L1	OCr	69	Not anemic	No Edema	Not jaundiced	83	110/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Harpriya	31	Sulur,Coimbatore	17892	Nil,significant	Regular cycles	G2P1L1	Nil	57	Not anemic	No Edema	Not jaundiced	90	110/70	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Preetha	25	Karunatharampatti,Coimbatore	17997	Nil,significant	Regular cycles	G2P1L1	Cu T	78	Not anemic	No Edema	Not jaundiced	84	120/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Ramya	25	AGS purduh,Coimbatore	18003	Nil,significant	Regular cycles	G2P1L1	Nil	61	Not anemic	No Edema	Not jaundiced	92	110/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Krushika	24	Avarampalayam,Coimbatore	18003	Nil,significant	Regular cycles	Primi	Nil	70	Not anemic	No Edema	Not jaundiced	76	110/70	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Saranya	26	Kinathukadavu,Coimbatore	18024	Nil,significant	Regular cycles	G2P1L1	Nil	67	Not anemic	No Edema	Not jaundiced	80	120/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Dheebalaxmi	24	Arispalayam,Coimbatore	18036	Nil,significant	Regular cycles	Primi	Nil	62	Not anemic	No Edema	Not jaundiced	78	120/70	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Rambharathi	22	Chelubayam,Coimbatore	18045	Nil,significant	Regular cycles	Primi	Nil	51	Not anemic	No Edema	Not jaundiced	82	110/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Smitra	31	Kalveerampalayam,Coimbatore	18067	Nil,significant	Regular cycles	G2P1L1	Nil	72	Not anemic	No Edema	Not jaundiced	84	120/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Leela	27	Veerapandi piruvu,Coimbatore	18074	Nil,significant	Regular cycles	G2P1L1	Cu T	68	Not anemic	No Edema	Not jaundiced	88	110/70	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Banumathy	21	SS Kilam,Coimbatore	18087	Nil,significant	Regular cycles	Primi	Nil	67	Not anemic	No Edema	Not jaundiced	80	120/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Chitradevi	23	Lovedale,Nilgiris	18094	Nil,significant	Regular cycles	Primi	Nil	86	Not anemic	No Edema	Not jaundiced	78	110/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Evamgeline	27	Pogalur,Coimbatore	18134	Nil,significant	Regular cycles	G2P1L1	Nil	59	Not anemic	No Edema	Not jaundiced	84	110/70	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good
Fathima	24	Rathnapur,Coimbatore	18145	Nil,significant	Regular cycles	Primi	Nil	67	Not anemic	No Edema	Not jaundiced	76	120/80	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Uterus term,acting,head engaged,FH good

Date of Delivery	Intervention Group	Baby Wt	Blood loss	other uterotonic agents	blood transfused	Post delivery details-Soon after delivery					rs after del		
						PR	BP	Temp	RR	Suivering	Pyrexia	Hb	Hct
11/26/2018	Group II(Oxytocin alone)	3.460ml	Nil		Nil	82	110/70	Normal	14	No	No	12.1	36
11/26/2018	Group II(Oxytocin alone)	3.2360ml	Nil		Nil	70	120/80	Normal	12	No	No	12	36
11/26/2018	Group II(Miso+Oxytocin)	3.1680ml	Nil		Nil	76	110/70	Normal	14	No	No	11	33
11/24/2018	Group II(Miso+Oxytocin)	2.2390ml	Nil		Nil	88	110/70	Normal	12	No	No	11.2	33
11/22/2018	Group II(Miso+Oxytocin)	3.2320ml	Nil		Nil	84	110/70	Normal	13	Yes	No	10	30
11/20/2018	Group II (Oxytocin alone)	2.4370ml	Nil		Nil	90	110/70	Normal	16	No	No	11.4	34
11/14/2018	Group II(Miso+Oxytocin)	3.000ml	Nil		Nil	78	110/70	Normal	14	No	Yes	11.2	33
11/14/2018	Group II(Oxytocin alone)	2.8380ml	Nil		Nil	90	110/70	Normal	12	No	No	10.2	31
11/14/2018	Group II(Miso+Oxytocin)	3.51390ml	Nil		Nil	87	110/70	Normal	17	No	No	12	36
11/14/2018	Group II (Oxytocin alone)	2.7320ml	Nil		Nil	92	110/70	Normal	14	No	No	11.2	33
11/9/2018	Group II(Miso+Oxytocin)	2.1520ml	Nil		Nil	92	110/70	Normal	12	Yes	Yes	10.8	32
11/6/2018	Group II (Oxytocin alone)	3.580ml	5		1	89	110/70	Normal	11	No	No	9.8	29
11/6/2018	Group II(Miso+Oxytocin)	3.5320ml	Nil		Nil	74	110/70	Normal	16	No	No	11.6	34
11/2/2018	Group II(Oxytocin alone)	2.7480ml	5		1	88	110/70	Normal	14	No	No	11.6	34
11/2/2018	Group II(Miso+Oxytocin)	3.260ml	Nil		Nil	78	110/70	Normal	14	Yes	No	11	33
11/2/2018	Group II(Oxytocin alone)	3.41320ml	5	Smith hysterectomy	4	118	110/70	Normal	16	No	No	8.9	27
11/1/2018	Group II(Miso+Oxytocin)	3.8300ml	Nil		Nil	90	110/70	Normal	11	No	Yes	10	30
11/1/2018	Group II (Oxytocin alone)	3.380ml	Nil		Nil	88	110/70	Normal	12	No	No	9.8	29
10/31/2018	Group II (Oxytocin alone)	2.9460ml	5		2	96	110/70	Normal	16	No	No	10.8	32
10/31/2018	Group II(Miso+Oxytocin)	3.230ml	Nil		Nil	98	110/70	Normal	13	No	Yes	12	36
10/31/2018	Group II (Oxytocin alone)	2.5340ml	Nil		Nil	94	110/70	Normal	15	No	No	11	33
10/31/2018	Group II(Miso+Oxytocin)	2.8120ml	Nil		Nil	85	110/70	Normal	12	No	No	8.9	27
10/30/2018	Group II(Oxytocin alone)	3.21620ml	5		3	102	110/70	Normal	10	No	No	19	27
10/30/2018	Group II(Miso+Oxytocin)	2.9280ml	Nil		Nil	78	110/70	Normal	12	No	No	11	33
10/29/2018	Group II (Oxytocin alone)	3.7290ml	Nil		Nil	74	110/70	Normal	14	No	No	10.2	33
10/29/2018	Group II(Miso+Oxytocin)	3.320ml	Nil		Nil	86	110/70	Normal	14	Yes	Yes	9.8	29
10/27/2018	Group II (Oxytocin alone)	2.8139ml	Nil		Nil	76	110/70	Normal	17	No	No	11.2	33
20-10-20	Group II(Miso+Oxytocin)	3.7260ml	Nil		Nil	87	110/70	Normal	16	No	No	11	33
10/20/2018	Group II(Oxytocin alone)	2.8290ml	Nil		Nil	73	110/70	Normal	18	No	No	11	33
10/17/2018	Group II(Oxytocin alone)	3.170ml	5		2	98	110/70	Normal	17	No	No	9	27
10/17/2018	Group II(Miso+Oxytocin)	2.3680ml	Nil		Nil	88	110/70	Normal	14	Yes	No	12.2	36
10/17/2018	Group II(Miso+Oxytocin)	2.7260ml	Nil		Nil	86	110/70	Normal	13	No	Yes	11	33
10/16/2018	Group II (Oxytocin alone)	2.5310ml	Nil		Nil	90	110/70	Normal	16	No	No	11.8	35
10/16/2018	Group II(Miso+Oxytocin)	3.7280ml	Nil		Nil	89	110/70	Normal	14	No	No	11	33
10/15/2018	Group II(Oxytocin alone)	3.5480ml	5		1	79	110/70	Normal	17	No	No	10	30
10/15/2018	Group II(Miso+Oxytocin)	4.120ml	5		4	118	110/70	Normal	16	No	No	7.8	23
10/15/2018	Group II (Oxytocin alone)	2.8375ml	Nil		Nil	84	110/70	Normal	14	No	No	11	33
10/10/2018	Group II(Miso+Oxytocin)	3.2180ml	Nil		Nil	88	110/70	Normal	12	Yes	Yes	11.6	34
10/10/2018	Group II (Oxytocin alone)	2.6300ml	Nil		Nil	89	110/70	Normal	18	No	No	9.8	29
10/6/2018	Group II(Miso+Oxytocin)	2.5260ml	Nil		Nil	90	110/70	Normal	16	No	No	11	33
10/6/2018	Group II (Oxytocin alone)	2.8290ml	Nil		Nil	88	110/70	Normal	17	No	No	9.8	29
10/6/2018	Group II(Miso+Oxytocin)	3.1320ml	Nil		Nil	92	110/70	Normal	16	No	No	10	30
10/4/2018	Group II(Oxytocin alone)	3.2290ml	Nil		Nil	89	110/70	Normal	12	No	No	11.6	34
10/2/2018	Group II(Miso+Oxytocin)	3.810ml	5		2	100	110/70	Normal	15	Yes	No	9.2	27
10/1/2018	Group II (Oxytocin alone)	2.8260ml	Nil		Nil	78	110/70	Normal	18	No	No	11.4	37
10/1/2018	Group II(Miso+Oxytocin)	2.5180ml	Nil		Nil	87	110/70	Normal	16	No	No	11.8	35
10/1/2018	Group II (Oxytocin alone)	3.2240ml	Nil		Nil	78	110/70	Normal	15	No	No	11	33
10/1/2018	Group II(Miso+Oxytocin)	3.11590ml	Nil		Nil	86	110/70	Normal	17	Yes	Yes	11	36
9/29/2018	Group II(Oxytocin alone)	2.3220ml	Nil		Nil	80	110/70	Normal	15	No	No	12	36
9/28/2018	Group II(Miso+Oxytocin)	2.9390ml	Nil		Nil	72	110/70	Normal	17	Yes	No	12	36
9/29/2018	Group II(Oxytocin alone)	3.2780ml	Nil		2	98	110/70	Normal	13	No	Yes	9.6	28
9/29/2018	Group II(Miso+Oxytocin)	2.7100ml	5		5	124	110/70	Normal	16	Yes	No	8	24
9/20/2018	Group II (Oxytocin alone)	2.9270ml	Nil		Nil	86	110/70	Normal	13	No	Yes	12.6	37
9/20/2018	Group II(Miso+Oxytocin)	3.1360ml	Nil		Nil	88	110/70	Normal	12	No	Yes	12	36
9/19/2018	Group II(Oxytocin alone)	3.2380ml	5		Nil	74	110/70	Normal	16	No	No	10.6	31
9/9/2018	Group II(Miso+Oxytocin)	2.9240ml	Nil		Nil	88	110/70	Normal	13	Yes	Yes	11	33
9/9/2018	Group II (Oxytocin alone)	3.2260ml	Nil		Nil	80	110/70	Normal	12	No	No	9.8	28
9/3/2018	Group II(Miso+Oxytocin)	2.6270ml	Nil		Nil	84	110/70	Normal	17	Yes	No	11	33
8/30/2018	Group II (Oxytocin alone)	3.1240ml	Nil		Nil	92	110/70	Normal	14	No	No	10.2	30
8/28/2018	Group II(Miso+Oxytocin)	2.6180ml	Nil		Nil	74	110/70	Normal	12	No	No	11.2	33
8/28/2018	Group II(Oxytocin alone)	3.6176ml	5		2	100	110/70	Normal	14	No	No	9	27
8/28/2018	Group II(Miso+Oxytocin)	2.5170ml	Nil		Nil	78	110/70	Normal	18	No	No	12	36

8/18/2018 Group II (Oxytocin alone)	2.8 390ml	Nil	Nil	82	110/70	Normal	16	No	10.4	33	
8/18/2018 Group I (Miso-Oxytocin)	3 400ml	Nil	1	102	110/70	Normal	14	Yes	9.8	29	
8/18/2018 Group II (Oxytocin alone)	2.75 240ml	Nil	Nil	76	110/70	Normal	13	5	11.2	33	
8/10/2018 Group I (Miso+Oxytocin)	2.8 180ml	Nil	Nil	98	110/70	Normal	15	No	10	30	
8/7/2018 Group II (Oxytocin alone)	3.1 210ml	Nil	Nil	86	110/70	Normal	13	No	12	36	
8/7/2018 Group I (Miso+Oxytocin)	3 210ml	Nil	Nil	92	110/70	Normal	17	Yes	10.8	32	
8/2/2018 Group II (Oxytocin alone)	2.8 340ml	Nil	Nil	86	110/70	Normal	16	No	10.6	31	
8/2/2018 Group I (Miso+Oxytocin)	2.9 320ml	Nil	Nil	94	110/70	Normal	13	No	9	27	
7/19/2018 Group II (Oxytocin alone)	2.7 150bml	Swish Hysterectomy	6	122	110/70	Normal	13	No	7.8	22	
7/17/2018 Group I (Miso+Oxytocin)	2.8 270ml	Nil	Nil	92	110/70	Normal	17	Yes	10	30	
7/17/2018 Group II (Oxytocin alone)	2.6 280ml	Nil	Nil	88	110/70	Normal	15	No	11	33	
7/8/2018 Group I (Miso+Oxytocin)	3.7 290ml	Nil	1	98	110/70	Normal	17	No	9.8	29	
7/8/2018 Group II (Oxytocin alone)	3.1 440ml	5	Nil	98	110/70	Normal	14	Yes	12	36	
7/3/2018 Group I (Miso+Oxytocin)	2.8 150ml	5	Nil	76	110/70	Normal	14	Yes	10.2	30	
7/3/2018 Group II (Oxytocin alone)	2.8 360ml	5	Nil	88	110/70	Normal	17	No	10.2	30	
7/1/2018 Group I (Miso+Oxytocin)	3.6 160ml	Nil	Nil	76	110/70	Normal	13	No	11.2	33	
6/29/2018 Group II (Oxytocin alone)	2.8 190ml	Nil	Nil	72	110/70	Normal	14	No	12.8	39	
6/29/2018 Group I (Miso+Oxytocin)	2.7 110ml	Nil	Nil	86	110/70	Normal	12	No	10	30	
6/18/2018 Group II (Oxytocin alone)	2.5 390ml	5	1	88	110/70	Normal	16	No	9	27	
6/17/2018 Group I (Miso+Oxytocin)	2.3 220ml	Nil	Nil	90	110/70	Normal	14	No	11	33	
6/15/2018 Group II (Oxytocin alone)	2.6 370ml	5	Nil	86	110/70	Normal	19	No	12.2	36	
6/15/2018 Group I (Miso+Oxytocin)	2.5 300ml	5	Nil	92	110/70	Normal	15	Yes	10	30	
6/7/2018 Group II (Oxytocin alone)	2 120bml	5	4	110	110/70	Normal	14	No	7.2	27	
6/7/2018 Group I (Miso+Oxytocin)	2.6 270ml	Nil	Nil	89	110/70	Normal	17	Yes	12	36	
6/1/2018 Group II (Oxytocin alone)	2.3 410ml	5	1	92	110/70	Normal	14	No	10	30	
5/31/2018 Group I (Miso+Oxytocin)	3 210ml	Nil	Nil	88	110/70	Normal	16	No	10	30	
5/27/2018 Group II (Oxytocin alone)	3.2 520ml	5	1	92	110/70	Normal	15	No	11	33	
5/27/2018 Group I (Miso+Oxytocin)	2.1 210ml	Nil	Nil	86	110/70	Normal	13	Yes	12	36	
5/11/2018 Group II (Oxytocin alone)	2.6 290ml	Nil	Nil	88	110/70	Normal	16	No	10	30	
5/11/2018 Group I (Miso+Oxytocin)	2.7 170ml	Nil	Nil	72	110/70	Normal	14	Yes	11.2	33	
5/9/2018 Group II (Oxytocin alone)	3 1850ml	5	3	94	110/70	Normal	16	No	7.2	28	
5/9/2018 Group I (Miso+Oxytocin)	3 310ml	5	Nil	87	110/70	Normal	12	No	11.2	33	
5/1/2018 Group II (Oxytocin alone)	2.6 420ml	5	1	90	110/70	Normal	15	No	9	27	
30-04-20 Group I (Miso+Oxytocin)	2.1 270ml	Nil	Nil	89	110/70	Normal	16	Yes	10.2	34	
30-04-20 Group II (Oxytocin alone)	2 290ml	Nil	Nil	88	110/70	Normal	14	No	10	30	
21-04-20 Group I (Miso+Oxytocin)	2.4 320ml	Nil	Nil	90	110/70	Normal	16	No	11.2	33	
21-04-20 Group II (Oxytocin alone)	2.6 610ml	5	2	100	110/70	Normal	12	No	8	24	
21-04-20 Group I (Miso+Oxytocin)	3.4 270ml	Nil	Nil	82	110/70	Normal	15	No	11.6	34	
11-04-20 Group II (Oxytocin alone)	2.7 360ml	5	Nil	82	110/70	Normal	16	No	10.2	30	
11-04-20 Group I (Miso+Oxytocin)	2.1 320ml	Nil	Nil	80	110/70	Normal	15	Yes	10.7	32	
07-04-20 Group II (Oxytocin alone)	2.6 290ml	Nil	Nil	84	110/70	Normal	14	No	11	33	
04-04-20 Group I (Miso+Oxytocin)	2.8 210ml	Nil	Nil	80	110/70	Normal	17	No	10	30	
04-04-20 Group II (Oxytocin alone)	2.6 340ml	Nil	Nil	78	110/70	Normal	15	No	8.7	25	
02-04-20 Group I (Miso+Oxytocin)	3 1120ml	5	4	122	110/70	Normal	12	Yes	7	22	
02-04-20 Group II (Oxytocin alone)	3.1 1740ml	5	2	94	110/70	Normal	13	No	8	24	
02-04-20 Group I (Miso+Oxytocin)	2.6 270ml	Nil	Nil	86	110/70	Normal	13	Yes	11	33	
3/30/2018 Group II (Oxytocin alone)	2.7 320ml	Nil	Nil	84	110/70	Normal	14	No	10.4	31	
3/30/2018 Group I (Miso+Oxytocin)	3.1 280ml	Nil	Nil	90	110/70	Normal	15	Yes	10.2	30	
3/26/2018 Group II (Oxytocin alone)	2 290ml	Nil	Nil	84	110/70	Normal	13	5	Yes	11	33
3/21/2018 Group I (Miso+Oxytocin)	3 370ml	Nil	Nil	90	110/70	Normal	16	No	11	33	
3/20/2018 Group II (Oxytocin alone)	2.7 410ml	5	1	88	110/70	Normal	12	No	8.2	25	
3/12/2018 Group I (Miso+Oxytocin)	2.4 270ml	Nil	Nil	92	110/70	Normal	14	Yes	9.6	30	
3/12/2018 Group II (Oxytocin alone)	2.1 169ml	Nil	Nil	78	110/70	Normal	14	No	13	38	
3/6/2018 Group I (Miso+Oxytocin)	2.7 320ml	Nil	Nil	90	110/70	Normal	16	Yes	Yes	10.4	30
3/6/2018 Group II (Oxytocin alone)	2.7 370ml	5	Nil	94	110/70	Normal	12	No	10.8	31	
3/3/2018 Group I (Miso+Oxytocin)	2 170ml	Nil	Nil	78	110/70	Normal	14	No	11.2	33	
3/2/2018 Group II (Oxytocin alone)	3.7 680ml	5	2	98	110/70	Normal	15	No	8.8	27	
2/27/2018 Group I (Miso+Oxytocin)	2.8 190ml	Nil	Nil	76	110/70	Normal	12	No	11	33	
2/26/2018 Group II (Miso+Oxytocin)	2.5 280ml	Nil	Nil	84	110/70	Normal	15	Yes	No	10	30
2/26/2018 Group I (Miso+Oxytocin)	2.2 270ml	Nil	Nil	88	110/70	Normal	16	No	12	36	
2/26/2018 Group II (Miso+Oxytocin)	2.4 570ml	5	1	90	110/70	Normal	14	No	9	27	
2/26/2018 Group I (Miso+Oxytocin)	3.5 190ml	Nil	Nil	72	110/70	Normal	12	No	10.2	30	
2/26/2018 Group II (Oxytocin alone)	3.4 810ml	5	2	89	110/70	Normal	16	No	7	21	
2/20/2018 Group I (Miso+Oxytocin)	2.4 690ml	Nil	1	96	110/70	Normal	13	No	10.2	30	
2/20/2018 Group II (Oxytocin alone)	2.7 390ml	5	Nil	98	110/70	Normal	14	No	12	36	
2/20/2018 Group I (Miso+Oxytocin)	2.1 290ml	Nil	Nil	86	110/70	Normal	16	No	10.8	32	
2/17/2018 Group II (Oxytocin alone)	3.8 1300bml	Swish H	4	112	110/70	Normal	15	No	8	24	
2/17/2018 Group I (Miso+Oxytocin)	2.9 280ml	Nil	Nil	87	110/70	Normal	13	No	Yes	10	30

2/15/2018	Group II (Oxytec'n alone)	2.7 680ml	5	2	102	110/70	Normal	14	No	8	24
2/15/2018	Group I (Misa+Oxytec'n)	2.7 290ml	Nil	Nil	98	110/70	Normal	16	Yes	10	30
2/17/2018	Group II (Oxytec'n alone)	2.6 260ml	Nil	Nil	86	110/70	Normal	14	No	9	27
2/17/2018	Group I (Misa+Oxytec'n)	3.4 660ml	Nil	Nil	75	110/70	Normal	13	Yes	12	36
2/6/2018	Group II (Oxytec'n alone)	3 179ml	5	3	118	110/70	Normal	15	No	7.8	23
2/6/2018	Group I (Misa+Oxytec'n)	3.2 180ml	Nil	Nil	72	110/70	Normal	15	No	11	33
2/4/2018	Group II (Oxytec'n alone)	2.1 300ml	Nil	Nil	86	110/70	Normal	15	5	10	30
2/4/2018	Group I (Misa+Oxytec'n)	2.9 290ml	Nil	Nil	92	110/70	Normal	16	No	10	30
2/3/2018	Group II (Oxytec'n alone)	3 610ml	5	1	86	110/70	Normal	14	No	8	24
2/3/2018	Group I (Misa+Oxytec'n)	2.4 310ml	Nil	Nil	87	110/70	Normal	15	Yes	10	30
2/3/2018	Group II (Oxytec'n alone)	3 580ml	5	Nil	92	110/70	Normal	13	No	9.2	27
2/2/2018	Group I (Misa+Oxytec'n)	2.5 340ml	Nil	Nil	78	110/70	Normal	14	Yes	10.9	33
1/2/2018	Group II (Oxytec'n alone)	2.5 190ml	5	Nil	86	110/70	Normal	12	No	9.2	28
2/2/2018	Group I (Misa+Oxytec'n)	2.7 240ml	Nil	Nil	90	110/70	Normal	14	No	10	30
2/2/2018	Group II (Oxytec'n alone)	3.7 240ml	Nil	Nil	89	110/70	Normal	16	No	9	27
2/2/2018	Group I (Misa+Oxytec'n)	3.5 510ml	5	Nil	78	110/70	Normal	17	No	8.8	26
2/1/2018	Group II (Oxytec'n alone)	2.5 720ml	5	1	100	110/70	Normal	13	No	8.9	27
2/1/2018	Group I (Misa+Oxytec'n)	3.7 320ml	Nil	Nil	88	110/70	Normal	14	No	11	33
1/30/2018	Group II (Oxytec'n alone)	3.2 490ml	5	Nil	90	110/70	Normal	13	No	11	33
1/30/2018	Group I (Misa+Oxytec'n)	3 320ml	Nil	Nil	86	110/70	Normal	16	Yes	9	27
1/30/2018	Group II (Oxytec'n alone)	2.5 680ml	Nil	Nil	78	110/70	Normal	15	No	10	30
1/28/2018	Group I (Misa+Oxytec'n)	2.7 290ml	Nil	Nil	82	110/70	Normal	13	Yes	9.8	29