A COMPARATIVE STUDY OF INJ. OXYMETRIN AND RECTAL MISOPROSTAL IN THE PREVENTION OF POST PARTUM HAEMORRHAGE

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CERTIFICATE

This is to certify that this dissertation titled **"A COMPARATIVE STUDY OF INJ. OXYMETRIN AND RECTAL MISOPROSTAL IN THE PREVENTION OF POST PARTUM HAEMORRHAGE"** submitted by **Dr.S. SIVANANDAVALLI** to the faculty of Obstetrics and Gynaecology, The Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree Branch II (Obstetrics and Gynaecology) is a bonafide research work carried out by her under our direct supervision and guidance.

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CONTENTS

INTRODUCTION

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Third stage of labour commences with the delivery of the fetus and ends with the delivery of the placenta. In view of the maternal risk, the third state of labour is the most important phase of parturition. Although it occupies an insignificant period of time compared with many hours devoted to labour, this short period involves many hazards for the maternal life and health. Prolonged third stage of labour is often associated with its related complications and increased risk of maternal mortality and morbidity.

In a developing country like ours postpartum haemorrhage contributes appreciably to maternal illness and is a leading cause of maternal death. WHO statistics suggest that 25% of maternal deaths are due to postpartum haemorrhage. The primary aim in the management of postpartum haemorrhage should be its prevention. Several methods have been developed to encourage early delivery of the placenta and thereby reduce the risk of postpartum haemorrhage.

Uterine atony accounts for about 80% of cases of PPH (Predivelle and Elboume 1990). There are several factors which may predispose to uterine atony, include overdistended uterus, multipara, prolonged labour, antepartum haemorrhage etc.

By following protocols of active management of third stage of labour, atonic Postpartum haemorrhage should be identified early and action should be prompt. The obstetric team could prevent it if atony is there which may be attended immediately.

The present study was designed to evaluate and compare the efficacy of oxytocic drugs Inj oxymetrin 1amp im and rectally administered T.Misoprostal 800 mcg Inj oxymetrin 1amp contains oxytocin 5 IU and Ergometrine maleate 0.5mg

AIM OF THE STUDY

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1. To evaluate the efficiency of Inj oxymetrin l amp Im in third stage of labour as a prophylactic oxytocic drug.

2. To study the effect of Inj.Oxymetrin in III stage critical events.
    (i) Duration of III stage.
    (ii) Blood loss of III stage.
    (iii) Complication of III stage.

3. Comparison of Inj. oxymetrin with Rectal misoprostal in III stage management.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

One of the primary objectives of third stage of labour is prevention of postpartum haemorrhage.

Active management of third stage is usually implemented as a package including.

- ❖ Early oxytocic therapy (with delivery of the anterior shoulder or shortly after delivery of the baby.
- ❖ Early cord clamping and placental delivery by controlled cord traction following signs of placental separation.

Oxytocices include syntocinon, methyl ergometrine and prosta glandins. -**Bonner**

Recent review of randomised trials showed a significant reduction in the risk of postpartum blood loss of 500ml (or) more for women receiving the combination drug syntometrine (Oxytocin and ergometrine) when compared with oxytocin 5 units Im. The advantage was smaller but still significant (**Bonner – 21**).

In another randomised double blind prospective study, Intramuscular syntometrine was better choice than syntocinon in the management of third

stage of labour. 2 Inj syntometrine not only reduced blood loss after delivery but was associated with a 40% reduction of in risk of PPH and the need for repeat oxytocin injection. It's use is however contra indicated in women with hypertensive disorders. Rectal misoprostal 600 mg was significantly less effective than 10 units Im syntocinon in active management of third stage (**17th studd**).

In a larger uncontrolled study misoprostal 1000 mg given rectally was effective in 16 of 18 women unresponsive to usual oxytocin. The mean response time was 14 minutes – **Williams 21** (Abdul Aleem and associated 2001 Brien and collegues 1997).

Villar and coworkers found in their systematic review that oxytocin and ergot preparations administered during third stage of labour was more effective than misoprostal for prevention of PPH.

Syntomctrine given In. immediately after the delivery of the child is associated with a small but statistically significant reduction in PPH compared to giving oxytocin alone (Prevention of PPH 70 **Fogsifocus** Prof. P.K. Sekharan).

Cochrane database comparing the effects of oxytocin and syntometrine. The analysis showed that there was a significant reduction in the risk of postpartum haemorrhage 500 to 1000ml by using syntometrine

when compared to oxytocin 5 units Im (Mcdonald et al 2000) - **Arulkumaran** – Second).

The oxytocic response of

- Iv ergometrine is 41 seconds.
- Im ergometrine in 7 minutes
- Im syntometrine in 2 ½ minutes **(Ian Donald)**
- maximum action for rectal misoprostal was achieved in 21minutes.

In a study published in British journal of obstetrics and Gynaecology of 2198 vaginal single ton deliveries, it was concluded that administration of combination of oxytocin ergometrine at the end of second stage of labour was significantly more effective in preventing postpartum haemorrhage also it was found that administration of oxytocin – ergometrine combination after delivery of fetal head was significantly more effective in preventing postpartum haemorrhage compared with administration after the placenta was expelled.

Prostaglandins are well known to be useful in treatment of postpartum haemorrhage (Bigrigg et al 1991). Misoprostol PGE1 analogue has a long shelf life and does not require any storage conditions.

Drape estimation Vs visual assessment for estimating postpartum haemorrhage.

John H stroger Jr. Hospital of cook county chicago USA.

A randomized controlled study was performed with 123 women delivered at District hospital, Belgaum, India. The women were randomized to visual or drape estimation of blood loss. Result – The visual estimation of blood loss was 33% less than the drape estimate. They have concluded drape estimation of blood loss is more accurate than visual estimation and have particular utility in the developing world.

Reducing PPH:

Oxytocics include syntocinon, methyl ergometrin and prostaglandins.

1. Randomised comparison of Im syntometrine with rectal Misoprostal 400 mcg for management of III stage of labour was done by **Dept of O&G Natalsprult Hospital Johannessburg** (Bamiyboyaa Merrell DA) Duration of III stage, postpartum blood loss and postpartum haemoglobin estimation were similar.

2. **Department of O&G Royal free and universal college London School U.K.** The objectives of study is to compare Im Syntometrine

plus syntocinon versus rectal Misoprostal 800 mg in prevention of PPH.

The primary outcome measured was whether haemorrhage ceased with in 20 minutes of administration of first line treatment. Conclusion – Inj, syntometrine plus syntocinon and rectal misoprostal was equally effective in prevention of Postpartum haemorrhage.

3. **Department of O&G Ainsham university Cairo Egypt.** They conducted a study with of rectal misoprostal and compared the effectiveness with Im Oxytocin & ergometrine.

   Clinical and haemorrhagic parameters were compared using ‘t’ and ‘chi’ square test. Results in both groups were well matched and had similar duration of III stage of labour. Postpartum hypertension was more in oxymetrin group.

4. **Department of O&G the Chinese University of Hong Kong Prince of Whales Hospital Station**. A total of 2058 patient with singleton pregnancy, low risk for postpartum haemorrhage and vaginal delivery were randomized to receive of 2 inj, syntometrine (or) 600 mg misoprostal for management of III stage of labour. There was no significant difference between 2 groups in mean blood loss, incidence

of postpartum haemorrhage and fall in haemoglobin concentration. The need for additional oxytocin injection was higher in misoprostal group. Shivering and transient pyrexia were more common in misoprostal group.

5. **Department of O&G university of Sydney New South Wales**. Randomized trial to compare efficacy of Im syntometrin with oral misoprostal 400 mcg. Main out come measured blood loss, use of second uterotonic agent, difference in Hblevel from antepartum to postpartum.

   Increase in blood loss and rate of Postpartum haemorrhage >500 ml in misoprotal group. Use of second uterotonic agent is higher in misoprostal group. Inference. Oral misoprostal 400 mcg is significantly less effective than the Inj. syntometrine

6. **British Journal of O&G Jan 2001 Vol 108.** Cochrane database studies comparing the effect of use of oxytocin and syntometrine. Advantages of syntometrine was smaller but significant in decrease in postpartum haemorrhage of 500 – 1000ml. No difference seen in large postpartum haemorrhage. Need for blood transfusion manual removal of placenta were similar.

7. **JC Schellenberg Department of O&G Geneva university hospital**. They have done a study comparing use of rectal administration of 1 gm misoprostal with oxytocin and ergometrine. Duration of III stage and blood loss in III stage were similar in both groups. But diastolic hypertension was increased in syntometrine group.

8. **The Salford Third Stage Trial**. Study of Oxytocin plus ergometrine versus oxytocin alone in the active management of III stage.

   Oxytocin plus ergometrine is more effective than oxytocin alone in the prevention of PPH. But ergometrine component caused nausea, vomiting and raised BP.

THIRD STAGE OF LABOUR

THIRD STAGE OF LABOUR

It commences with the delivery of the fetus and ends with the delivery of the placenta. Average duration of third stage of labour is around 15 minutes.

Signs of Placental Separation

- Uterus becomes globular and firmer.
- Sudden gush of fresh blood from the vagina.
- Uterus rises in the abdomen because the placenta having separated, passes down into the lower uterine segment where its bulk pushes the uterus upward.
- Extra vulval lengthening of cord.

Physiology of Third Stage

- Uterine contractions continue after birth of the fetus and intrauterine pressure continues to be rhythmically raised.
- Uterus spontaneously contracts around its diminishing contents.
- Sudden diminishing in uterine size is inevitably accompanied by a decrease in the area of placental implantation.
- Separation of placenta results primarily from disproportion created between the unchanged size of the placenta and the reduced size of the underlying implantation site.

- **Two methods of placental delivery**
  - Maternal lower edge of the placenta presents at the vulva – Dirty Duncan Method.
  - Placental fetal surface appears first at vulva – Shiny Shultz Method

- **Blood loss after placental delivery is minimised by**
  - Effective contraction of the uterine muscles
  - Blood vessels supplying placental site are compressed by oblique fibres of middle layer of the myometrium.
  - Thrombosis of open ends of blood vessels at the placental site

The degree of compression of the vessels depends on the force acting on the vessels.

Force obeys the Young Laplace relationship $F = \frac{2T}{r}$

F = The compressive force acting on the blood vessels

T = Wall tension (generated by uterine contraction)

r = Radius of the uterus

It is essential that the radius of the uterus be made small by emptying the uterus from any blood or placental tissue and increasing the wall tension

of the uterus (T) by giving Ecbolics - Oxytocics. This is the scientific basis of the initial treatment and the prevention of primary PPH.

Active management of third stage

Active management of third stage of labour include

1. Prophylactic use of oxytocic drugs
2. Early cord clamping
3. Controlled cord traction for delivery of the placenta.

Use of oxytocic drugs

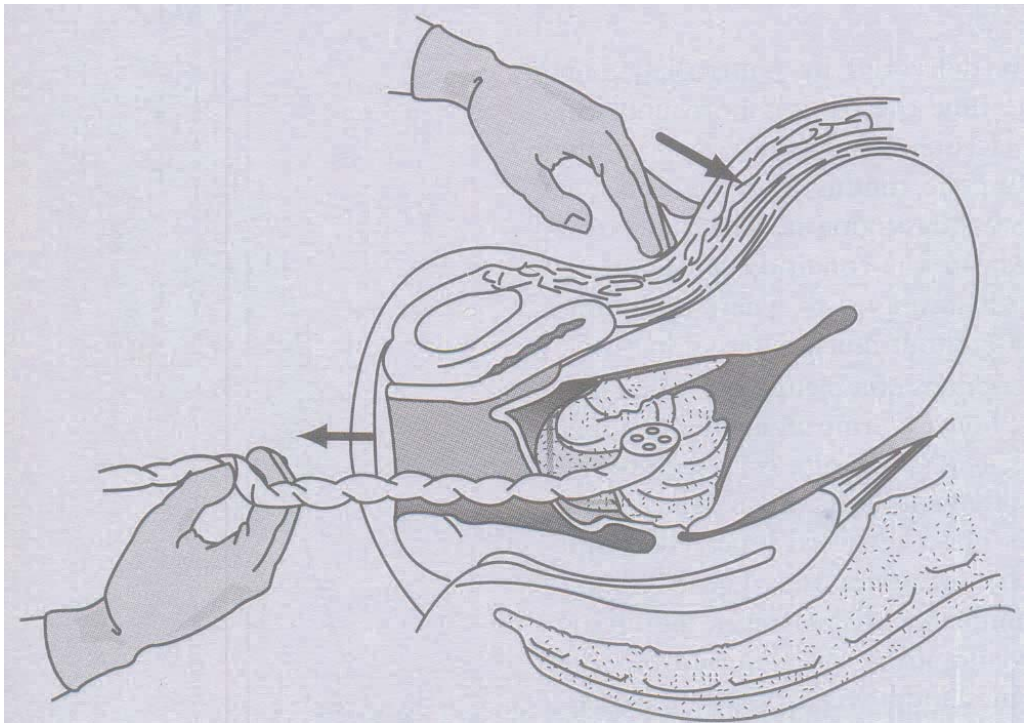
The objective of prophylactic oxytocics is to ensure efficient contractions of the uterus after the delivery of the fetus, thus minimizing the amount of blood loss.

If an oxytocic drug is given before the delivery of the placenta, the procedure of controlled traction should be applied for subsequent delivery of placenta.

Clamping of the cord

Active management of the third stage, usually entails the clamping and dividing the umbilical cord early.

DELIVERY OF PLACENTA



Delivery of the placenta

It is usually done by modified Brandt-Andrews method by controlled cord traction.

Once the signs of placental separation are recognised the palmar surface of the left hand is placed approximately below the level of the fundus. The body of the uterus is displaced upwards and backwards, towards the umbilicus while by the right hand steady gentle tension is given in downward direction until the placenta comes outside the introitus.

POSTPARTUM HAEMORRHAGE

POSTPARTUM HAEMORRHAGE

Postpartum haemorrhage is defined as a loss of more than 500 ml of blood from genital tract following delivery (or) any loss even less than 500 ml if associated with hemodynamic changes in the mother.

PPH are of two types:

- **Primary PPH**

  Loss of blood in excess of 500ml during the first 24 hours after birth of an infant.

- **Secondary PPH**

  When blood loss occurs after the first 24 hours upto six weeks, it is designated as secondary PPH.

  PPH is a major contributor of maternal mortality. It accounts for 25% of all global deaths.

Causes of PPH include

- ❖ Atony of the uterus
- ❖ Trauma to the genital tract
- ❖ Coagulation disorder

Uterine Atony

It accounts for the majority of cases of PPH 76-81 %. Immediately after delivery of the infant and placenta, uterine bleeding associated with a soft 'boggy' uterus on palpation is characteristic of uterine atony.

A. Predisposing factors include

- Prolonged labour
- Uterine overdistension
- Antepartum haemorrhage
- Uterine fibroids
- High parity
- Excessive (or) prolonged use of oxytocics in labour
- Magnesium sulphate in labour
- General anaesthesia mainly halogenated anaesthetics
- Precipitate labour
- Chorioamnionitis
- Uterine abnormalities

Measurement of blood loss

After delivery of the baby, the amniotic fluid is allowed to drain away and a specially designed blood collection drape was kept in position by slipping under woman’s buttock and left in place to collect blood loss over the next hour.

Blood and clots from the drape is measured in a measuring cylinder blood soaked swabs and linen savers are weighed the known dry weight subtracted.

Clinical symptoms and signs related to the amount of blood loss

Blood Loss % of Blood volume	Systolic Blood Pressure mmHg	Symptoms and signs
10 – 15	Normal	Postural Hypotension mild tachycardia
15 – 30	Slight fall	Tachycardia, thirst, weakness
30 – 40	60 – 80	Pallor, Oliguria, confusion, restlessness
40 +	40 – 60	Anuria, air hunger, coma, death

Prophylaxis of PPH

1. Every pregnant woman should have haemoglobin estimation during her antenatal period. Her blood grouping and Rh typing should be done.
2. Antepartum anaemia is corrected.
3. Certain patients are susceptible to develop PPH in labour and and certain conditions predispose to

PPH which include

i. Multi parity

ii. H/o. PPH (or) manual removal of placenta.

iii. Abruptio placenta

iv. Placenta praevia

v. Multiple pregnancy

vi. Polyhydramnios

vii. Intrauterine death with prolonged retention of dead fetus

viii. Prolonged labour

ix. Difficult labour

x. Caesarean section

4. In the above patients practice active III stage management of labour.
5. As long as the child is in good condition and there is no need for rapid extraction, the body is delivered slowly. This facilities placental separation and permits the uterus to retract sufficiently to control bleeding.
6. In cases where uterine atony is anticipated, an IV infusion is set up before the delivery
7. Squeezing and kneading the uterus before the placenta has separated is traumatic and harmful. Look for uterine atony.
8. Careful postpartum observation of the patient is made.
9. Excessive and prolonged inhalatory anaesthesia should be avoided.

10. Fibrinogen studies are done incases of placental abruption and retained dead fetus.
11. When haemorrhage is anticipated adequate amounts of blood should be cross matched and kept available.

Treatment of Primary Postpartum Haemorrhage

Most maternal deaths are avoidable and are due to underestimation of blood loss, inadequate volume replacement and delay in operative intervention.

Any delay in achieving haemostasis results in terminal coagulopathy. At this stage even surgery may be too late. Hence rapid and resolute action is paramount.

Management include

- General management
- Specific management
  - Medical Management
  - Surgical Management

General Management

1. Assess the general condition of the patient, the amount of blood loss and the degree of hypoxemia.

2. Vital parameters such as the level of consciousness, pulse rate, blood pressure, input / output, level of the uterine funds and amount of blood should be monitored.
3. Two intravenous lines should be set up.
4. Catheterize the bladder.
5. Blood should be sent for full blood count and cross matching with a request for 4-6 units.
6. Crystalloids (or) colloids should be given in the meantime
7. Uterine atony is the cause of PPH in about 80% of cases in the meantime, so uterus should be massaged.

Medical Management

Uterotonic agents in PPH. Usually bleeding will get arrested in 5 – 15 minutes duration with Oxytocics.

Agent	Route of Administration	Dose	Comments
Oxytocin	Inravenous	10-40 units in 1000 ml of RL (or) NS	Not to exceed 100ml/min
Methyl Ergometrine	Intramuscular intravenous	0.2mg 6^{th} hourly	Avoid in Hypertensive patients, cardiac disease patients
15 Methyl PGF2$\propto$	Intramuscular intramyometrial	0.25μg 15 – 90 mins	Bronchospasm

Agent	Route of Administration	Dose	Comments
Misoprostol (PGE_1 Analogues)	Intracervial vaginal, rectal	400μg – 1000μg	Nausea, vomiting diarrhoea.
Oxymetrin	Intra Muscular	Oxytocin 5 I.U Ergometrine maleate 0.5 mg	Avoid in Hypertensive patients, cardiac disease patients

8. **Bimanual compression** - Bimanual compression of the uterus prevents an increase in the radius of the uterus due to bleeding in the uterus. Simultaneously, the uterus is pushed caphalad, which puts the uterine arteries under tension and reduces blood flow to the uterus.

Specific Management

Other methods

Uterine Package

It is a controversial subject. It is impossible to pack an atonic uterus so tightly that the blood sinuses are closed off.

Uterus simply balloons and fills up with more blood. Despite these anti packing arguments, many obstetricians believe that is worth trying to control bleeding by this method before more radical measures are employed. If bleeding is not controlled cases to be shifted to the tertiary care centre.

Embolization of pelvic arteries

This technique can be used instead of Hysteretomy or ligation of internal iliac artery for the treatment of pelvic haemorrhage.

Procedure

Under radiologic angiographic control, a polyethylene catheter is introduced into the aorta in the Right Femoral Artery. Each internal iliac artery is catheterized and occluded with small fragments of gelfoam.

It can be carried out in less than 2hours.

Advantages

- Distal blood vessels are occluded, so that bleeding from reconstituted distal vessels is rare.
- Uterus is retained and further child bearing is possible.

Surgery :

B Lynch suture for Post partum haemorrhage (Ferguson et al 2000)

- It is a type of compression suture applied over the uterus to control PPH.
- It has the advantage of maintaining the patient's child bearing potential.

Ligation of the uterine arteries

Since most of the uterine blood is supplied by the uterine arteries, their ligation can control PPH. The collateral supply is sufficient to maintain the viability of the organ.

The suture is placed through the myometrium of the lower segment of the uterus 2-3 cm medial to the vessels.

Ligation of Internal iliac artery (Allahbadia 1993)

Ligation of internal iliac arteries at times, reduces the haemorrhage appreciably. Most important mechanism of action with this ligation is an 85% reduction in pulse pressure in those arteries distal to the ligation, thus turning an arterial pressure system into one with pressure in the venous circulation and amenable to haemostasis via simple clot formation.

Hysterectomy

- It is performed when all other treatment options have failed.
- In most of the cases, hysterectomy results in the prompt and definitive cessation of PPH.

PHARMOCOLOGY OF

UTEROTONIC DRUGS

PHARMOCOLOGY OF UTEROTONIC DRUGS

1. Methylergotamine
2. Oxytocin
3. Prostaglandins

Oxymetrin Injection

(Oxytocin + Ergometrine Maleate injections)

Composition

Each 1 ml ampoule contains:

Oxytocin 5 1.U.

Ergometrine maleate 0.5 mg

Description

Oxymetrin injections contain two potent uterine oxytocics i.e. oxytocin and ergometrine maleate. Oxytocin is a cyclic nonapeptide secreted by the hypothalamus which causes contraction of the uterus, the effect increasing with the duration of pregnancy due to proliferation of oxytocin receptors. It is chemically designated as Cys-Tyr-lle-Gin-Asn-Cys-Pro-Leu-Gly-Nh2 cyclic (16) disulphide with a structural formula of C43H66N12012S2 and a molecular weight of 1007.2.

Ergometrine maleate is an ergot alkaloid which produces intense uterine contractions, especially on the puerperal uterus. It is chemically designated as N-[(S)-2-Hydroxy-1 –methylethyl] –D-lysergamide hydrogen maleate with a structural formula of $C_{19}H_{23}N_3O_2$, $C_4H_4O_4$ and a molecular weight of 441.5.

Pharmacology

Oxymetrin injections combine the rapid uterine action of oxytocin with the sustained uterotonic effect of ergometrine.

Following intramuscular administration, the latent period for the occurrence of the uterine response is considerably shorter with OXYMETRIN injections (about 2 ½ minutes) than with ergometrine given alone (about 7 minutes), whereas the uterotonic effect of Oxymetrin injections lasts for several hours compared with only ½ to 1 hour when oxytocin is given alone.

These properties make Oxymetrin injections suitable for the active management of the third stage of labour and for the prevention or treatment of postpartum haemorrhage, particularly in situations where for any reason the intravenous administration of a uterotonic agent is impracticable.

Pharmacokinetics

Oxytocin undergoes enzymatic destruction in the gastrointestinal tract but it is rapidly absorbed from the mucous membranes when administered

buccally or intranasally. It is metabolized by the liver and kidneys with a plasma half-life of only a few minutes. Only small amounts are excreted unchanged in the urine.

Ergometrine is reported to be rapidly absorbed after administration by mouth and by intramuscular injection, with onset of uterine contractions in about 5 to 15 minutes and 2 to 7 minutes respectively. Elimination appears to be principally by hepatic metabolism.

Indications

Oxymetrin Injections are indicated for the following:

- Active management of the third stage of labour (as a means to promote separation of the placenta and to reduce blood loss)
- Prevention and treatment of postpartum haemorrhage associated with uterine atony.

Contraindications

Oxymetrin Injections are contraindicated in the following conditions:

- Hypersensitivity to any of the components.
- Pregnancy, labour (except in second stage of labour following the delivery of the anterior shoulder).
- Severe hypertension, pre-eclampsia, eclampsia

- Severe disorders of cardiac, hepatic or renal functions; occlusive vascular disease; sepsis.

Precautions and Warnings

In breech presentation and other abnormal presentations, Oxymetrin injections should not be given until after delivery of the child is completed. When Oxymetrin injections are used for the management of the third stage of labour the possibility of multiple pregnancy must be assessed; Oxymetrin injections should not be given until the last child has been delivered.

Active management of the third stage of labour requires expert obstetric supervision.

If in the treatment of postpartum haemorrhage, bleeding is not arrested by Oxymetrin injections, the possibility of a retained placental fragment, or soft tissue injury (cervical or vaginal laceration), or of a clotting defect should be considered and appropriate measures taken before a further injection is given.

Caution is required in patients with mild or moderate hypertension, or with mild or moderate degress of cardiac, hepatic or renal disease (severe forms are contraindications). Caution is also required in patients with respiratory disease, chronic anaemia and toxaemia of pregnancy.

Drug Interactions

Oxymetrin Injections may enhance the pressor effect of vasoconstrictors (e.g. of sympathomimetic agents contained in local anaesthetics) and potentiate the uterine action of prostaglandins.

Halothane anaesthesia may diminish the uterotonic effect of Oxymetrin Injections.

Adverse Effects

Oxymetrin injections may cause nausea, vomiting, uterine hypertonicity associated with abdominal pain, headache, dizziness and skin rashes. On rare occasions, it may give rise to hypertension, bradycardia, cardiac arrhythmias, chest pain or to anaphylactoid reactions associated with dyspnoea, hypotension, collapse or shock.

Dosage and Administration

Active management of third stage of labour

1 ml intramuscularly following delivery of the anterior shoulder, or immediately after delivery of the child. Expulsion of the placenta, which is normally separated by the first strong uterine contraction following the injection of Oxymetrin injections should be manually assisted by applying gentle fundal pressure.

Prevention and treatment of postpartum haemorrhage:

1 ml i.m. following expulsion of the placenta, or when bleeding occurs: If necessary, the injection of 1 ml may be repeated after an interval of not less than 2 hours. The total dose given within 24 hours should not exceed 3 ml.

Intravenous administration of Oxymetrin injections (0.5 to 1 ml by slow injection) is possible, but not generally recommended. It is advisable to monitor blood pressure during intravenous administration.

Over Dosage

No cause of overdosage with OxymetriniInjections have so far been reported. The symptoms most likely to occur would be those of acute ergometrine intoxication, nausea, vomiting, hypertension or hypotension, vasospastic reactions, respiratory depression, convulsions, coma. Treatment would have to be symptomatic.

Inadvertent administration of the newborn infant has proved fatal. Other than general resuscitative measures, no treatment is available.

Presentation

1 ml ampoule containing 5 I.U. Oxytocin & 0.5 mg Ergometrine maleate.

Storage Conditions

Store at 2^0-8^0C (Refrigerate, do not freeze). Protect from light.

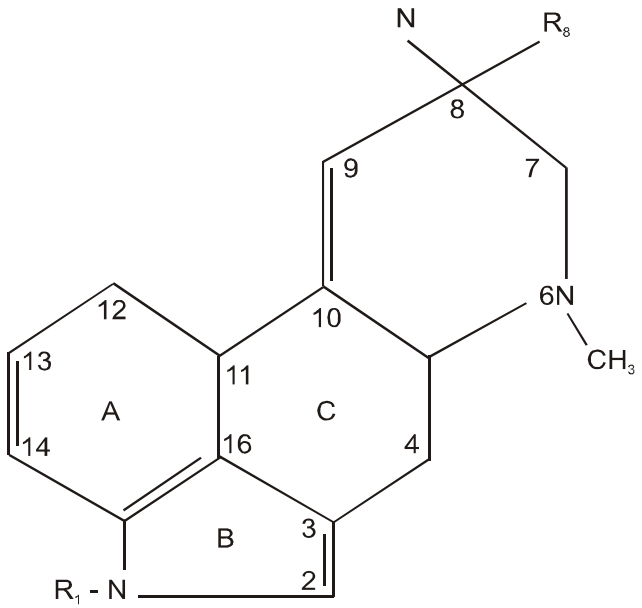
Ergot Alkaloids

They are produced by claviceps purpurea a fungus that infects grain. These alkaloids affect alpha adrenoceptors, dopamine receptors, 5 HT receptors.

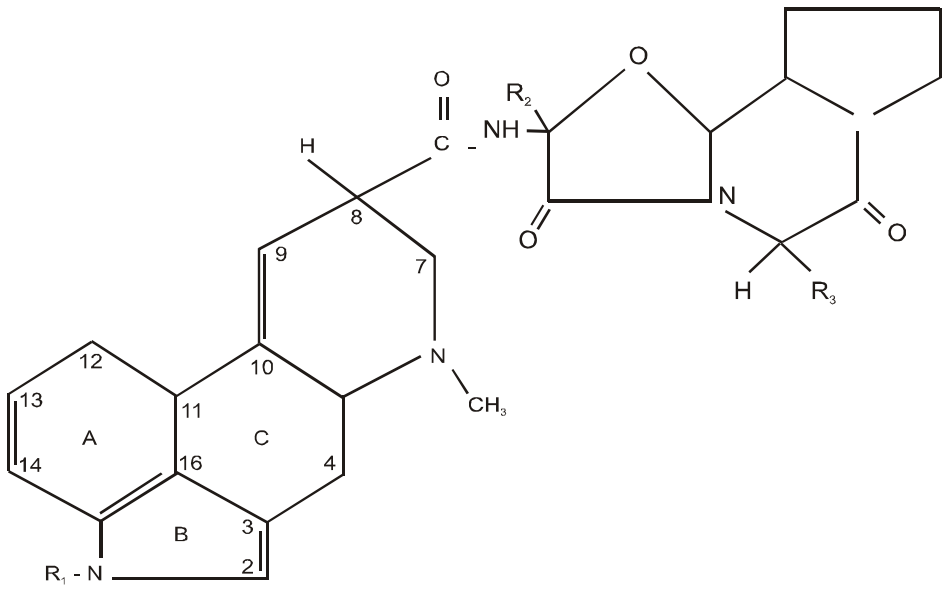
Chemistry & Pharmacokinetics

Two major families of compounds that incorporate the tetracyclic ergo line nucleus may be identified.

1) Amine Alkaloids



2) Peptide Alkaloids



Pharmacokinetics

They are variably absorbed from the Gastro intestinal tract. The oral dose of ergotamine is about ten times larger than the intramuscular dose.

Amino alkaloids are also absorbed from the rectum and the buccal cavity and after administration by aerosol inhaler. Absorption after intramuscular injection is slow but usually reliable.

They are extensively metabolized in the body. Primary metabolites are hydroxylated in the A ring and peptide alkaloids are also modified in the peptide moiety.

Pharmacodynamics

Mechanism of Action

They act on several types of receptors. Their effects include agonist, partial agonist and antagonistic actions at α - adreno receptors and serotonin receptors and agonist action at CNS dopamine receptors.

They have a powerful stimulant effect on the uterus that seems to be most closely associated with agonist effects at 5 HT2 receptors.

Effects

1. **CNS**

   Certain alkaloids are powerful hallucinogens. Bromocriptine directly suppresses prolactin secretion from pituitary cells by activating and regulating dopamine receptors.

2. **Vascular Smooth Muscle**

   Ergotamine and related compounds, constrict most human blood vessels in a predictable, prolonged and potent manner.

3. **Uterine Smooth Muscle**

   The stimulation action of ergot alkaloids on the uterus as on vascular smooth muscle, appears to combine alpha agonist, serotonin and other effects.

Because of increasing dominance of receptors as pregnancy progresses, uterus at term is more sensitive than earlier in pregnancy.

4. Other Smooth muscle organs

It produces visceral smooth muscle contractions. It does not act on the bronchiolar smooth muscle.

Preparations commonly used

Preparations	Strength	Dosage
Ergometrine injections	0.5mg/ml	0.2mg/im 0.1 –0.5mg/iv
Methyl ergometrine	0.2 mg/ml	0.2 mg/ml 0.2 mg sc, im & iv
Syntometrine	0.5 mg methyl ergometrine	in 5 units of oxytocin

Side Effects

Most common side effects of the ergot derivatives are gastro intestinal disturbances including nausea, vomiting and diarrhoea. Activation of the medullary vomiting center and of the gastrointestinal serotonin receptors is involved.

Dangerous tonic effects with ergotamineand ergonorine is prolonged vasopasm.

Oxytocin

It means 'Quick birth'. It is synthesized in the hypothalamus and then transported to the posterior pituitary, where they are stored and released into the circulation.

Chemistry & Pharmacokinetics

It is a nine amino acid peptide composed of six amino acid disulfide ring and three membered tail containing the carbonyl terminus.

Cys - Tyr - lie - Gln - Asn - Cys - Pro - Leu - Gly - NH2

Absorption, Metabolism and Excretion

It is usually administered intravenously for stimulation of labor, though buccal absorption is possible.

It is inactive if swallowed, because it is destroyed in the stomach and intestine. It is catabolized by the kidneys and liver and plasma t½ is 5 – 10 minutes.

Pharmacodynamics

Oxytocin alters transmembrane ionic currents in myometrial smooth muscle cells to produce sustained uterine contraction. The sensitivity of the uterus to oxytocin increases during pregnancy. Oxytocin causes contraction of myo epithetial cells surrounding mammary alveoli which leads to milk injection.

Mechanism of Action and Effects

Uterus

It binds to the estrogen receptors on myometrial cell membrane, where CAMP is eventually formed and Ca++ is mobilised from sarcoplasmic reticulum to activate contractile proteins.

Other Actions

CVS

It decreases diastolic blood pressure and a reflex increase in cardiac output with tachycardia.

Anti diuretic effect

Oxytocin in high doses exerts an ADH like action. This can lead to water intoxication especially when given with dextrose which is electrolyte free.

Side effects

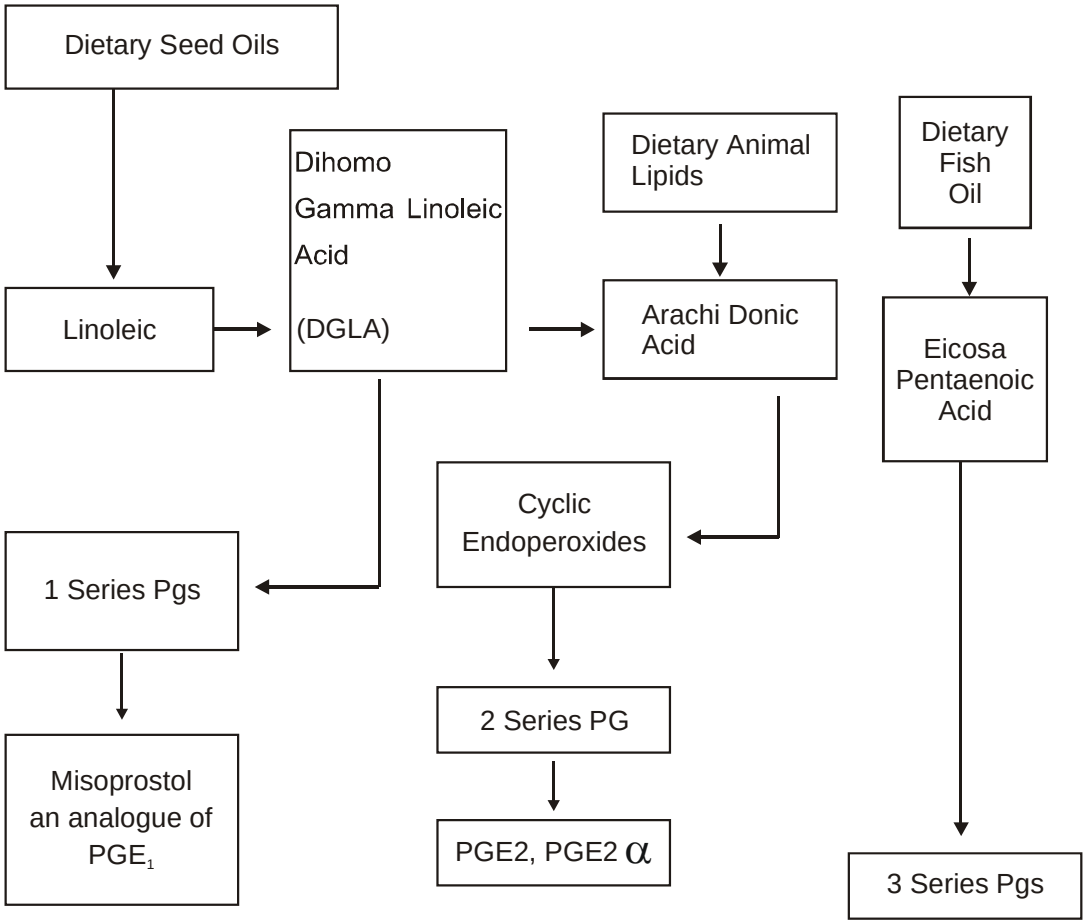
1) Hypotension, tachycardia
2) Water intoxication

3) Increased incidence of neonatal jaundice due to increased red cell fragility causing haemolysis.

PROSTAGLANDINS

Prostaglandins are the most potent naturally occuring bioactive autocoids. Vou Euler named this active principle prostaglandin because he assumed, it originated in the prostate gland.

Prostaglandin Biosynthesis



Degradation

Degradation of arachidonates occurs rapidly in most tissues, but fastest in the lungs. Prostaglandin is catabolized mainly in the kidney.

Actions

1) **CVS**

PGE2 cause vasodilatation but not in all the vascular beds.

PGE2 and F2 stimulate heart by weak direct but more prominent reflex action due to fall in BP.

2) Platelets

PGI 2 - is a potent inhibitor of platelet aggregation

3) Uterus

PGE2 & PGF2 uniformly contract human uterus. PGs increase tone as well as amplitude of uterine contractions.

4) Bronchial muscle

They are potent bronchoconstrictors expect PGE2, which is a powerful bronchodilator.

Uses

- Abortion – First trimester termination of pregnancy – PG are used
- Induction and Augmentation of labour
- Cervical priming

- PPH – for control of PPH due to uterine atony specially in patients unresponsive to ergometrine and Oxytocin.

Administration of prostaglandins in PPH

Intramyometrial injections

PgF2 – 250 – 1000 μg (microgram)

PGE2 100 – 200 μg

15 me PGF2 250 μg

Intramuscular

15 me PGF2 250 μg

Uterine lavage

PGF2 2000 μg / hr

Rectal administration

400 – 1000 μg

Vaginal Instillation

PGE2 20 mg

Side effects

- Nausea. vomiting, watery Diarrhoea.
- Uterine Cramps, flushing, shivering.
- Fall in BP, tachycardia, chest pain.

MATERIALS AND METHODS

MATERIALS AND METHODS

In this randomized comparative study, 100 patients attending Government Rajaji Hospital, Madurai for confinement during the period from June 2006 to October 2007 were recruited. They were grouped into 2 groups.

Group A – Prophylactic Inj. Oxymetrin Group – 50 patients

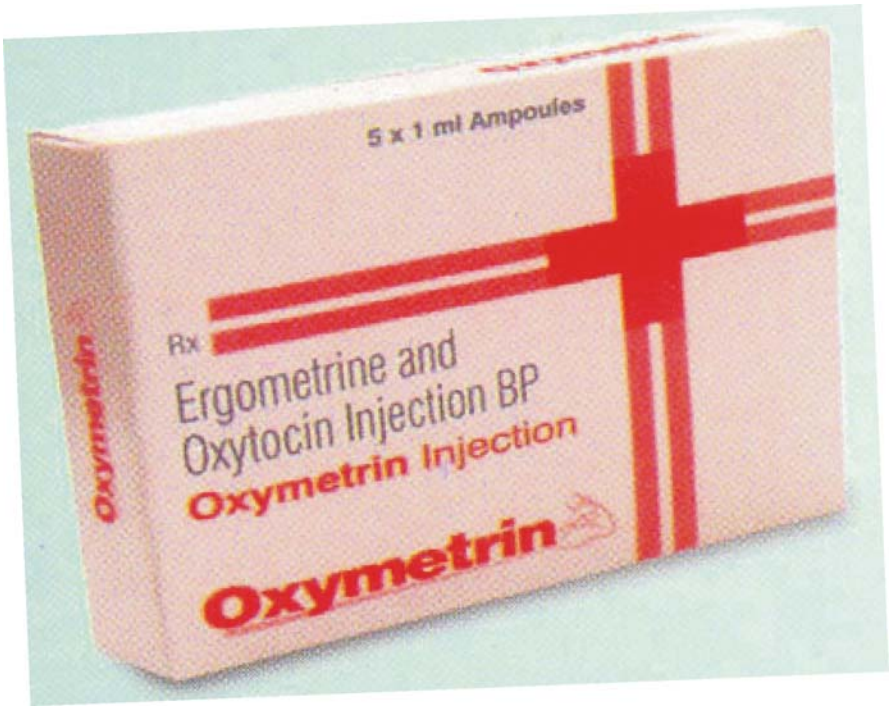
Group B – Prophylactic Rectal Misoprostol Group – 50 patients

Inclusion Criteria

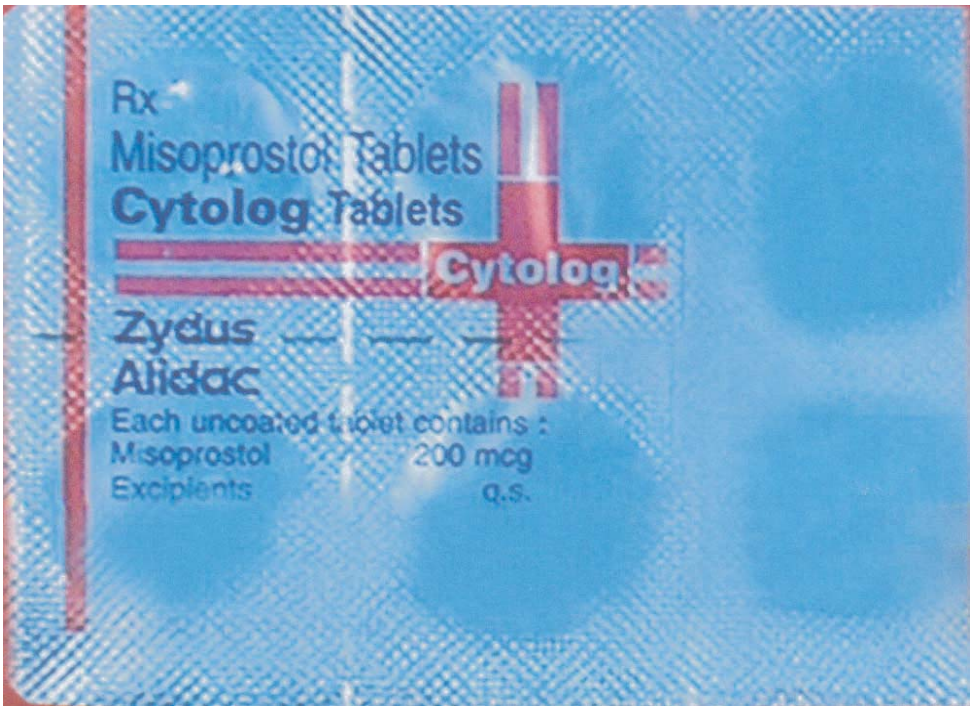
Pregnant women with gestational age more than 28 weeks in longitudinal lie either vertex (or) breech presentation who deliver vaginally including the following risk factors.

- Prolonged Labour
- Instrumental delivery
- Post dated pregnancy
- Anemia
- Elderly primi

Inj. Oxymetrin



T. Misoprostal



Exclusion Criteria

- Abruptio placenta
- Placenta previa
- Twins
- Heart disease
- Asthma complicating pregnancy
- Previous uterine surgery

Methods

Group A

50 Patients received Inj. oxymetrin 1 amp Im at the delivery of anterior shoulder.

Group B

50 Patients were given Rectal Misoprostal 800 μg administered at the time of delivery of anterior shoulder.

In each case, the following parameters were recorded.

1. Labour – Spontaneous (or) Induced
2. Labour – Accelerated or not
3. Duration of I Stage
4. Duration of II Stage

Drap Estimation

Measuring Jar

5. Mode of Delivery whether labour natural or assisted breech or instrumental
6. Oxytocin used pertaining to
    a. Time of administration, dosage
    b. Duration of III Stage
    c. Amount of blood loss
7. Side effects of drugs like nausea, vomiting and diarrhea
8. Need for other oxytocics
9. Requirement of blood transfusion
10. Presence of maternal complications after delivery like PPH and hypotension.
11. Coagulation profile before and after deliveries

Measure of Blood Loss

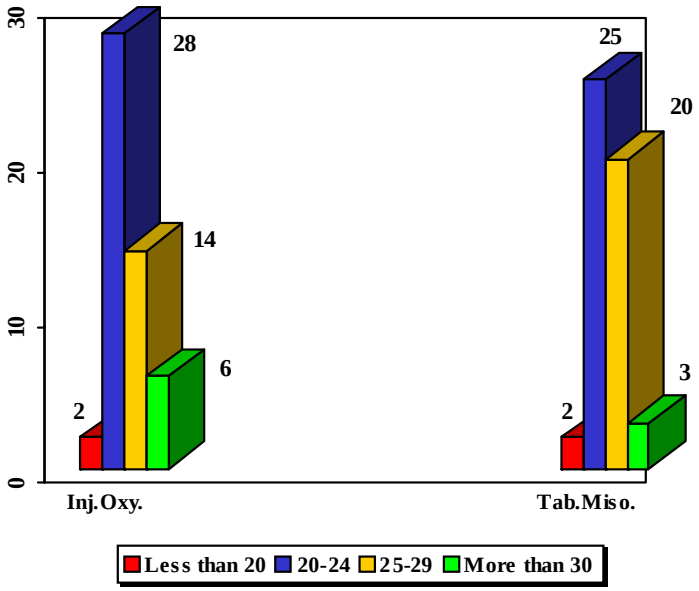
The amount of blood loss was measured by collecting the blood in blood collection, drape after amniotic fluid drained away. Blood loss was calculated 1 gm = 1 ml (Harding 1984). This gives only the approximate blood loss during the third stage.

Blood clot of the size of clenched fist in roughly equal to 500 ml.

After collecting all the data, the data were tabulated and analysed.

RESULTS

AGE DISTRIBUTION



RESULTS

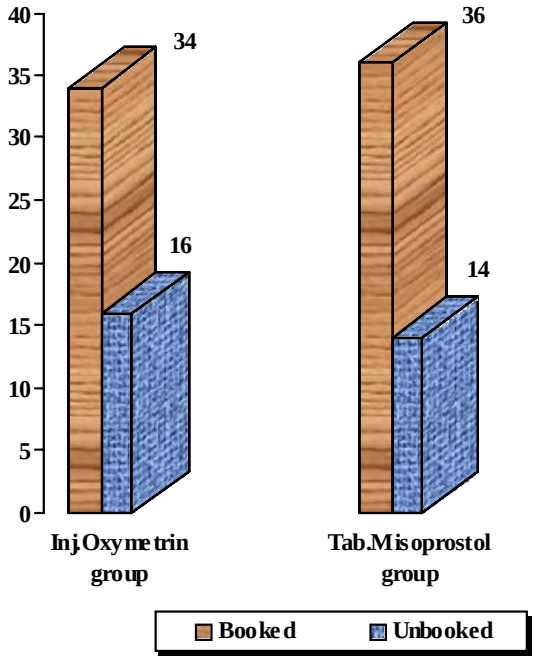
Profile of cases studied

Table 1 : Age Distribution

Age in Years	**No of cases in**			
	Inj.Oxymetrin Group		**Tab.Misoprostol Group**	
	No	**%**	**No**	**%**
Less than 20	2	4	2	4
20 – 24	28	56	25	50
25 – 29	14	28	20	40
30 & above	6	12	3	6
Total	50	100	50	100
Mean	24.4		23.9	
S.D	4.4		2.9	
'p'	0.742 (Not Significant)			

Comparing the age distribution in both the groups, majority of the patients were between 20-29 years of age 84% (42/50) in Group A and 90%(45/50) in Group B. Elderly age group contributes to minority of the population (i.e.) 12%(6/50) in Group A 6%(3/50) in Group B. Teenage group remains the same in both 4%(2/50) in both.

ANTENATAL CARE



There is no significant difference in the mean age of the cases in both the groups.

Table : 2 Antenatal care

Antenatal care	No of cases in			
	Inj.Oxymetrin Group		Tab.Misoprostol Group	
	No	%	No	%
Booked	34	68	36	72
Unbooked	16	32	14	28
Total	50	100	50	100
'p'	0.8273 (Not Significant)			

In Group A 68% (34/50) were booked and 32% (16/50) were unbooked. In Group B 72% (36/50) were booked and 28% (14/50) were unbooked.

The antenatal care received by the two groups does not exhibit statistically significant difference.

PARITY

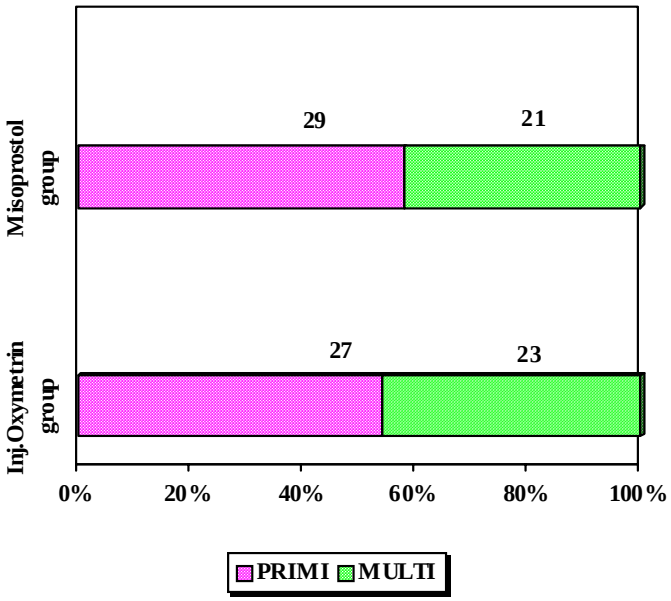

Misoprostol group
29
21
Inj.Oxymetrin group
27
23
0%
20%
40%
60%
80%
100%
PRIMI
MULTI

Table : 3 Parity

Parity	No of cases in			
	Inj.Oxymetrin Group		Tab.Misoprostol Group	
	No	%	No	%
Primi	27	54	29	58
Multi	23	46	21	42
Total	50	100	50	100
'p'	0.8403 (Not Significant)			

In this study, primi gravida were more compared to multigravida.

- In Group A – 54% Primi 46% multi
- In Group B – 58% Primi 42% multi

The parity of the two groups does not have statistically significant difference.

TYPE OF DELIVERY

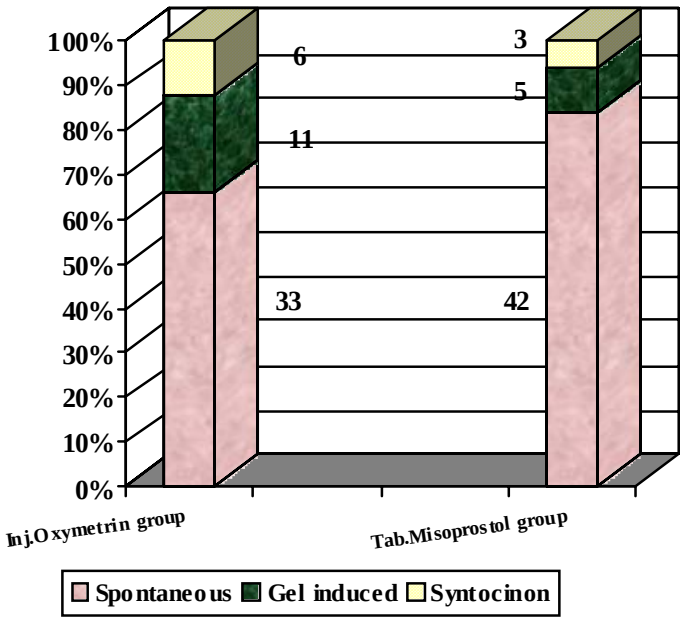


Table 4 : Type of Labour

Type of Labour	No. of cases in			
	Inj.Oxymetrin Group		Tab.Misoprostol Group	
	No	%	No	%
Spontaneous	33	66	42	84
Gel induced	11	22	5	10
Augmentation	6	12	3	6
Total	50	100	50	100
'p'	0.0647 (Not Significant)			

Type of labour was compared in both the groups. Majority of the patients in the groups had spontaneous onset of labour. (Group A 66%(33/50) Group B 84%(42/50).

Labour was induced in 22%(11/50) in Group A and in 10%(5/50) in Group B.

Type of Labour in the two groups does not differ significantly.

METHOD OF DELIVERY

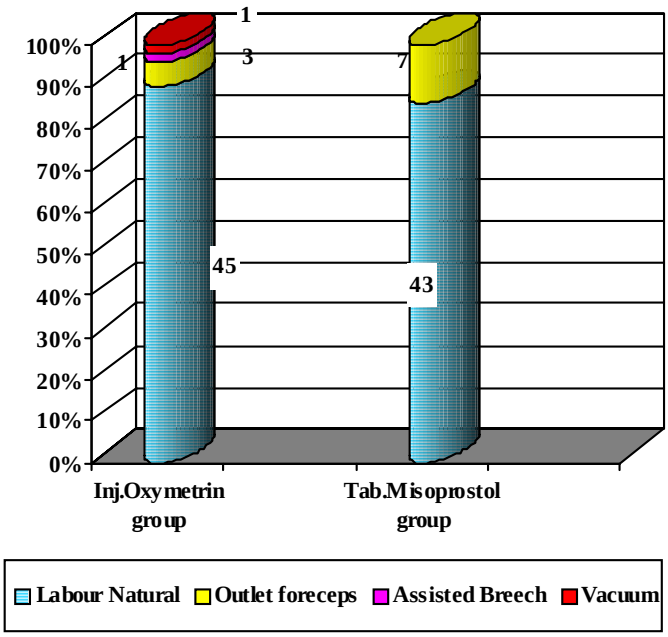
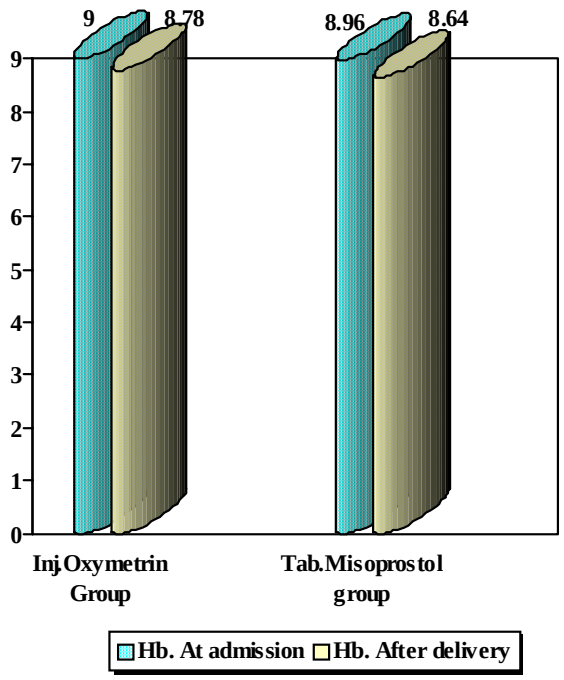


Table 5 : Method of Delivery

Method of Delivery	No. of cases in			
	Inj.Oxymetrin Group		Tab.Misoprostol Group	
	No	%	No	%
Labour Natural	45	90	43	86
Outlet forceps	3	6	7	14
Assisted Breech	1	2	-	-
Vacuum	1	2	-	-
Total	50	100	50	100
'p'	0.7583 (not significant)			

In comparing the mode of delivery in both the groups, maximum number of patients were delivered by Labour natural 90%(45/50) in Group A and 86%(43/50) in Group B. Minimal instrumentation was present 8%(4/50) in Group A 14%(7/50) in Group B.

CHANGES IN Hb.



Comparison of outcome parameters in the two groups

Table 6 : Changes in Hb.

Hb.	Inj.Oxymetrin Group		Tab.Misoprostol Group		'p'
	Mean	**S.D**	**Mean**	**S.D**	
At admission	9.0	0.89	8.96	0.89	0.9252 (Not Significant)
After delivery	8.78	0.98	8.64	0.87	0.3677 (Not Significant)

Haemoglobin level at admission is compared to haemoglobin level after delivery in both groups.

Statistically there was no significant difference in changes of haemoglobin in two groups.

MEAN DURATION OF III STAGE OF LABOUR

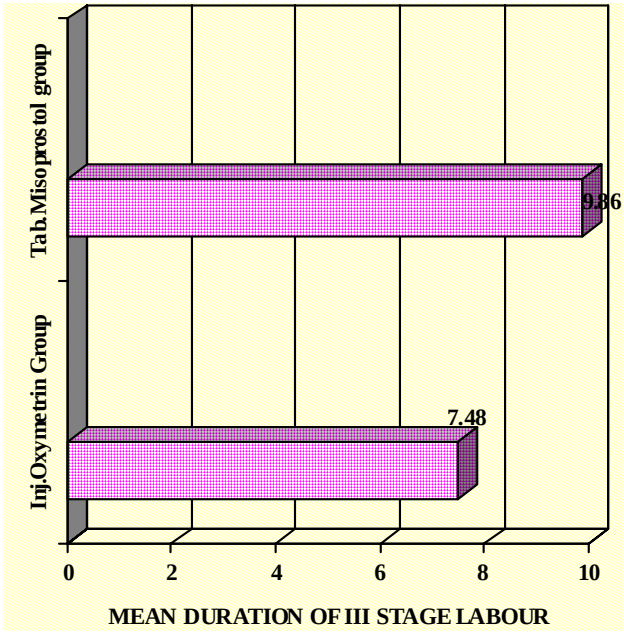


Table 7 : Duration of III stage of labour

Duration of III stage of labour (in minutes)	Inj.Oxymetrin Group		Tab.Misoprostol Group	
	No.	**%**	**No.**	**%**
≤ 2 minutes	-	-	-	-
3-4 minutes	10	20	5	10
5-6 minutes	16	32	6	12
7-8 minutes	10	20	4	8
9-10 minutes	4	8	15	30
More than 10 minutes	10	20	20	40
Mean S.D.	7.48 3.31		9.86 3.41	
'p'	0.0007 **Significant**			

20% of patients had III Stage duration upto 4 minutes in Group A 10% of Group B also 4 minutes.

In Group A 80% of patients upto 10 mins. In Group B 60% of patients upto 10 mins. In Group A mean duration of third stage – 7.48 minutes. In Group B Mean duration of third stage – 9.86

The mean duration of third stage of delivery in the Inj. Oxymetrin group is significantly lower than in the Tab.Misoprostol group.

BLOOD LOSS

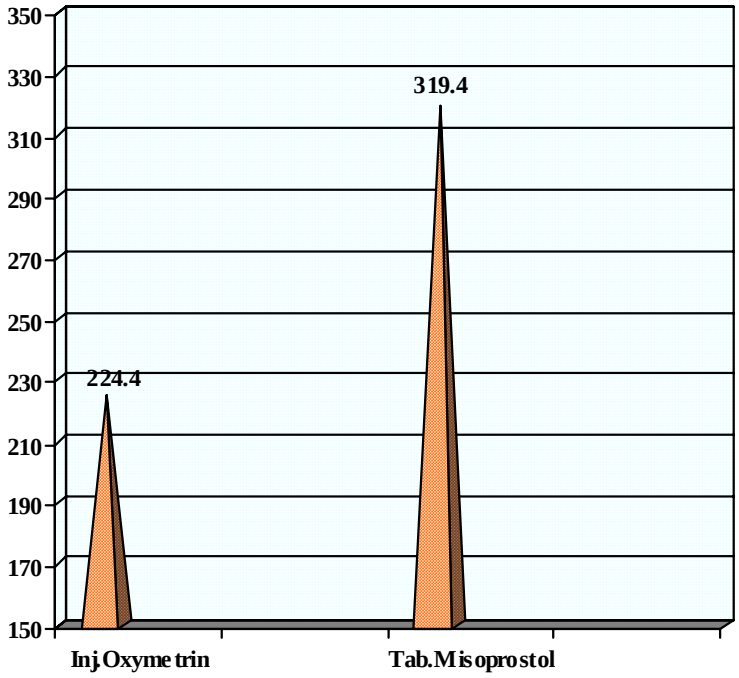

350
330
310
290
270
250
230
210
190
170
150
224.4
319.4
Inj.Oxymetrin
Tab.Misoprostol

Table 8 : Blood loss

Blood loss (in ml.)	Inj.Oxymetrin Group		Tab.Misoprostol Group	
	No.	**%**	**No.**	**%**
0-50	1	2	-	-
51-100	6	12	2	4
101-150	13	26	3	6
151-200	13	26	6	12
201-250	6	12	4	8
251-300	7	14	11	22
301-350	-	-	12	24
351-400	-	-	7	14
401-450	-	-	1	2
451-500	1	2	-	-
More than 500 ml	3	6	4	8
Mean S.D.	224.4 212.9		319.4 194	
'p'	**0.0001 Significant**			

- In Group A 66% had blood loss less than 200 ml
- In Group B 22% had blood loss less than 200 ml.

- In Group A more than 90% of patients had blood loss less than 300 ml.

- In Group B only 52% of patients had blood loss less than 300 ml.

- Mean Blood loss for Group A – 224.4 ml
- Mean Blood Loss for Group B – 319.4 ml

- More than 500 ml in Group A – 6%
- More than 500 ml in Group B – 8%

The mean blood loss in the Inj. Oxymetrin group is lower than in the Tab.Misoprostol group. This difference is statistically significant.

Table 9 (a)

Post partum complication - Inj. Oxymetrin group

PPH	Inj. Oxymetrin group	
	No.	**%**
> 1000 ml	2	4
500-1000 ml	1	2
Nil	47	94

Table 9 (b)

Post partum complication - T. Misoprostol group

PPH	T. Misoprostol Group	
	No.	**%**
> 1000 ml	2	4
500-1000 ml	2	4
Nil	46	92

The incidence of PPH is 6% in Group A and 8% in Group B. The difference is not statistically significant.

Table 10

Maternal Side Effects

	Group A		Group B	
	No.	**%**	**No.**	**%**
Shivering and fever	-	-	3	6%
Nausea and Vomiting	4	8%	1	2%
Increase in BP>10mm H	2	4%	-	-

Minor side effects like nausea and vomiting occurred in 8% in Group A. Shivering and fever occurred in 6% in Group B. Major side effects like increase in BP is found in 4% in Group A Nil in Group B.

Statistical Tools (To be included at the end of Materials and Methods)

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2002).

Using this software, frequencies, percentage, mean, standard deviation, x^2 and 'p' values were calculated. A 'p' value less than 0.05 is taken to denote significant relationship.

DISCUSSION

DISCUSSION

Patients undergoing normal progression in labour can become abnormal within few minutes and a successful delivery can turn swiftly to disaster if post partum haemorrhage enters the scene.

As the saying goes "prevention is always better than cure", prevent Post partum haemorrhage by available excellent oxytocic drugs given by different routes.

Here this study was conducted in Department of Obstetrics and Gynaecology, Government Rajaji Hospital, Madurai to assess the usefulness of two different groups of drugs Inj. Oxymetrin 1 amp Im and Rectal Misoprostal 800 mcg in the active management of third stage of labour.

In this study 50 patients were given Inj. Oxymetrin 1 amp In at the delivery of anterior shoulder.

Another 50 patients were given rectal misoprostal 800 mcg at the delivery of anterior shoulder.

Discussion of Profile of Cases Studied

Age Group and Patients Selection

In our study, the age group of patients included varied from 17-35 years. Maximum percentage of patients belong to the age group 21-30 years.

- 84% of Group A were between 20-29 years.
- 90% of Group B were between 20-29 years.

This is similar to a randomised controlled trial of oral misoprostal and Im Syntometrine in the management of III Stage of Labour by Department of Obstetrics and Gynaecology. The Chinese University of Honkong, Prince of Wales Hospital,where the mean age was 28 years.

Antenatal Care

In our study in Group A 68% were booked and 32% unbooked. In Group B 72% were booked and 28% were unbooked. Antenatal care received by the two groups were comparable.

Parity

In our study primi gravida were more in both groups compared to multi gravida. All were singleton pregnancies.

- In Group A – 54% primi 46% multi
- In Group B – 58% primi 42% multi

This is similar to study done at chinese university of Hongkong Prince of Wales Hospital where primis consisted of 52.7% in Misoprostal group and 54.3% in Syntometrine group.

Type of Labour

In our study majority of patients in both groups had spontaneous onset of labour.

- Group A – 66% Spontaenous onset of labour
- Group B – 84% spontaenous onset of labour

Augmentation with Syntocinon drug were done in Group A – 12% and Group B – 6%.

This is similar to chinese University Study Prime of Wales were 80.9% had spontaneous onset of labour in Inj. Syntometrine group 83.9% in rectal misoprostal group. 18% were augmented in syntometrine group 15% were augmented in misoprostal group.

Method of delivery

In our study maximum number of patients were delivered by labour natural 90% in Group A 86% in Group B. In Group B minimal instrumentation was present 8% in Group A 14% in Group B.

This is similar to study done by CMY Choy Wc Hau, WH Tam where Inj. Syntometrine was compared to Iv Oxytocin 10 Iu. Here 79.2% of Syntometrine group had spontaneous vaginal delivery. 77.6% of syntocinon group had spontaneous vaginal delivery.

- Instrumental delivery 20.8% in Syntometrine.
- 22.4% in Syntocinon.

Comparison of outcome parameters in both groups

Changes in Haemoglobin

Here haemoglobin level at admission is compared to haemoglobin level after delivery (on 3rd postnatal day) in both groups.

Mean Haemoglobin level of Group A

- At admission is 9 gm%
- After delivery is 8.78 gm%

Mean haemoglobin level of Group B

- At admission is 8.96 gm%
- After delivery is 8.64 gm%

This is similar to study by Chinese University of Hongkong Prince of Wales Hospital were pre delivery Hb of Syntometrine 11.8 gms%

48 hrs post delivery Hb of Syntometrine group 10.5 gm%.

- Predelivery Hb of Misoprostal group 11.9 gm%
- 48 hours post delivery Hb of Misoprostal group is 10.6gm%

There was no significant difference in changes of haemoglobin statistically in above study.

In our study too, there was no significant difference in changes of haemoglobin in two groups.

In another study by Department of Obstetrics and Gynaecology Natal Spruit Hospital Johannesburg where Im Syntometrine was compared to rectal misoprostal post partum hemoglobin estimation had similar difference in both groups.

Duration of III Stage of Labour

In our study in Group A 80% of patients had duration of third stage upto 10 minutes. In Group B 60% of patients upto 10 minutes mean duration of third stage in Group A is 7.48 minutes and in Group B is 9.86 minutes.

In a study by Chinese university of Hongkong, the duration of third stage was < 10 minutes in 86.2% of cases in syntometrine group. The duration is < 10 minutes in 79% of cases in misoprostal group.

Blood Loss

In our study 66% of Inj. Oxymetrin group had blood loss less than 200 ml. Only 22% of Rectal Misoprostal group had blood loss less than 200 ml.

- Mean Blood loss for Group A – 224.4 ml
- Mean Blood loss for Group B– 319.4 ml

This is similar to the study by Chinese University of Hongkong, Prince of Wales Hospital,

- Mean Blood loss of Syntometrine group – 254 ml
- Mean Blood loss of misoprostal group – 290 ml

In our study more than 90% of patients had blood loss less than 300 ml. In group B only 52% of patients had blood loss less than 300 ml.

The incidence of PPH i.e. more than 500 ml in Group A is 6% and more than 500 ml in Group B is 8%. This is similar to the study by Chinese university, where the incidence of PPH in misoprostal group is around 6.3% in syntometrine group is around 4.7%.

These results were like Salford Third stage trial where the inference was oxytocin plus ergometrine is more effective than oxytocin alone in the prevention of PPH.

These results were also similar to that done in Department of Obstetrics and Gynaecology, University, Sydney New South Wales which compared Inj. Syntometrine with oral misoprostal 400 mcg. In this trial there is increase in blood loss and rate of post partum haemorrhage > 500 ml in misoprostal group. Use of second utero tonic agent is higher in misoprostal group. Inference – oral misoprostal 400 mcg is significantly less effective than Inj. Syntometrine.

According to Williams, Villar and coworkers found in their systematic review that oxytocin and ergot preparations administered during third stage of labour was more effective than misoprostal in prevention of post partum haemorrhage.

Post partum complications

Main postpartum complications studied is post partum haemorrhage which required additional uterine atonic and blood transfusion. In our study Im Inj. Oxymetrin group, 6% of patients had massive post partum haemorrhage.

In T. Misoprostal group, 8% of patients had massive post partum haemorrhage. So, the incidence of Post partum haemorrhage is lower in Inj. Oxymetrine group. In Group A two patients needed blood transfusions three patients needed additional uterotonics. In Group B two patients needed blood transfusions and four patients needed additional uterotonics.

Maternal Side Effects

Minor Side effects like nausea, vomiting, occured in 8% in Group A. Shivering and fever occurred in 6% in Group B. Major side effects like increase in Blood pressure is found in 4% in Group A nil in Group B.

SUMMARY

SUMMARY

This study was conducted in the Department of Obstetrics and Gynaecology, Government Rajaji Hospital, Madurai. Hundred patients under this study were admitted in labour ward and with inclusion and exclusion criteria they were segregated into Group A and Group B.

- Group A patients were given Inj. Oxymetrin 1 amp Im.
- Group B Patients were given rectal Misoprostal 800 μg.

Results

- Inj. Oxymetrin reduce the duration of third stage more than rectal misoprostal.
- Inj. Oxymetrin reduce blood loss more effectively than rectal misoprostal.
- Inj. Oxymetrin has side effects like increased BP, Vomitting in small number of patients.
- Prophylactic use of inj. Oxymetrn in active management of third stage of labour reduces the blood loss and duration of third stage with minimal side effects.

CONCLUSION

CONCLUSION

- ☞ Inj. Oxymetrin is very effective in the active management of third stage labour.
- ☞ It reduces the blood loss and duration of third stage labour significantly. In oxymetrin group, 90% of the patients had blood loss less than 300 ml. In oxymetrin group the mean duration of III Stage was 7.48 minutes.
- ☞ Oxytocic response of Inj. Oxymetrin Im is 2 ½ minutes.
- ☞ On critical evaluation Inj. Oxymetrin is more potent in reducing the mean duration of third stage and amount of blood loss than Rectal Misoprostal.
- ☞ Because of its cost effectiveness, easy administration and avoidance of need for trained personnel, Inj. Oxymetrin Im. can be used as a alternative oxytocic agent in the third stage of labour in all developing countries.
- ☞ Side effects like nausea, vomiting, increased Blood pressure occurs in few patients.

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PROFORMA

PROFORMA

COMPARATIVE STUDY OF INJ. OXYMETRIN WITH RECTAL MISOPROSTAL IN PREVENTION OF PPH

Name : Age : IP.No. SE Status

Booked Obstetric Code

Un booked

LMP EDD Gestational Age

EXCLUSION CRITERIA

Abruption Twins Placenta Praevia Heart Diseases

Asthma complicating Pregnancy

Previous h/o. uterine surgery

History

H/o. Diabetes, Hypertension, Asthma, Epilepsy, Tuberculosis, Jaundice

H/o. Repeated MTP

H/o. Manual Removal of placenta

H/o. Previous surgery

H/o. Any chronic drug intake

H/o. Any other High Risk Factor

Whether labour was spontaneous (or) induced:

1. Spontaneous 2. Gel Induction

Whether labour was accelerated or not

If accelerated with

ARM	ARM with Oxytocin	Oxytocin

Duration of I Stage

Duration of II Stage

Duration of III Stage

Induction & Delivery interval

Mode of delivery

LN	Instrumental	Assisted Breech

Use of oxytocics during third stage of labour

Oxytocics used GP A Inj. Oxymetrin lamp Im

GP B Rectal misoprostal 800 mg

Maternal Complications:

T.Misoprostol Oxymetrin

PPH

Hypertension

Shivering & fever

Nausea

Vomiting

INVESTIGATION :

	Before Delivery	After Delivery
Hb (Gm %)		
CT (Min)		

MASTER CHART

	ge	IP.No	AN CARE	PARITY	Hb at Admn Gm%	MODE	Method	Duration (minutes)	Blood Loss (mn)	Hb. After deli. Gm%	Complicatio
	2	32999	Booked	Primi	9	Gel	LN with Epi	6	31	8.8	Absent
	0	32282	Unbooked	Primi	9	Spontaneous	LN with Epi	5	190	9	Absent
	1	33400	Unbooked	Primi	8.6	Gel	LN with Epi	6	230	8.2	Absent
	0	33789	Booked	Primi	12.2	Spontaneous	LN with Epi	5	120	12.2	Absent
	9	33746	Unbooked	Primi	9.8	Spontaneous	LN with Epi	12	90	9.8	Absent
	2	33720	Unbooked	Primi	7.8	Gel	LN with Epi	12	290	7.5	Prolonged induc time 18 hrs.
	3	33842	Booked	Multi	7.8	Assisted Breech	Assisted breech	10	120	7.5	Absent
	5	34121	Booked	Primi	8.6	Gel	LN with Epi	8	220	8.4	Prolonged induc time 16 hrs.
	5	35487	Booked	Multi	8.8	Spontaneous	LN with Epi	5	120	8.8	Absent
	9	34417	Booked	Multi	8.5	Spontaneous	LN with Epi	4	130	8.4	Absent
	5	35248	Unbooked	Multi	9	Gel	LN with Epi	8	220	8.8	Absent
	7	35731	Booked	Multi	8	Spontaneous	LN with Epi	6	100	8	Absent
	3	37712	Booked	Multi	10	Spontaneous	LN with Epi	5	60	9.8	Absent
	5	37989	Booked	Primi	8.6	Spontaneous	LN with Epi	11	280	8.4	Absent
	2	37841	Unbooked	Primi	9.2	Spontaneous	LN with Epi	16	120	9.2	Absent
	3	38595	Unbooked	Primi	8.6	Spontaneous	LN with Epi	4	180	8.4	Absent
	7	38415	Booked	Multi	6.8	Spontaneous	LN with Epi	4	130	6.6	4^{th} gravida
	3	38889	Booked	Primi	9.6	Syntocinon	LN with Epi	6	280	9.4	Absent
	2	42781	Unbooked	Primi	8.8	Gel	Outlet	6	470	8	Prolonged IInd st 1 hr 10 min
	4	42567	Booked	Multi	8	Spontaneous	LN with Epi	8	1080	6.8	PPH
	1	43418	Booked	Primi	11	Syntocinon	Outlet with Epi	4	240	10.8	Absent
	5	43476	Booked	Multi	9.4	Spontaneous	LN with Epi	12	160	9.2	Absent
	0	43433	Booked	Primi	8.8	Gel	LN with Epi	5	290	8.6	Absent

	ge	IP.No	AN CARE	PARITY	Hb at Admn Gm%	MODE	Method	Duration (minutes)	Blood Loss (mn)	Hb. After deli. Gm%	Complicatio
	2	45141	Booked	Multi	9	Spontaneous	LN with Epi	5	130	8.8	Absent
	0	43433	Unbooked	Primi i	8.8	Gel	LN with Epi	10	180	9.2	Absent
	3	45149	Booked	Multi	8.6	Syntocinon	Vacuumacuum	8	290	8.4	Absent
	7	45616	Unbooked	Multi	8.6	Spontaneous	LN with Epi	15	80	8.6	Absent
	5	35705	Unbooked	Primi	8	Syntocinon	LN with Epi	15	120	7.8	Absent
	3	60638	Booked	Multi	10.8	Spontaneous	LN with Epi	4	180	10.6	Absent
	9	61842	Booked	Primi	10	Spontaneous	LN with Epi	6	180	10	Absent
	2	62109	Booked	Primi	10	Spontaneous	LN with Epi	6	180	10	Absent
	3	62026	Booked	Primi	8.6	Spontaneous	LN with Epi	7	150	8	Absent
	2	60821	Unbooked	Primi	9	Gel	LN with Epi	10	1190	7.4	PPH
	3	62093	Booked	Primi	9.6	Spontaneous	LN with Epi	12	230	9	Big baby mor than 4 kg
	1	62026	Booked	Primi	9.8	Syntocinon	LN with Epi	4	160	9.4	Absent
	5	62108	Unbooked	Multi	9	Spontaneous	LN with Epi	8	80	9	Absent
	0	62592	Booked	Multi	9	Spontaneous	LN with Epi	4	160	8.8	Absent
	5	62591	Booked	Primi	9	Gel	LN with Epi	6	130	8.6	Absent
	4	62164	Booked	Primi	9	Spontaneous	LN with Epi	9	280	8.8	Absent
	9	62584	Booked	Multi	9	Spontaneous	LN with Epi	8	180	8.6	Absent
	2	62898	Booked	Multi	9.4	Spontaneous	LN with Epi	12	230	9	Absent
	2	62511	Booked	Primi	8.4	Gel	Outlet with Epi	8	630	7.8	Absent
	5	62648	Booked	Primi	8	Spontaneous	LN with Epi	12	170	8	Absent
	2	62542	Unbooked	Multi	8.8	Spontaneous	LN with Epi	8	90	8.8	Absent
	0	62138	Booked	Primi	9.2	Spontaneous	LN with Epi	6	260	9	Absent
	0	62816	Booked	Multi	9	Spontaneous	LN with Epi	5	150	8.8	Absent
	0	62848	Booked	Multi	9.6	Spontaneous	LN with Epi	4	200	9.6	Absent
	2	62807	Booked	Multi	8.4	Spontaneous	LN with Epi	7	140	8.8	Absent
	9	62144	Unbooked	Multi	9.6	Spontaneous	LN with Epi	3	120	9.6	Big baby 4kg
	0	62797	Unbooked	Multi	8	Spontaneous	LN with Epi	4	180	8	Absent
	5	45148	Booked	Multi	9	Spontaneous	LN with Epi	6	390	8.6	Absent
	5	46148	Booked	Multi	8	Spontaneous	LN with Epi	4	250	8	Absent

	ge	IP.No	AN CARE	PARITY	Hb at Admn Gm%	MODE	Method	Duration (minutes)	Blood Loss (mn)	Hb. After deli. Gm%	Complicatio
	27	46208	Unbooked	Multi	7	Spontaneous	LN with Epi	6	100	7	Absent
	25	47034	Booked	Multi	8.6	Spontaneous	LN with Epi	10	280	8.2	Absent
	21	48923	Booked	Primi	8.6	Gel	LN with Epi	12	330	8	Prolonged induc > 14 hrs
	20	49390	Booked	Primi	9.6	Syntocinon	LN with Epi	14	280	9.4	Absent
	21	50101	Unbooked	Primi	8.6	Spontaneous	LN with Epi	5	190	8.4	Absent
	24	50202	Unbooked	Primi	6.8	Spontaneous	LN with Epi	10	320	6.4	Absent
	25	49940	Booked	Multi	10.2	Spontaneous	LN with Epi	10	290	10	Absent
	25	50203	Booked	Primi	8.8	Spontaneous	LN with Epi	15	320	8.6	Absent
	23	50216	Booked	Multi	8.8	Spontaneous	LN with Epi	13	340	8.6	Absent
	20	50177	Booked	Primi	9.6	Gel	Outlet	8	520	9	Prolonged II Sta 1 hr 10 min
	24	50409	Unbooked	Multi	8.6	Spontaneous	LN with Epi	5	270	8.4	Absent
	24	50422	Booked	Multi	9.6	Spontaneous	LN with Epi	10	1160	8.6	PPH
	27	50200	Booked	Primi	9	Gel	LN with Epi	10	320	9	Absent
	23	50229	Booked	Primi	9	Spontaneous	Outlet	12	180	8.4	Absent
	27	50231	Unbooked	Multi	8	Syntocinon	LN with Epi	12	220	8.4	Absent
	25	50440	Booked	Multi	8.6	Spontaneous	LN with Epi	10	340	8.2	Absent
	23	50445	Booked	Primi	9	Spontaneous	LN with Epi	14	240	8.6	Absent
	25	50441	Booked	Primi	9.6	Spontaneous	Outlet	5	360	9.2	Absent
	23	50504	Booked	Primi	11.6	Spontaneous	LN with Epi	10	170	11.6	Absent
	22	50519	Unbooked	Multi	9.2	Spontaneous	LN with Epi	12	280	9	Absent
	20	50234	Booked	Primi	9.6	Spontaneous	LN with Epi	9	120	9.4	Absent
	25	50444	Booked	Primi	12	Spontaneous	LN with Epi	15	360	11.6	Absent
	21	50237	Booked	Primi	9	Spontaneous	LN with Epi	10	240	8.6	Absent
	29	54311	Unbooked	Primi	9	Spontaneous	LN with Epi	4	1100	8	PPH
	25	53847	Booked	Primi	9.6	Spontaneous	Outlet	15	340	9	Absent
	21	54301	Booked	Primi	9.2	Spontaneous	LN with Epi	12	290	9	Absent
	25	54166	Unbooked	Multi	8	Spontaneous	LN with Epi	3	140	7.6	4th gravida
	20	53849	Booked	Primi	8	Syntocinon	Outlet	15	580	7.6	PPH
	23	54034	Unbooked	Multi	7.2	Spontaneous	LN with Epi	10	170	7	Absent
	25	55330	Unbooked	Multi	8.8	Spontaneous	LN with Epi	8	80	8.6	Absent

	ge	IP.No	AN CARE	PARITY	Hb at Admn Gm%	MODE	Method	Duration (minutes)	Blood Loss (mn)	Hb. After deli. Gm%	Complicatio
	25	55321	Booked	Multi	9	Spontaneous	LN with Epi	4	120	8.6	Absent
	23	54373	Booked	Primi	9.8	Spontaneous	LN with Epi	10	280	9.6	Big baby 4.2k
	23	54366	Booked	Primi	9.4	Spontaneous	LN with Epi	13	290	9.2	Absent
	25	54388	Booked	Multi	8.6	Spontaneous	LN with Epi	9	180	8.6	Absent
	24	54328	Booked	Multi	9	Spontaneous	LN with Epi	12	320	8.6	Absent
	24	62858	Unbooked	Primi	9.2	Spontaneous	LN with Epi	8	280	9	Absent
	27	62865	Booked	Primi	9	Spontaneous	LN with Epi	9	160	9	Absent
	20	72442	Booked	Multi	9.2	Spontaneous	LN with Epi	12	380	8.4	Big baby 4.3 kg
	21	73642	Unbooked	Primi	8.8	Spontaneous	LN with Epi	11	260	8.2	Absent
	25	75821	Booked	Primi	9	Spontaneous	LN with Epi	14	360	8.4	Absent
	20	73342	Booked	Primi	8.6	Spontaneous	LN with Epi	10	330	8.2	Absent
	23	74109	Booked	Multi	8.4	Spontaneous	LN with Epi	12	420	8	Absent
	21	74058	Unbooked	Primi	9	Spontaneous	LN with Epi	11	380	8.6	Absent
	20	74038	Booked	Primi	9.2	Gel	Outlet	10	280	8.8	Absent
	20	74077	Unbooked	Multi	8.8	Gel	Outlet	6	340	8.8	Absent
	23	74018	Booked	Primi	8.4	Spontaneous	LN with Epi	4	360	8	Absent
	20	74027	Booked	Primi	9	Spontaneous	LN with Epi	16	340	9	Absent
	24	74175	Booked	Multi	9.2	Spontaneous	LN with Epi	8	320	9	Absent