

**COMPARATIVE STUDY OF  
“MIFEPRISTONE PLUS VAGINAL MISOPROSTOL”  
VERSUS  
“VAGINAL MISOPROSTOL ALONE”  
FOR SECOND TRIMESTER ABORTION**

*Dissertation submitted to*

**THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY  
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**INSTITUTE OF OBSTETRICS AND  
GYNAECOLOGY  
MADRAS MEDICAL COLLEGE  
CHENNAI.**

## **CERTIFICATE**

This is to certify that the dissertation on **COMPARATIVE STUDY OF “MIFEPRISTONE PLUS VAGINAL MISOPROSTOL” VERSUS “VAGINAL MISOPROSTOL ALONE” FOR SECOND TRIMESTER ABORTION** is a bonafide work done by **Dr.T.A.ARUNADEVI**, in Institute of Obstetrics and Gynaecology, Egmore, Chennai – 8, Madras Medical College, Chennai–3 during 2009-2011 under my supervision and guidance in partial fulfillment of the regulation laid down by the Tamil Nadu Dr. M.G.R. Medical University for MD (Obstetrics & Gynaecology) Branch – II Degree Examination to be held in April 2011.

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## **DECLARATION**

I, **Dr.T.A.ARUNADEVI**, solemnly declare that the dissertation titled **COMPARATIVE STUDY OF “MIFEPRISTONE PLUS VAGINAL MISOPROSTOL” VERSUS “VAGINAL MISOPROSTOL ALONE” FOR SECOND TRIMESTER ABORTION** has been prepared by me.

This is submitted to the Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D.Degree Examination in Obstetrics and Gynaecology. This has not been submitted previously by me for the award of any degree or diploma from any other university.


**Place : Chennai**  
**Date :**

**Dr.T.A.ARUNADEVI**

**ETHICAL COMMITTEE CERTIFICATE**

I, **Dr. T.A.Arunadevi** apply for the ethical committee certificate for the project of **“Comparative study of “Mifepristone plus Misoprostol {vaginal} versus “Misoprostol {Vaginal} alone” for 2<sup>nd</sup> Trimester Abortion** under the guidance of **Dr. K. Jayashree MD., DGO., DNB.** Institute of Obstetrics and Gynaecology, Egmore, Chennai-8.

I understand the implications of doing research with human subjects and will fully comply with the regulations and keep the dignity and protect the health of subjects at all costs.



**Signature of Postgraduate student**

I have no objection to guide this postgraduate student in the project mentioned above. I shall supervise that all the human rights are protected and research is carried on with the utmost humanitarian principles.



**Signature of the guide**

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**Seal of guide**

I certify that this project has been presented in front of the Ethical Committee, duly formatted in this institution and that all the members of the Ethical Committee have given permission to conduct this research.



**Chairman of Ethical Committee**

**Seal of Chairman**

Date: 21/12/2009

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## **INTRODUCTION**

Mid trimester termination of pregnancy is one of the controversial issues in obstetrics and gynecology which has moral, technical, emotional and social issues. Many Indian women opt for MTP (Medical Termination of Pregnancy) in second trimester inspite of increased morbidity like excessive hemorrhage, uterine perforation and infection because of unplanned pregnancies. In addition, there is a continuous need for termination of pregnancy in second trimester as there are advanced antenatal diagnostic tests which enable us to identify lethal fetal anomalies.

Termination of pregnancy in second trimester is associated with much more morbidity and mortality than when it is done in the first trimester. The various methods for second trimester termination of pregnancy are still under scrutiny and the search for the ideal method which is the safest, easiest, cheapest and optimally most effective is still going on.

Second trimester pregnancy termination can be carried out by both medical and surgical methods. Medical methods are comparatively



safer and have superseded the surgical methods because of risks involved in surgical methods.

The various drugs used for bringing about induction of abortion have undergone tremendous change. From instillation of intra-amniotic hypertonic saline, urea and then to extra-amniotic ethacridine lactate and now to prostaglandin analogues, the entire scenario is undergoing a metamorphosis.

The Prostaglandin analogue misoprostol introduced in the late 1970's was cheap and stable at room temperature. It has the ability of being administered by any route (Vaginal/Oral/Buccal/Sublingual). Hence Misoprostol is being extensively evaluated for being used in second trimester abortion.

The subsequent introduction of anti progestin ,mifepristone in 1980 has shortened the induction abortion interval and reduced the dosage of misoprostol required though the cost is high.

The present study was undertaken to evaluate the efficacy of Mifepristone and vaginal misoprostol combination with vaginal misoprostol alone in the termination of second trimester pregnancy.

## **REVIEW OF LITERATURE**

The unmet need of safe abortion among women with unwanted pregnancy continues to be a major obstetric challenge in the efforts to provide better health care to an increasing number of women currently subject to repeated unsafe abortions. The estimated maternal deaths directly due to consequences of unsafe abortions amounts to 300 - 500 per day<sup>1</sup>.

### **MTP ACT**

Medical termination of pregnancy (MTP) under supervision is an important way to reduce the mortality due to septic abortions. Although MTP has been legalised in India (MTP Act, 1971), the incidence of unsafe septic induced abortions has not decreased. Septic abortion is a significant health problem with short and long term complications that affect the quality of life. Both spontaneous and induced abortion can result in septic complications, with the latter disproportionately higher.

MTP Act was introduced with the aim of reducing these unsafe and subsequent septic abortions. The MTP Act was passed in the Indian parliament in 1971 and came into force in 1972.

## **THE LAW SPECIFIES**

### 1. Grounds for performing MTP:

- a. Medical
- b. Eugenic
- c. Humanitarian
- d. social

### 2. Persons who can perform MTP:

Only a registered medical practitioner having postgraduate training or qualification in obstetrics and gynaecology in a specialized and recognized training centre for MTP can perform the procedure.

### 3. Place where MTP can be performed:

MTP can be performed only in:

- a. A hospital established and maintained by the government.
- b. A place recognized and approved by the government under this act.

## **METHODS OF MEDICAL TERMINATION OF PREGNANCY**

### **(MTP):**

MTP can be performed either in the first or second trimester by either surgical or medical means. An ideal method would be one which is safe, quick, 100% effective, inexpensive and without any immediate or late side effects. Since no ideal method is available at present we have to choose a method that is effective with minimal side effects and complications.

### **FIRST TRIMESTER:**

The two modes of termination of first trimester pregnancy are medical and surgical<sup>2</sup>.

#### **MEDICAL**

- Mifepristone ,Misoprostol, Gemeprost

#### **SURGICAL**

- Menstrual regulation, Manual vacuum aspiration, Suction evacuation

## **SECOND TRIMESTER**

Termination of second trimester pregnancy can be done by either medical or surgical means. Majority are performed medically to reduce the incidence of complications associated with surgical methods like hemorrhage, Pelvic infections, uterine and cervical injuries.

### **MEDICAL**

#### ❖ INTRA AMNIOTIC INSTILLATION

Hypertonic solutions , 20% saline ,30% urea,  
15-methylPGF<sub>2</sub> α

Complications with hypertonic saline include hemorrhage, infection, hypernatremia and coagulation disorders. Hence, hypertonic saline is not used for induction of abortion in recent times<sup>3</sup>.

#### ❖ EXTRA AMNIOTIC INSTILLATION

Ethacridine lactate , PGF<sub>2</sub>α

#### ❖ SYSTEMIC

#### ❖ ORAL

Mifepristone, Misoprostol.

❖ INTRA MUSCULAR

PGF<sub>2</sub>α

❖ VAGINAL

Prostaglandins-PGE<sub>1</sub>, PGE<sub>2</sub>

❖ INTRAVENOUS

High dose oxytocin

❖ SURGICAL

Aspirotomy ,Hysterotomy ,Hysterectomy<sup>2</sup>

**DRUGS USED IN SECOND TRIMESTER PREGNANCY**

**TERMINATION: PROSTAGLANDINS:**

Prostaglandins, oxygenated metabolites Of C<sub>20</sub> carboxylic acid, are naturally found in most biological tissues where they act as modulators of cell function. They act through receptors of G-protein family that are coupled to a variety of intracellular signal mechanisms. Believing that the active principle originated in the prostate, von Euler coined the term PROSTAGLANDINS. Prostaglandins of E and F family can produce uterine contractions at any period of gestation.

## CHEMISTRY:

Prostaglandins are a family of polyunsaturated 20-carbon fatty acids containing a cyclopentane ring and two aliphatic side chains. Chemically they are derivatives of the hypothetical prostanoic acid. Prostaglandins are divided into groups (A, B, C, D, E, F, G, H, I) according to differences in the structure of the five membered cyclopentane ring<sup>4</sup>. Sune K Bergstrom, Bengt I Samuelsson and John R Vane jointly received Nobel Prize (1982) in Physiology or Medicine for their research on prostaglandins<sup>5</sup>.

## BIOSYNTHESIS<sup>5</sup>:

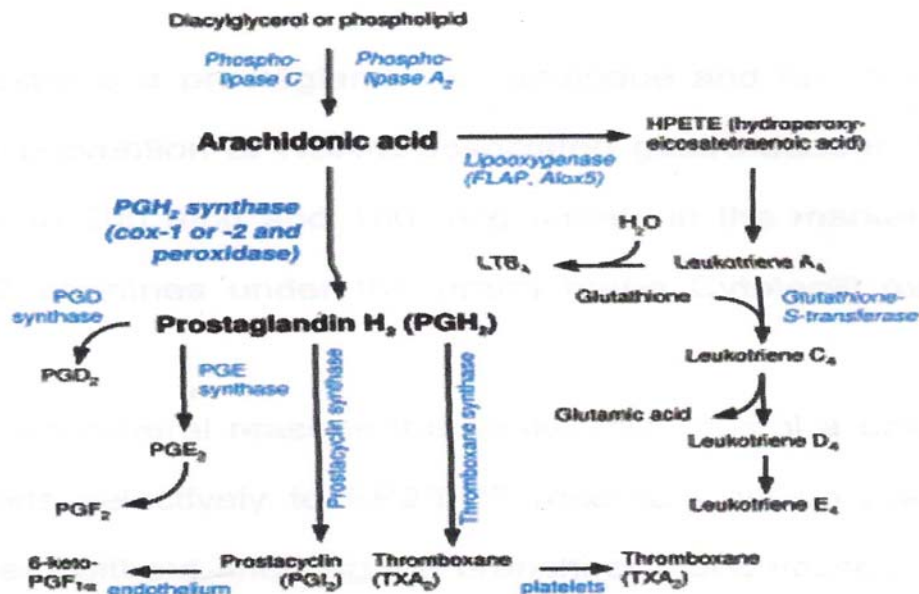


FIG 1: BIOSYNTHESIS OF PROSTAGLANDINS

Prostaglandins are derived from arachidonic acid present in membrane phospholipids. On its release from membrane phospholipids in response to cellular signals, arachidonic acid is acted upon by two types of enzymes -

- Cyclo-Oxygenase which leads to prostaglandin formation, which are compounds with ring structure.
- Lipo-Oxygenase which leads to leukotriene formation, which are compounds with open chain structure.

Natural prostaglandins are unstable compounds, lack specificity and are poorly tolerated. The advent of synthetic prostaglandins like misoprostol has greatly evaded these disadvantages.

## **MISOPROSTOL**

Misoprostol is a prostaglandin E<sub>1</sub> analogue and has been licensed for treatment and prevention of NSAID-associated gastro-duodenal ulcers. It has been available in 200 mcg and 100 mcg tablets in the market since 1985 in more than 87 countries under the trade name Cytotec® manufactured by SEARLE<sup>6</sup> (now Pfizer),but other brand name and Generic formulations are now available as well.



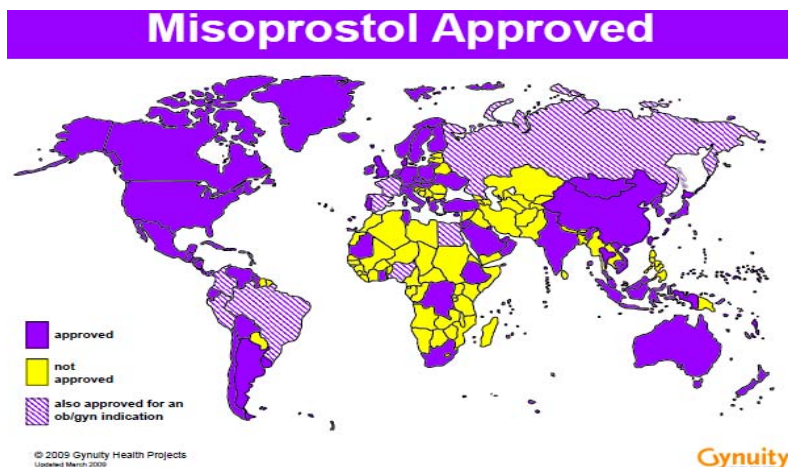
There are several reasons that make misoprostol a unique drug in the market. It binds selectively to EP2/EP3 receptors, which makes it a potent uterotonic agent without affecting the bronchi or blood vessels. This effect has made misoprostol very beneficial and a widely used drug for several indications within reproductive health such as postpartum hemorrhage, labour induction, missed abortion, intrauterine foetal death, induced abortion and cervical ripening prior to curettage. Prostaglandins like misoprostol have two important modes of action in the female reproductive system; they induce the ripening of the uterine cervix and stimulate uterine contractions.



**FIG 2: COMMERCIAL PREPARATION OF MISOPROSTOL**

Other advantages of misoprostol are that it is very cheap compared to other prostaglandins available in the market, it can be stored at room temperature for years, it can be administered orally, sublingually, rectally and vaginally and it has no severe side effects apart from those related to its uterotonic effects. All these attributes

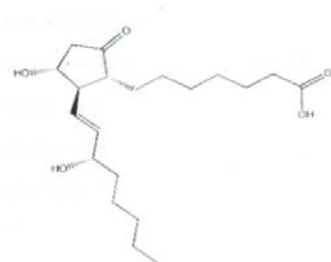
make misoprostol very suitable for use in settings with limited resources.



**FIG 3: AVAILABILITY & APPROVAL STATUS OF MISOPROSTOL WORLD WIDE**

## CHEMISTRY

Misoprostol is a 15-deoxy-16-hydroxy-16-methyl synthetic analog of prostaglandin E<sub>1</sub> and is a water soluble viscous gel. The commercial preparation usually contains inactive ingredients hydrogenated castor oil hydroxyl-propyl methyl cellulose, micro crystalline cellulose and sodium starch glycolate<sup>6</sup>



**FIG 4: STRUCTURE OF MISOPROSTOL**



**FIG 5 : STEREOTACTIC CONFIGURATION OF MISOPROSTOL**

## **PHARMACOKINETICS**

The half life of misoprostol is 20-40 minutes and plasma concentrations peak in approximately 30 minutes and decline rapidly thereafter. It is metabolized by the fatty acid oxidation processes that take place in numerous organs in the body, primarily the liver and less than 1 percent of its active metabolite is excreted in the urine. Misoprostol has no known drug interactions nor does it induce the hepatic cytochrome P-450 enzyme system.

After oral administration, misoprostol is rapidly absorbed and converted to its pharmacologically active metabolite misoprostol acid. The bioavailability of misoprostol is decreased by concomitant intake of food or antacids<sup>7</sup>.

## **ROUTES OF ADMINISTRATION**

Many studies comparing the efficacy of the different routes of administration of misoprostol have been carried out. There is still no consensus on what is the most effective route of administration or dosage. Most studied routes of administration are oral and vaginal. It was shown that the systemic bioavailability, measured as the Area Under Curve, was higher after vaginal misoprostol than after oral

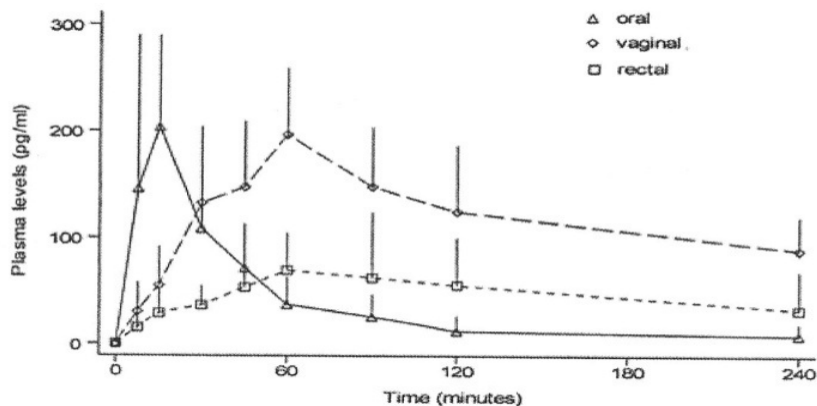
misoprostol. It is faster absorbed orally than vaginally with higher peak serum level, but vaginally absorbed levels are more prolonged.

Since misoprostol is only approved for oral administration and most women prefer to take the tablets orally, this route of administration seems to be the most convenient but high doses have a greater risk of causing uterine hyperstimulation. Vaginal use of lower doses seems to be associated with less uterine hyperstimulation, less side effects and a higher efficacy rate in inducing medical abortion.

There have also been recent studies on buccal administration of misoprostol where it was found to be effective for cervical ripening in labour induction but also resulted in a higher incidence of tachysystole compared to the intravaginal route of administration<sup>7</sup>.

(Error bars represent 1 standard deviation.)

**FIG6: MEAN PLASMA CONCENTRATIONS OF MISOPROSTOL ACID OVER TIME WITH ORAL, RECTAL, AND VAGINAL ADMINISTRATION**



## **ADVERSE REACTIONS**

The most common adverse effects of misoprostol are nausea, vomiting, diarrhoea, abdominal pain, chills, shivering and fever all of which are dose dependent<sup>7</sup>. Both PGE<sub>2</sub> and PGF<sub>2</sub>α can cause myocardial infarction and bronchospasm but this has not been observed with misoprostol.

## **TERATOGENICITY**

Mobius syndrome (congenital facial palsy) and limb defects have occurred in infants of women who have taken misoprostol in the first trimester in an unsuccessful attempt to induce abortion. There was also an increased incidence of transverse limb defects, ring shaped constrictions of extremities, arthrogyrosis, hydrocephalus, holoprosencephaly and exstrophy of bladder<sup>7</sup>.

## **USES IN OBSTETRICS**

### **MISOPROSTOL IN FIRST TRIMESTER**

#### **1. Medical Abortion**

For first trimester abortions, misoprostol is used extensively with either mifepristone or methotrexate.

2. For cervical ripening before surgical abortion.

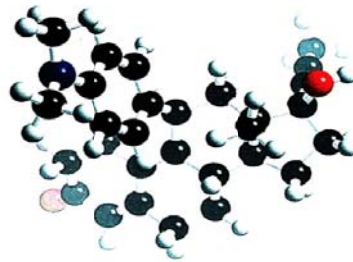
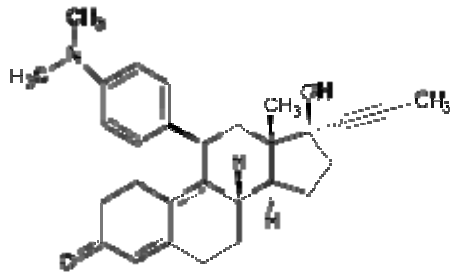
3. Failed pregnancy.

4. Inevitable or incomplete abortion.

#### **OTHER USES:**

- Second trimester for induction of abortion.
- third trimester for induction of labour.
- as second line drug for control of post partum hemorrhage.

#### **MIFEPRISTONE**



**FIG 7: STRUCTURE OF MIFEPRISTONE**

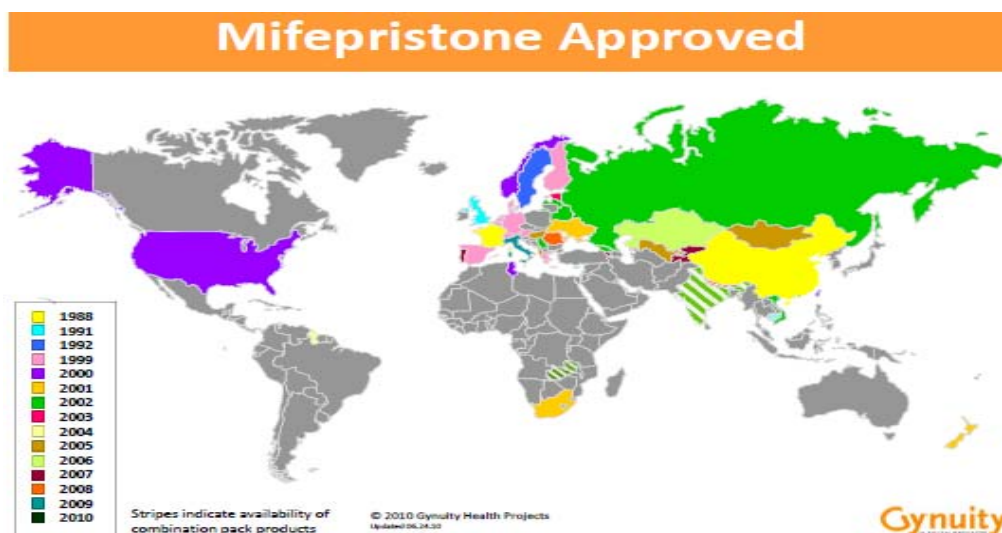
**FIG 8: STEREOTACTIC  
CONFIGURATION OF  
MIFEPRISTONE**

Mifepristone is a synthetic steroid compound used as a pharmaceutical abortifacient. It is used as an abortifacient in the first two months of pregnancy, and in smaller doses as an emergency contraceptive. During early trials it was known as RU-486, its designation at the Roussel Uclaf company, which designed the drug. The drug was initially made available in France and other countries then followed often amid controversy. In France and countries other than the United States it is marketed and distributed by Exeigyn Laboratories under the tradename Mifegyne. In the United States it is sold by Danco Laboratories under the tradename Mifeprex. (The drug is still commonly referred to as "RU-486")<sup>5</sup>.

#### **FIG-9 COMMERCIAL PREPARATION OF MIFEPRESTONE**



**FIG 10 MIFEPRESTONE AVAILABILITY**



## PHARMACOLOGY

Mifepristone is a 19-nor steroid with a bulky *p*-dimethylamino phenyl substituent above the plane of the molecule at the 11  $\beta$  position responsible for inducing or stabilizing an inactive receptor conformation and a hydrophobic 1propynyl substituent above the plane of the molecule at the 17 $\alpha$ -position that increases its progesterone receptor binding affinity. In the presence of progesterone, mifepristone acts as a competitive receptor antagonist at the progesterone receptor (in the absence of progesterone, mifepristone acts as a partial agonist).

In addition to being an antiprogestogen, mifepristone is also an antiglucocorticoid and a weak antiandrogen. Mifepristone's relative



binding affinity at the progesterone receptor is more than twice that of progesterone. Its relative binding affinity at the glucocorticoid receptor is three times more than that of dexamethasone and ten times more than that of cortisol, its relative binding affinity at the androgen receptor is less than one third that of testosterone. It does not bind to the oestrogen or mineralocorticoid receptors.

Mifepristone as a regular contraceptive at 2 mg daily prevents ovulation (11 mg daily does not). A single preovulatory 10 mg dose of mifepristone delays ovulation by 3 to 4 days and an emergency contraceptive as a single 1.5 mg dose of the progestin levonorgestrel. In women, mifepristone at doses greater or equal to 1 mg/kg antagonizes the endometrial and myometrial effects of progesterone. In humans, an antiglucocorticoid effect of mifepristone is manifested at doses greater than or equal to 4.5 mg/kg by a compensatory increase in ACTH and cortisol. In animals, a weak antiandrogenic effect is seen with prolonged administration of very high doses of 10 to 100 mg/kg.

In medical abortion regimens, mifepristone blockade of progesterone receptors directly causes endometrial decidual degeneration, cervical softening and dilatation, release of endogenous prostaglandins and an increase in the sensitivity of the myometrium to

the contractile effects of prostaglandins. Indeed mifepristone administration gradually elicits a 5 fold increase in sensitivity to PG 24-48 hrs after its administration.

In women undergoing 2<sup>nd</sup> trimester abortion, a single 100 mg oral dose produced fetal cord blood concentrations of mifepristone ranging from 20 ng/ml {30 minutes} to 400 ng/ml {18 hours}. The peak maternal concentration {1500 ng/ml} was attained in 12 hours and the average fetal : maternal ratio was approximately 0.33. An active transport mechanism was suggested because of the fetal concentration increase exponentially<sup>8</sup>.

When followed sequentially by a prostaglandin, mifepristone in a dose of 200 mg is as effective as 600 mg in producing a medical abortion<sup>9,10</sup>.

### **PHARMACOKINETICS :**

The half life of mifepristone is 18 hrs. Bio availability is 64%. It is metabolized in liver and mainly excreted through feces (83%) and renal(9%).

**Adverse Effects :**

Neonatal exposure to a single large dose of mifepristone in rats were not associated with any reproductive problems, although chronic low-dose exposure of newborn rats to mifepristone was associated with structural and functional reproductive abnormalities.

Teratology studies in mice, rats and rabbits revealed teratogenicity for rabbits, but not rats or mice. The rate of birth defects in human infants exposed in utero to mifepristone and misoprostol is very low, and may be due to misoprostol alone.

**CONTRAINDICATIONS :**

In the presence of an intrauterine device (IUD) ,Ectopic pregnancy, Adrenal failure, Hemorrhagic disorders, Inherited porphriya, and Anticoagulant or long-term corticosteroid therapy.

**OTHER USES**

Regular long term use as an oral contraceptive, and treatment of: Uterine fibroids, endometriosis, major depression with psychotic features, glaucoma, meningiomas, breast cancer, ovarian cancer, prostate cancer, and some types of Cushing's syndrome.

## VARIOUS STUDIES OF MISOPROSTOL

### *Route of Administration:*

#### **Vaginal versus Oral:**

**Bebbington et al<sup>11</sup>** compared two protocols for the use of misoprostol in mid trimester pregnancy termination - oral vs vaginal ,14 women were included in the study. They were randomly assigned to receive misoprostol 200 mcg vaginally every hour for three hours followed by 400 mcg every four hours orally or vaginally. Induction to abortion interval was significantly shorter in the vaginal group (14.5 hours) than in the oral group (19.6 hours). Febrile morbidity was higher in the vaginal group (25%) vs oral group (6.7%) but this subsided without any specific treatment.

#### **Sublingual versus Vaginal:**

**Tang et al<sup>12</sup>** compared sublingual or vaginal misoprostol 400 mcg every three hours for a maximum of five doses in second trimester abortion. They concluded that the use of vaginal misoprostol resulted in a higher success rate of 85% than sublingual misoprostol of 64% at 24 hours but the abortion rates were similar at 48 hours.

### **Sublingual versus Oral versus Vaginal:**

A study by **Aronsson et al**<sup>13</sup> (2004) reported on the effect of misoprostol on uterine contractility following different routes of administration (sublingual, vaginal and oral). The study showed that the increase in uterine activity 24h after administration and thereafter was similar for both the sublingual and vaginal groups. These findings suggest that sublingual administration results in a more rapid effect on uterine contractility and may explain the higher requirement for intramuscular opiates.

### **Interval of Administration**

**Jain et al**<sup>14</sup> randomized One hundred pregnant women between 12-22 weeks gestation to receive 200 mcg of misoprostol intravaginally either every 6hrs or every 12 hrs for up to 48 hours. The incidences of abortion within 48 hours after initial drug administration were 87.2% and 89.2% , the mean abortion intervals 13.8 hrs and 14.0 hrs in the 6hrs and 12hrs group respectively. Side effects were similar between the two groups. They concluded that misoprostol administered vaginally is effective for terminating second-trimester pregnancies and that

shortening the dosing interval from 12 to 6 hours produced no significant benefit.

### **Comparison of dosage /Dosage Administration**

**Herabutya et al<sup>15</sup>** randomized One hundred and forty three pregnant women between 14-26 weeks gestation into 2 groups to receive either 600mcg or 800mcg of intravaginal misoprostol every 12 hours until abortion was induced The incidences of abortion within 24 hours after initial drug administration were 82.1% and 78.9%, within 48 hours 92.5% and 92.1% , the mean abortion intervals were 15.2 hours and 15.3 hours, the complete abortion rates 77.6% and 72.4% , and body temperature of more than 38<sup>0</sup> C was noted in 26.9% and 71.1% ( p < 0.001) in the 600 and 800 mcg group, respectively. All other side-effects were similar between the two groups. They concluded that considering the effectiveness and febrile complications, 600 mcg applied every 12 hours is the most appropriate dose for second trimester termination.

**Ramsey et al<sup>16</sup>** evaluated the cardiovascular effects of high dose vaginal misoprostol 600 mcg by trans thoracic electrical bioimpedance monitoring concluded that high dose vaginal misoprostol does not alter

maternal cardiac function but further clinical data is needed to validate these findings in view of small sample size.

In a study on **Ramin KD, Ogburn PL, Danilenko DR, Ramsey PS<sup>17</sup>** reviewed the experience with high-dose oral misoprostol for mid-trimester pregnancy interruption. Patients received 400 mcg misoprostol orally every 4 h. Women undelivered within 24 h were considered failures and were treated with high-dose oxytocin. For comparison, a group of women treated with high-dose oxytocin were evaluated.

Induction-to-delivery interval was significantly shorter in the misoprostol cohort (15.2 hrs) compared with those treated with oxytocin (21.7 hrs). Misoprostol group delivered within 24 h (91.0%) compared with the oxytocin group (62.0%;  $p = 0.04$ ). Adverse outcomes and side effects were not significantly different between the study groups.

High-dose oral misoprostol is more effective than concentrated oxytocin infusion for mid-trimester pregnancy interruption.

### **Comparison of Misoprostol with other methods**

In a study by **Chauduri et al<sup>18</sup>** compared extraamniotic instillation of ethacridine lactate with vaginal misoprostol in second trimester abortion.

The mean interval from induction to abortion was shorter in misoprostol group (15.5 hrs vs 31.3 hrs). The rate of complete abortion was 66.6% for misoprostol and 70% for ethacridine lactate. Side effects were uncommon and did not differ between the two groups. They concluded that the success rates of misoprostol and ethacridine lactate were comparable but the induction abortion interval was almost half in misoprostol group when compared with that in ethacridine lactate group.

**Yapar et al<sup>19</sup>** compared the efficacy of five different methods for second trimester pregnancy termination between 14 and 28 weeks gestation. Three hundred and forty patients with poor cervical condition (Bishop score : < 4) were subjected to one of five termination methods were subsequently assessed: (i) extra amniotic administration of ethacridine lactate (82 patients) (ii) intracervical prostaglandin PGE<sub>2</sub> gel (100 patients) (iii) intravenous infusion of concentrated oxytocin (36 patients) (iv) vaginal misoprostol (49 patients) and (v) balloon insertion (73 patients). They concluded that in comparison with the five methods, the use of extraamniotic ethacridine, intravenous concentrated oxytocin, and balloon was found to provide more effective treatment than intracervical PGE<sub>2</sub> and misoprostol in terms of achievement of abortion within 24 and 48 h.



In a study by **Jain et al**<sup>20</sup>, 55 women were studied to compare the efficacies of PGE<sub>1</sub> and PGE<sub>2</sub> in inducing second trimester abortion. Misoprostol was administered at a dose of 200 mcg every 12 hourly while 20 mg PGE<sub>2</sub> was administered every three hours and concluded that misoprostol is as effective as PGE<sub>2</sub> for the termination of second trimester pregnancy but it is less costly, easier to administer and is associated with fewer side effects.

In a study by **Blumenthal et al**<sup>21</sup>, misoprostol application was compared with PGE<sub>2</sub> and it was concluded that misoprostol was effective in achieving mid trimester abortion, had comparable induction abortion interval, low incidence of side effects and cost savings over PGE<sub>2</sub>.

**Nuutila et al**<sup>22</sup> compared two doses of intravaginal misoprostol and gemeprost for induction of second trimester abortion. Eighty one patients were recruited and were randomized to receive either 100 mcg every 6 hours, 200 mcg every 12 hours or gemeprost every 3 hours. I – A interval were respectively 23.1 hrs 27.8 hrs and 14.5 hrs.

**Ho et al**<sup>23</sup> studied the effect of vaginal vs oral misoprostol in terminating second trimester pregnancy after pretreatment with

mifepristone. Thirty six hours after 200 mg of oral mifepristone, women were given oral or vaginal misoprostol 200 mcg every three hours for a maximum of five doses. I-A interval, misoprostol required were reduced and success rate increased in vaginal group and maximum dose of Misoprostol used in vaginal group was 600mcg and in oral group was 1000mcg.

**Eng et al**<sup>24</sup> compared the efficacy of vaginal misoprostol and gemeprost in inducing second trimester abortion. Fifty patients participated in the study and the misoprostol group received 200 mcg every three hours upto a maximum dose of 1200 mcg. Gemeprost group received 1 mg of the same three hourly upto a maximum dose of 5 mg. They found that majority of patients in misoprostol group aborted between 7 to 12 hours whereas majority of patients in gemeprost group aborted in the first six hours after induction.

They concluded that intravaginal misoprostol was at least as effective as gemeprost as an abortifacient in second trimester pregnancy with intrauterine death but it was less costly, did not require refrigeration and was associated with lesser side effects.

In a study by **Akoury et al**<sup>25</sup>, the efficacy, outcome and acceptability of oral misoprostol, vaginal misoprostol and intra amniotic PGF<sub>2α</sub>. (IAPG) were compared in second trimester abortion. Their results were that the oral misoprostol group had significantly longer delivery time (29 hours) than vaginal misoprostol group (16 hours) and IAPG (18 hours). Women in the vaginal misoprostol group were most satisfied with the procedure and had fewer side effects than the other two groups. Failure rates for umbilical cord cultures were maximum for IAPG.

**Dickinson et al**<sup>26</sup> conducted a prospective randomized, double-blind, controlled clinical trial in 100 women between 14 and 28 weeks gestation using either:

- 1 mg gemeprost 3 hourly for 5 doses or
- 200 mcg vaginal misoprostol 6 hourly for 4 doses.

Delivery within 24 hours occurred in 75.1 % of women receiving gemeprost and 74.9% receiving misoprostol (NS). They concluded that intravaginal misoprostol performs as effectively as gemeprost in achieving delivery in the second trimester without an increase in adverse effects and displaying a significant cost advantage.

In a study by **Biswas et al**<sup>27</sup> in group 1, 600 mcg misoprostol was given vaginally followed by 400 mcg 8 hourly upto a maximum of 48 hours. In group 2, 150 ml of ethacridine was instilled extra amniotically.

They found that mean induction abortion interval in group 1 was 13.94 hrs and in group 2 it was 28.86 hrs ( $p < 0.0001$ ). Complications were noted in 32% women in group I and 44% in group 2.

Vaginal administration of misoprostol appears to be effective and well tolerated with less side effects and no complications and was cheaper.

The evidence based regimen of the **Royal College of Obstetrics and Gynecology{RCOG}** is 400 mcg of Vaginal misoprostal every 3 hours up to 5 doses in pregnancy between 13-22 weeks<sup>28</sup>.

### **Prior uterine scar / Prior Cesarean**

Increasing rates of cesarean delivery mean that more women with a history of uterine scarring will confront second trimester induction. Although the absolute risk of uterine rupture during second-trimester induction is unknown, most studies suggest that misoprostol can safely be used in postcesarean pregnancies.<sup>30,31,32</sup>

Case reports describe uterine rupture among women with and without prior uterine scars undergoing PG induction throughout a wide range of gestational ages<sup>33</sup> between 15 and 35 weeks, prior cesarean section did not increase the risk of hemorrhage (2% vs 0.9%; P=.56) or the median induction-abortion interval (8.5 vs 9.0 hours; P=.26). 1 case of uterine dehiscence were noted, both in women with prior cesarean section and women without uterine scar. Conversely, a series reported by **Daskalakis et al**<sup>34</sup> of 108 women with prior cesarean undergoing second-trimester misoprostol induction reported only 1 case of uterine rupture but it occurred in 1 of the 216 nonscarred control subjects. Because rates of rupture may increase with advancing gestational age some author's have advocated avoiding its use in the third trimester.<sup>35</sup>

## **VARIOUS STUDIES OF MIFEPRISTONE**

### ***Dosage of Administration***

In a randomized study by **Webster D, Penney GC, Templeton A**<sup>9</sup>, The intervention is administration of either 600mg or 200mg mifepristone 36 to 48 hours prior to prostaglandin.

The geometric mean induction abortion interval was 6.9h and 6.9h in the 600mg and 200mg groups, respectively (no significant

difference). The median dose of misoprostol was 1600 micrograms in each group.

As with first-trimester abortion, randomized studies consistently indicated 200 mg of mifepristone is equally effective as 600 mg for termination of pregnancy in the second trimester.<sup>9,10</sup>

### **INTERVAL BETWEEN MIFEPRISTONE AND MISOPROSTOL**

When the interval between mifepristone and misoprostol administration was reduced to 24 hours, the induction-to-abortion interval was somewhat longer than after a 48-hour interval. In a retrospective study, time to fetal expulsion was 9.8 hours in the 24-hour interval group compared with 7.5 hours when the interval was 48 hours ( $P < .01$ ), and in a randomized study it was 7.3 vs 6.2 hours ( $P < .05$ ), respectively.<sup>36-37</sup> This latter study also reported a higher rate of uterine curettage with the 24-hour interval ( $P < .001$ ).

In this study by **D.R. Urquhart and A.A. Templeton**<sup>38</sup>, mifepristone (600 mg) was administered 24, 36 and 48 h prior to extra-amniotic infusion of prostaglandin. No bleeding was observed prior to prostaglandin infusion in any of the groups and it is suggested that

mifepristone could be administered safely prior to hospital admission for termination.

### **Mifepristone with misoprostol studies:**

In this randomized study by **Suk Wai Ngai, Oi Shan Tang and Pak Chung Ho**<sup>39</sup>, the hypothesis that oral misoprostol 400 µg is as effective as vaginal misoprostol 200 µg when given every 3 h in termination of second trimester pregnancy after priming with mifepristone was tested.

For the oral group, both the incidence of diarrhoea (40% versus 23.2%,  $P = 0.03$ ) and the amount of drug used (1734 compared with 812 µg,  $P < 0.0001$ ) were significantly higher than that of the vaginal group but the incidence of fever appeared to be lower (not significant).

There was no significant difference in complete abortion rate: 81.4% in the oral group and 75.4% in the vaginal group. The median induction–abortion interval was similar in the two groups (10.4 versus 10.0 h). Overall, 82.0% of women preferred the oral route. Oral misoprostol (400 µg) given every 3 h up to five doses, when combined with mifepristone, was as effective as the vaginal (200 µg) route in second trimester termination of pregnancy. This regimen could also be

offered to those women who found repeated vaginal administration unacceptable. There are several advantages in using the oral route like (i) It is more convenient to administer; (ii) It is preferred by the majority of women & (iii) Misoprostol is manufactured for administration by the oral route.

In the study by **El-Refaey *et al***<sup>40</sup>(1995), women were pretreated with 600 mg oral mifepristone. After 36–48 h, they were randomized to group 1: vaginal misoprostol 600 µg followed by vaginal misoprostol 400 µg given at a 3 h interval; group 2: vaginal misoprostol 600 µg followed by oral misoprostol 400 µg doses given at a 3 h interval of four doses. They achieved an overall successful abortion rate of 97% and a mean induction to abortion time of 6.4 h (95% confidence interval 5.6–7.0 h).

**Ashok *et al.***<sup>41</sup> (1999) reviewed 500 women who underwent second trimester termination of pregnancy. Women were given a single oral dose of mifepristone 200 mg and 36–48 h later, vaginal misoprostol 800 µg. Three hours following the first dose of misoprostol, 400 µg doses were administered orally at 3 h intervals, to a maximum of four doses, and 97% aborted successfully. The median induction-to-abortion interval after the first prostaglandin administration was 6.5 h. It seems



that the first dose of misoprostol, when it is given vaginally at high dose, is important in reducing the induction–abortion interval.

In a study by **Haitham Hamodal, Premila W. Ashok, Gillian .M. Flett and Allan Templeton**<sup>42</sup> Mifepristone (200 mg) was followed 36–48 h later by sublingual administration of oral misoprostol 600 µg or vaginal misoprostol 800 µg. This was followed by 3 hourly doses of misoprostol 400 µg administered sublingually or vaginally.

Sublingual administration of misoprostol following mifepristone is an acceptable and effective alternative to vaginal administration for medical abortion at 13–20 weeks gestation.

A retrospective audit by **Rose SB, Shand C, Simmons A**<sup>43</sup> shows prospectively collected notes for 272 women presenting for mid-trimester termination of pregnancy by Mifepristone with vaginal misoprostol.

The median time to abortion was 6 hrs, and mean number of doses of misoprostol was three. The proportion of women who aborted within 24 hrs was 95.9%. Immediate surgical evacuation of retained

placenta was required in 22 women (8.1%). Heavy bleeding occurred in 22 women (8.1%), and seven required a transfusion (2.6%). The proportion of women who required parenteral narcotics was 78.2%.

Our experience supports the finding that the use of mifepristone as pretreatment to misoprostol results in a shorter induction-to-delivery interval than the use of misoprostol alone as has been reported by other groups.

A retrospective analysis was carried out by **Sin Ee Goh, Kok Joo Thong**<sup>44</sup> of 386 women who underwent termination of pregnancy between 12 and 24 weeks gestation. Each woman received 200 mg mifepristone orally followed by vaginal misoprostol 800 µg 36 to 48 h later. Three hours after the initial misoprostol administration, 400mcg doses of vaginal misoprostol were administered every 3 h, to a maximum of four doses in 24 h. If abortion failed, 200 mg mifepristone is given again 3 h after the last misoprostol dose, followed by 12 h of rest before vaginal misoprostol administration is repeated as per previous course of treatment.

Overall, 97.9% and 99.5% of the women aborted within 24 and 36 h, respectively. The median induction-to-abortion interval was 6.7 h

(range: 1.4–73.8 h), and nulliparous women took significantly longer time to abort (6.0 h in multiparous women compared to 7.6 h in nulliparous women;  $p < .0001$ ). One woman failed to abort within 48 h. Surgical evacuation of the uterus was performed in 5% of women for incomplete abortion or retained placenta. Multiparous women were less likely to need analgesic administration for pain relief, and to experience vomiting and diarrhea, than nulliparous women.

**Kapp N, Borgatta L, Stubblefield P, Vragovic O, Moreno N.<sup>45</sup>**

did a randomized, placebo-controlled, double-blind trial of mifepristone in second-trimester induction termination using misoprostol after fetocidal digoxin. Women seeking abortion between 18 and 23 weeks of gestation were offered enrollment.

Of 64 women, 32 received mifepristone and 32 received placebo. Median procedure time was significantly shorter for those who received mifepristone, 10 hours (95% confidence interval [CI] 8-12), than those who did not, 18 hours (95% CI 15-22),  $P < .01$ , and those parous, 10 hours (95% CI 9-14), compared with nulliparous, 16 hours (95% CI 12-22,  $P = .02$ ). Other findings in the mifepristone compared with placebo group included rates of placental retention, 3.1% compared with 6.3% ( $P = .61$ ), length of hospitalization, 0.66 days compared with 0.8 days

( $P=.23$ ), and analgesic requirements, 27.2 mg compared with 39.3 mg morphine ( $P=.22$ ). Side effects during induction were similar between groups.

Addition of mifepristone in second-trimester termination inductions using misoprostol significantly reduces the abortion time interval.

**DICKINSON, J. E., BROWNELL, P., MCGINNIS, K. and NATHAN, E. A.** <sup>46</sup> (2010), did a study in 388 women with prenatally recognised fetal anomalies between 14 and 24 weeks gestation underwent medical termination: 189 with misoprostol alone and 199 with mifepristone priming followed by misoprostol. The median abortion duration was 15.5h in the misoprostol group and 8.6 h in the mifepristone primed group ( $P < 0.001$ ). In both the groups, nulliparity and advancing gestation were associated with a significant prolongation of the abortion interval.

In a ongoing study by **Gynuity health projects**<sup>47</sup>, Mifepristone Plus buccal Misoprostol Versus buccal Misoprostol Alone for 2nd Trimester Abortion (14 - 21 Weeks) were studied. This study is currently recruiting participants.

Mifepristone 200 mg orally → 36 hours later: Misoprostol 800mcg vaginally → 3 hours later: Misoprostol 400mcg (buccal) every 3 hours until delivery or a maximum of 5 doses in 24 hours or 10 doses in 48 hours. In the misoprostol alone group, the same protocol was used without Mifepristone. Placebo was used instead.

In the study of **Hammond recent advances** in second trimester abortion<sup>48</sup>, the recommended regimen of **Royal College of Obstetricians and Gynecologists** was given below:

Day One: Mifepristone 200 mg orally → 36-48 hours later: Misoprostol 800mcg vaginally → 3 hours later: Misoprostol 400mcg orally or vaginally every 3 hours until delivery or total of 4 doses. → If undelivered 3 hours after 4<sup>th</sup> dose: Repeat Mifepristone 200 mg and resume induction next day or consider surgical abortion.

In the study of **Bartley and Baird**<sup>49</sup> 200mg Mifepristone 36-48 hrs prior administration of 800mcg misoprostol vaginally followed by 400 mcg oral misoprostol every 3 hrs of 4 doses. I-A interval was 6.1 hrs and success rate was 94% in 24 hrs.

In the study of **Ngai et al**,<sup>50</sup> 200mg Mifepristone 36-48 hrs prior administration of 400mcg misoprostol orally at 3hrs interval of 5 doses and success rate was 81.4% in 24 hrs and induction abortion interval was 10.4hrs and mean misoprostol dose was 1200mcg.

## **AIMS AND OBJECTIVES**

- ❖ To compare the abortifacient efficacy of vaginal misoprostol with mifepristone and vaginal misoprostol alone in second trimester pregnancy termination.
- ❖ To compare the induction -abortion intervals.
- ❖ To compare side effects and complications.
- ❖ To compare the Cost effectiveness.
- ❖ To identify the suitable method for second trimester MTP by comparing the various parameters.

## **MATERIALS AND METHODS**

This study comparing the efficacy of mifepristone – vaginal misoprostol combination with vaginal misoprostol alone as a method of second trimester abortion conduct at Institute of obstetrics and Gynaecology, Chennai – 08 during October 2009 – October 2010.

**Study design:** Prospective randomized comparative study.

**Study Place :** Institute of obstetrics and Gynaecology, Chennai-8.

**Collaborating Unit :** Department of family welfare, IOG.

Study Population : Patients requesting abortion in their second trimester at Department of family welfare, IOG and patients requiring abortion at second trimester at IOG, Egmore.

Period of Study : OCT2009 – OCT2010.

Sample Size: 100 (Random allocation to either group),  
50 – mifepristone + vaginal misoprostol group,  
50 – vaginal misoprostol group

**Inclusion Criteria:**

- ❖ 14 – 20 weeks gestation, Woman full filling the MTP indicators as per the MTP act ,Single live fetus, Present with closed cervical os, No vaginal bleeding and Patients consenting to this procedure only.

**Exclusion Criteria :**

- ❖ History of previous uterine surgery (but not a contraindication), Known allergy / Contraindications to mifepristone (or misoprostol / prostaglandin), Multiple fetus, Intra uterine fetal demise, Presentation in active labour, Low lying placenta.

**METHODOLOGY:**

Mifepristone – misoprostol group:

Dosage schedule:

Day I: 200mg mifepristone was given orally and pt observed in ward itself, after 36 hrs Pt shifted to labour ward and misoprotol 800mcg administered vaginally  $\implies$  3 hrs Later Misoprostol 400 mcg vaginally every 3 hrs Until delivery (or total of 4 doses). If undelivered



3 hrs after 4<sup>th</sup> dose repeat mifepristone 200mg and resume induction next day or consider surgical abortion

**Misoprostol group:**

Patient was asked to empty the bladder and was asked to lie down in the dorsal position with knee semiflexed and hip abducted.

800mcg misoprostol moistened with saline inserted in posterior vaginal fornix , 3hrs later misoprostol 400mcg vaginally every 3hrs until delivery or total of 4 doses.

Additional measures were adopted in patients with incomplete abortion like instrumental evacuation, oxytocin infusion.

In patients who failed to expel at the end of 48hrs further management was determined by the unit policy.

Check USG done next day after expulsion to exclude retained products. If determined products present further management done .

**OUTCOME**

COMPLETE: When both placenta and fetus were expelled in 48 hours.

INCOMPLETE: When either placenta or fetus was retained.

FAILED: Neither fetus nor placenta was expelled.

**PARAMETERS STUDIED:**

1. Induction - Abortion Interval ,Complete abortion rate, Success rate ,

Side Effect Profile

Vomiting , Diarrhoea, Fever, Headache, Rigor, Hemorrhage,

Infection

3. Total Number of Misoprostol Doses Required

4. Need For Additional Procedures Like Curettage , Misoprostol or

Oxytocin

5. Requirement Of Transfusion

6. Cost in both groups

Data was analyzed using SPSS software using ANOVA, Independent sample test and Chi-Square test and significant p-value being less than 0.05.

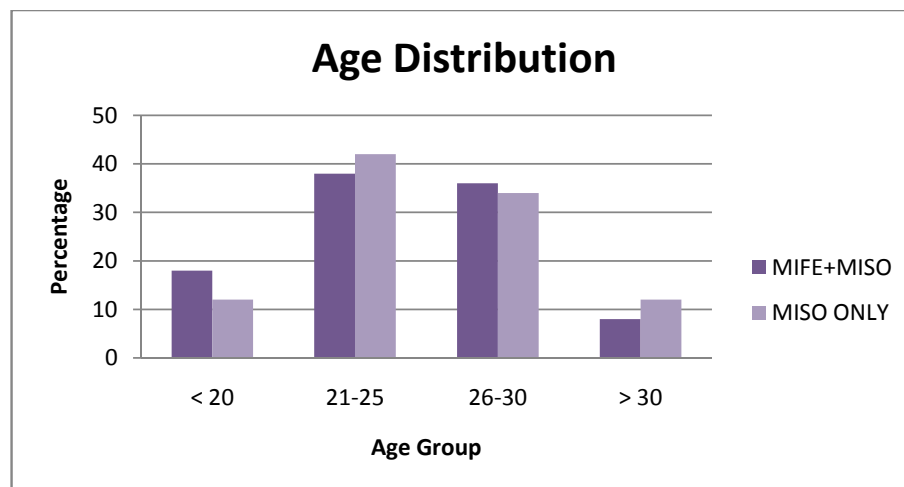
## OBSERVATIONS

### PATIENT CHARACTERISTICS: AGE DISTRIBUTION

**TABLE 1: AGE DISTRIBUTION**

Age Group {Years}	Mife+Miso n=50		miso only n=50		total	
	N	%	N	%	N	%
<20	9	18.0%	6	12.0%	15	15.0%
21-25	19	38.0%	21	42.0%	40	40.0%
26-30	18	36.0%	17	34.0%	35	35.0%
> 30	4	8.0%	6	12.0%	10	10.0%
<b>Total</b>	<b>50</b>	<b>100%</b>	<b>50</b>	<b>100.0%</b>	<b>100</b>	<b>100.0%</b>
<b>Mean Age in years</b>	<b>24.9400</b>		<b>25.1000</b>			
<b>SD</b>	<b>4.03763</b>		<b>4.22939</b>			

Age distribution was similar in both groups . Majority of patients in either group were in the age group of 21-25 years.

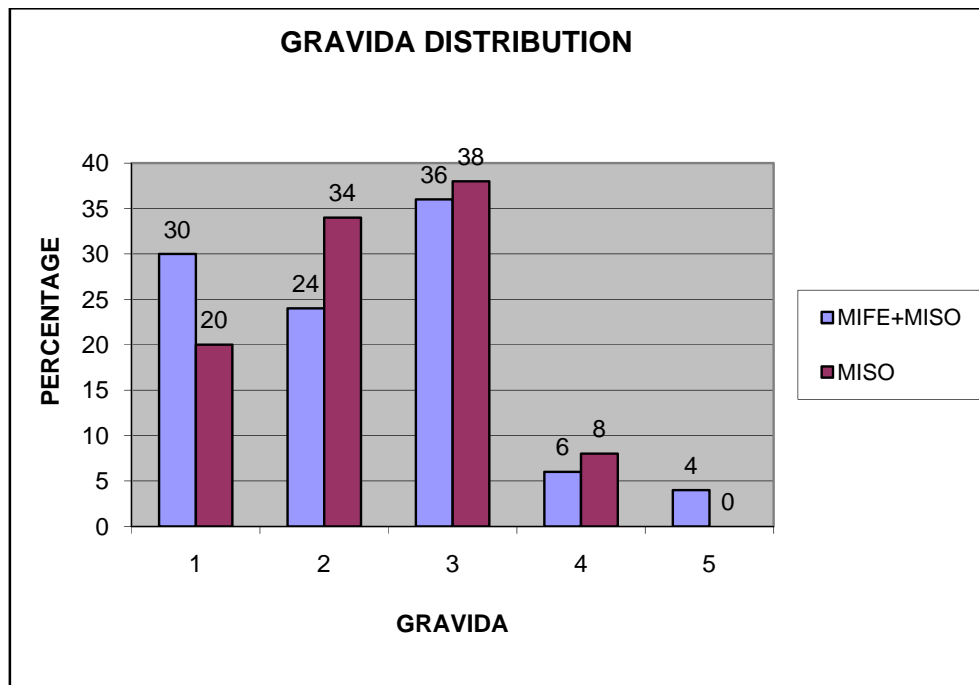


## GRAVIDA

**TABLE 2: GRAVIDA**

Gravida	Mife+miso N=50		Miso only N=50		Total	
	N	%	N	%	N	%
1	15	30%	10	20%	25	25%
2	12	24%	17	34%	29	29%
3	18	36%	19	38%	37	37%
4	3	6%	4	8%	7	7%
5	2	4%	0	0%	2	2%
<b>Total</b>	<b>50</b>	<b>100%</b>	<b>50</b>	<b>100.0%</b>	<b>100</b>	<b>100.0%</b>

Forty Six Percent of patients in both group was gravida Three and above.

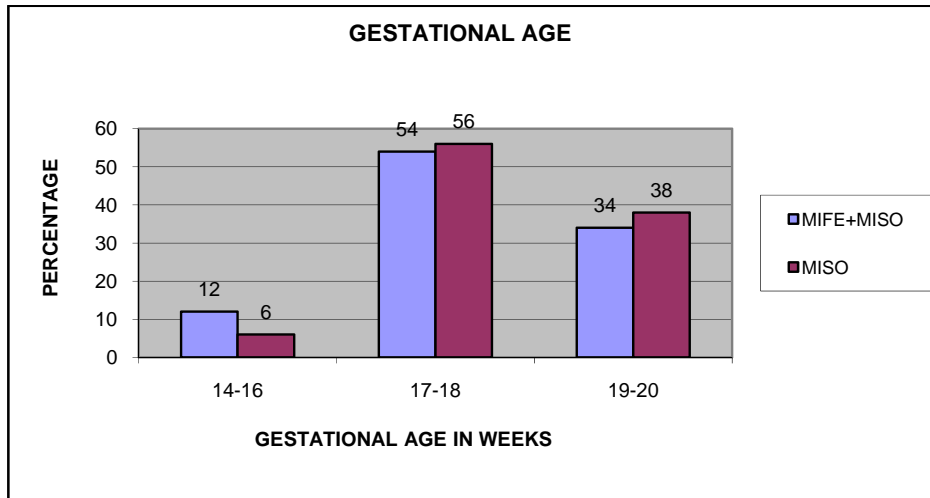


## GESTATIONAL AGE AT TIME OF TERMINATION

**TABLE 3: GESTATIONAL AGE GROUP**

GA {weeks}	Mife+miso N=50		Miso only N=50		Total	
	N	%	N	%	N	%
14-16 week	6	12%	3	6%	9	9%
17 -18 week	27	54%	28	56%	55	55%
19-20 week	17	34	19	38%	36%	36%
Total	50	100%	50	100%	100	100%
Mean	18.08		18.44			
pvalue	0.159					

Most of the pregnancies were terminated in 17 to 18 weeks of gestation in both groups



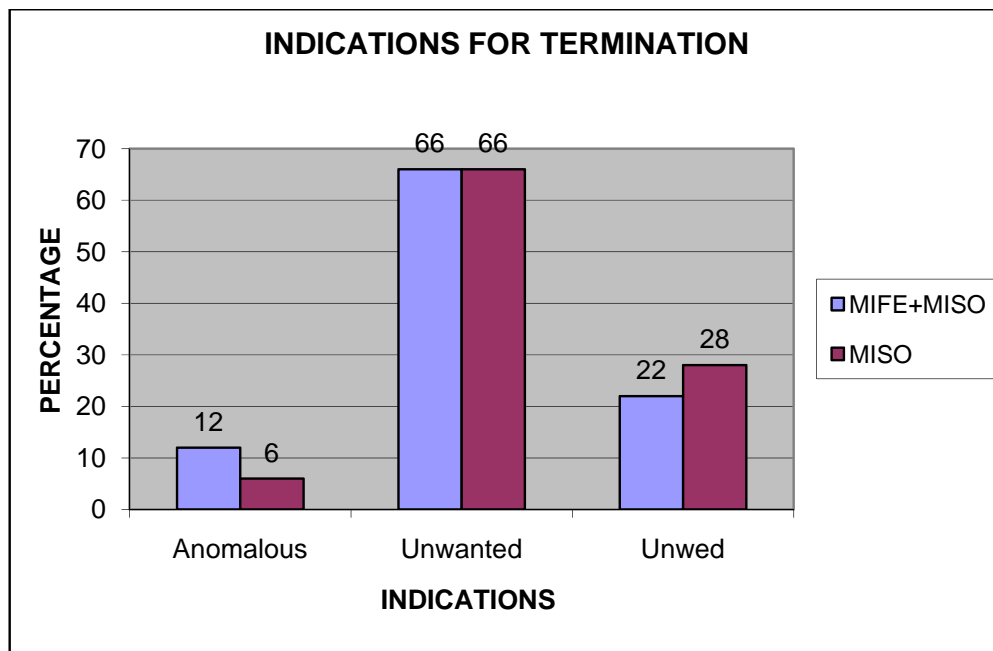
## INDICATIONS FOR TERMINATION

**TABLE 4: INDICATIONS FOR TERMINATION**

Indication	Mife+miso n=50		Miso only n=50		Total	
	n	%	n	%	n	%
ANOMALOUS	6	12.00%	3	6.00%	9	9.00%
UNWANTED	33	66.00%	33	66.00%	66	66.00%
UNWED	11	22.00%	14	28.00%	25	25.00%
Total	50	100.00%	50	100.00%	100	100.00%

Social reasons account for most of the reasons for MTP.

Unwanted Pregnancies accounts for Sixty Six percent in both groups.



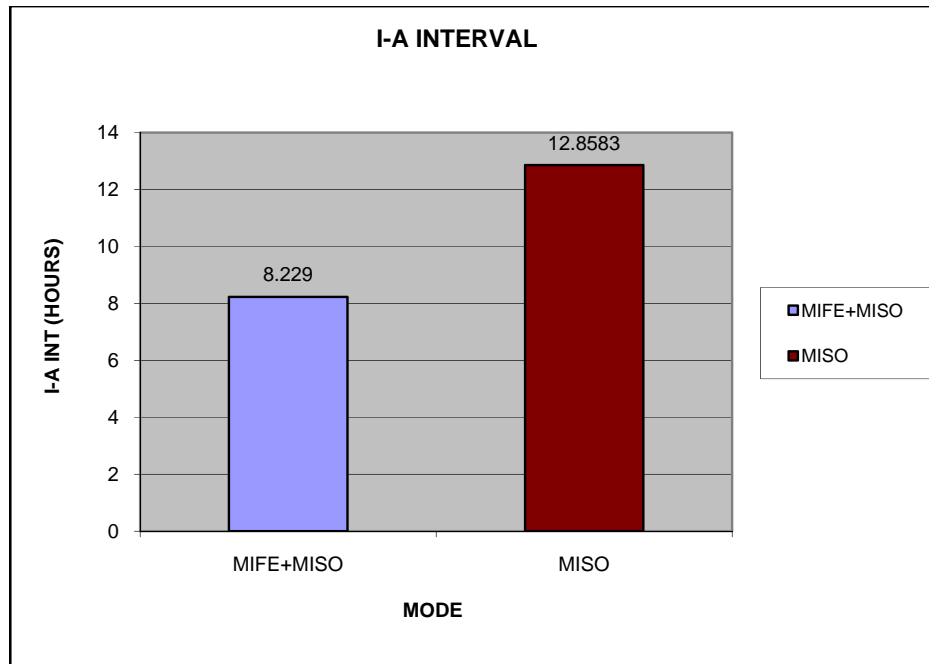
## PARAMETERS STUDIED

### INDUCTION-ABORTION INTERVAL

**TABLE 5: INDUCTION-ABORTION INTERVAL**

Induction Abortion	Mife+Miso n=50	Miso only n=50	P value
Mean	8.2290	12.8583	P=0.000 < 0.001 SIGNIFICANT.
Std. Deviation	3.29394	3.67504	
Std. Error Mean	.46583	.53045	

Mean Induction-Abortion (I-A) interval in mife+miso group was 8.2 hrs and in miso group was 12.8 hrs. The difference between them was found to be statistically significant (p value 0.000).

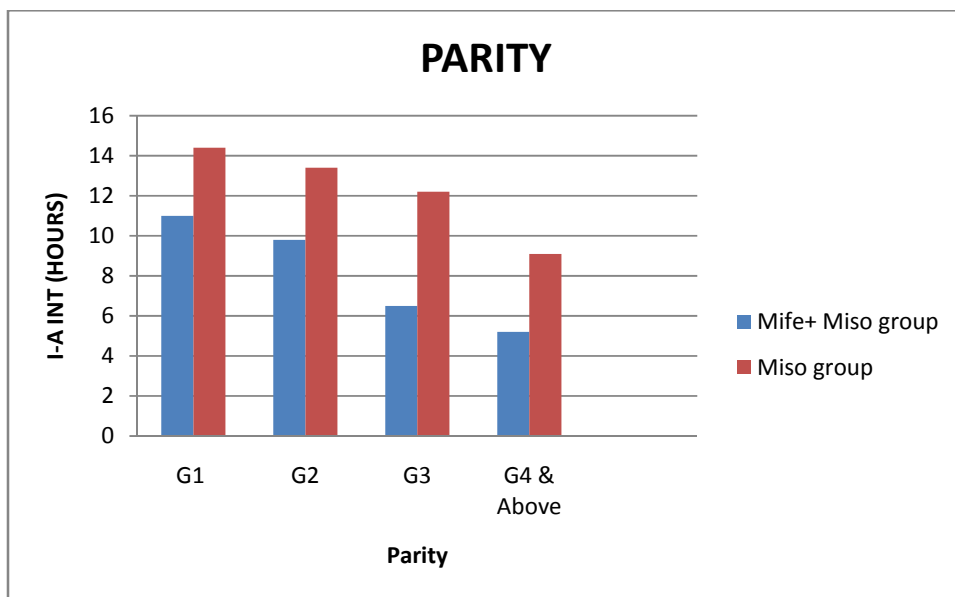


## INDUCTION – ABORTION INTERVAL

**TABLE 6: INDUCTION-ABORTION INTERVAL& PARITY**

<b>Parity</b>	<b>Mife+ Miso group Hrs</b>	<b>Miso group Hrs</b>
G1	11	14.4
G2	9.8	13.4
G3	6.5	12.2
G4 & Above	5.2	9.1
P Value	0.01	0.54

I-A Interval is shortened in Multigravida Compared to Primigravida in both groups. In Mife+miso group it is statistically significant (P Value 0.01)



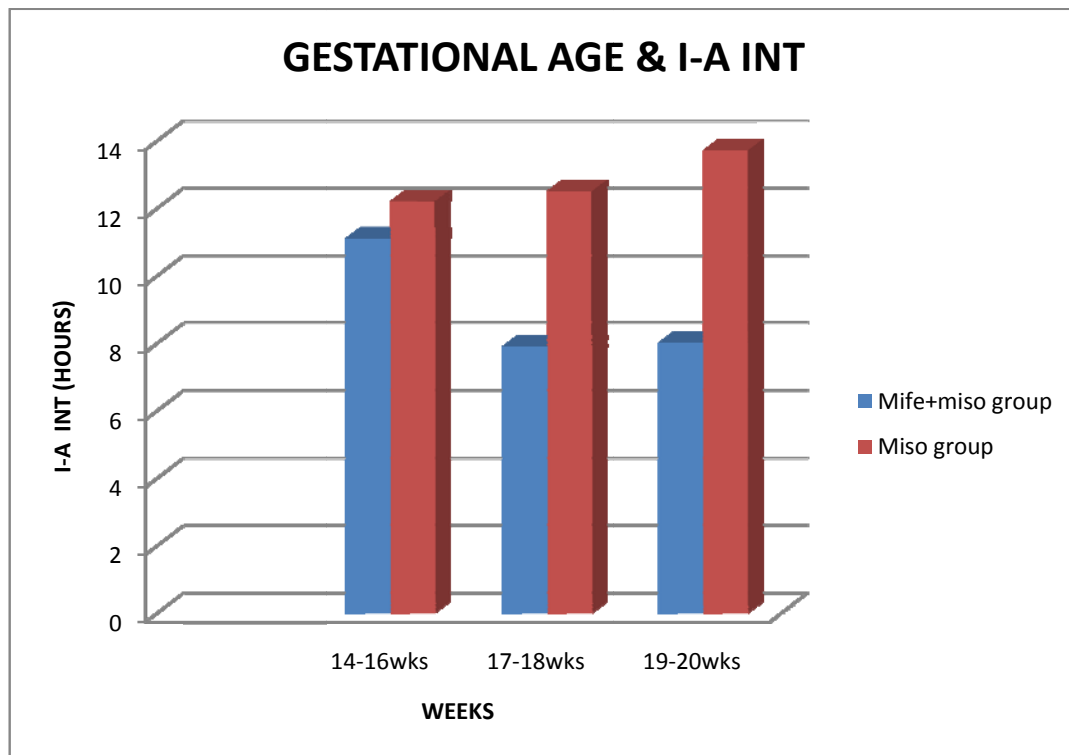


## INDUCTION – ABORTION INTERVAL

**TABLE 7: INDUCTION-ABORTION INTERVAL & GESTATIONAL AGE**

<b>Gestational Age</b>	<b>Mife+miso group Hrs</b>	<b>Miso group Hrs</b>
14-16wks	11.1	12.2
17-18wks	7.9	12.5
19-20wks	8	13.7
P Value	0.124	0.978

According to GA, I-A Interval is not statistically significant

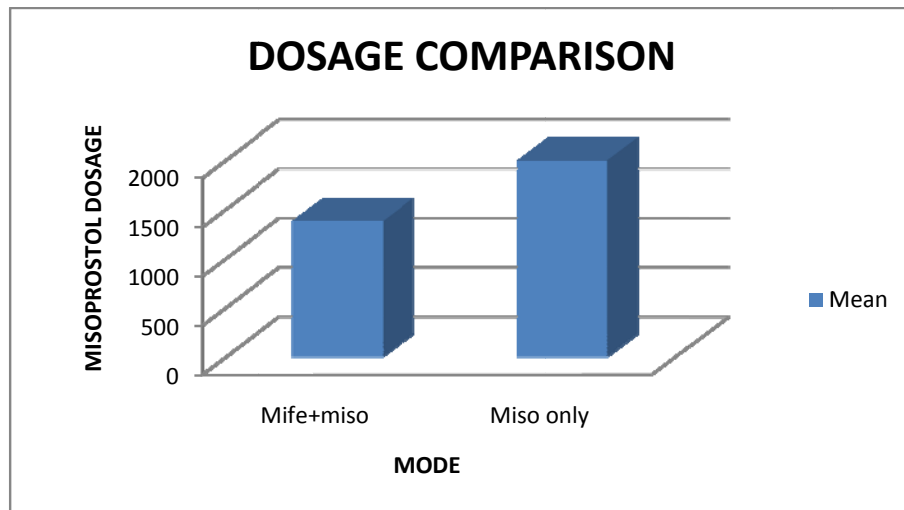


## DOSES REQUIRED

**TABLE 8: DOSES REQUIRED**

	<b>Method group</b>	<b>N</b>	<b>Mean</b>	<b>Std. Deviation</b>	<b>Std. Error mean</b>
Total dosage	Mife+miso	50	1376.0000	512.12243	72.42505
	Miso only	50	1992.0000	438.84821	62.06251

Mean dose required in mife+miso group was 1376 mcg while that in the miso group was 1992 mcg.

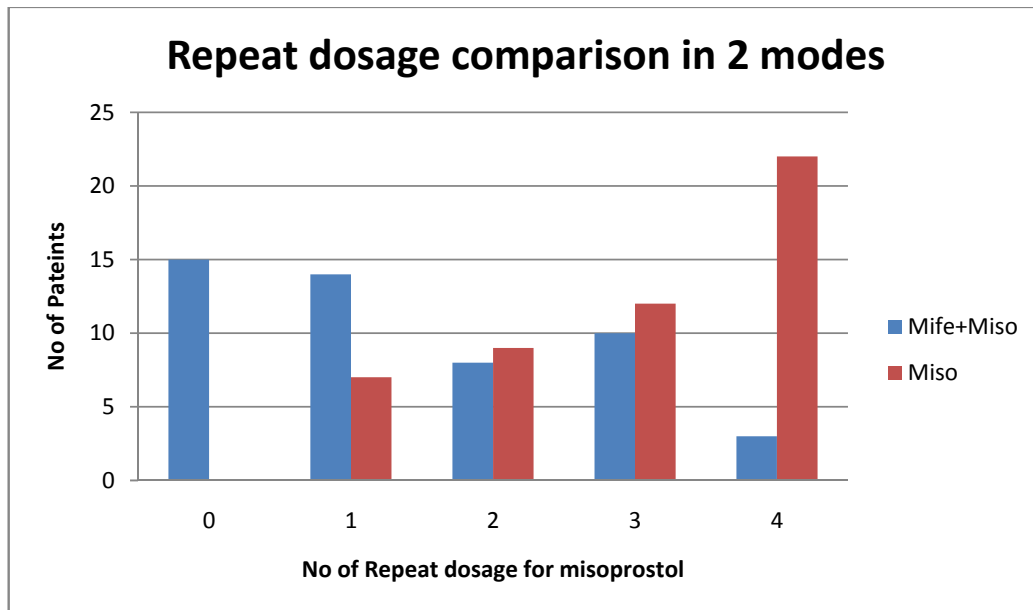


## Repeat Dosage

**TABLE 9: Repeat Dose of Misoprostol Required for Abortion**

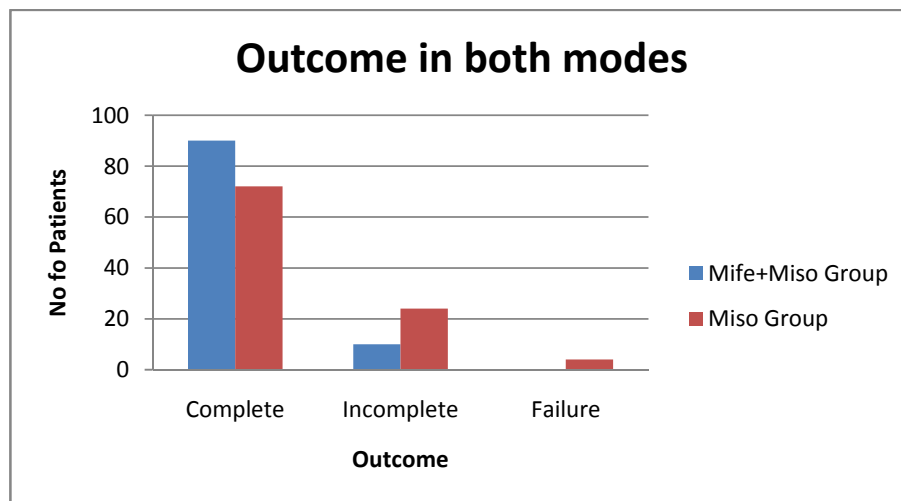
Mode	Number of doses				
	0	1	2	3	4
Mife+Miso	15	14	8	10	3
Miso	0	7	9	12	22

The Repeat dose required in mife+miso group was lesser while that in the miso group was comparatively more.



**TABLE 10: OUTCOME IN BOTH GROUPS**

	Mife+Miso Group		Miso Group		p - Value
	N	%	N	%	
Complete	45	90	36	72	0.53 (NS)
Incomplete	5	10	12	24	
Failure	0	0	2	4	



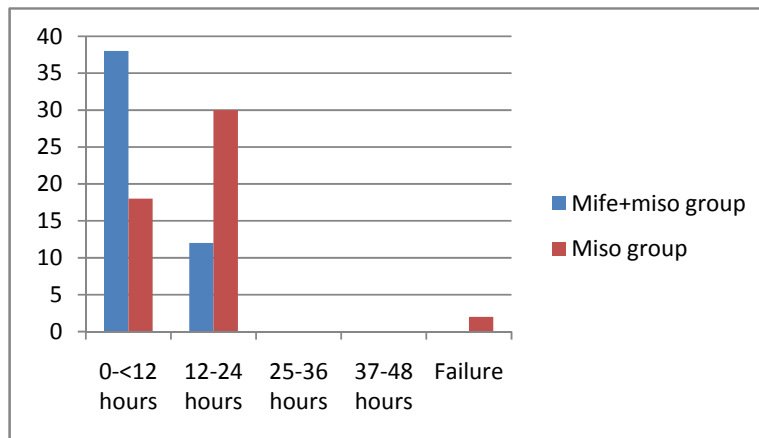
The percentage of complete abortion in Mife + Miso group was 90% while that in Miso group was 72%. The difference between the two group was not statistically significant. The percentage of incomplete abortion was 10% in Mife + Miso group and 24% in Miso group which was not statistically significant. There is no failure in Mife + Miso group and 4% in miso group which was not significant statistically.

**TABLE 11: SUCCESS RATES IN BOTH GROUPS**

<b>Hours</b>	<b>Mife+miso group</b>	<b>Miso group</b>
0-<12 hours	38	18
12-24 hours	12	30
25-36 hours	-	-
37-48 hours	-	-
Failure		2

Successful abortions included those patients who expelled completely or incompletely within forty eight hours. The number of successful abortions in Mife + Miso group was 100% and that in miso group was 96%.

Seventy Six percent of patients in Mife + Miso group expelled within twelve hours as apposed to Thirty Six percent in Miso group. With Mife + Miso group, 100% of the women had expelled in 24 hours while with Miso group, 94% had expelled in the same time.



## ADDITIONAL INTERVENTIONS

**TABLE 12: ADDITIONAL INTERVENTIONS**

<b>Intervention</b>	<b>Mife + Miso</b>	<b>Miso</b>	<b>P Value</b>
Instrumental Evacuation	3	9	0.154 (NS)
Misoprostol	-	2	
Oxytocin	2	1	
Mife + miso	-	2	
Total	10%	28%	

Overall 10% in mife + miso group and 28% patients in miso group required some form of interventions for completion of the abortion process. The commonest intervention in both group was instrumental evacuation.

Additional procedures like CUT insertion and tubectomy done in multigravida. There was no incidence of postprocedural infections or sepsis in either group.

## ANALYSIS OF SYMPTOMS

**TABLE 13: ANALYSIS OF SYMPTOMS**

S.No	Symptoms	Mife+miso group		Miso group		P Value
		N	%	N	%	
1.	Nausea	11	22	17	34	0.181
2.	Vomiting	7	14	13	26	0.1337
3.	Rigor	6	12	11	22	0.183
4.	Pain	10	20	19	38	0.473
5.	Fever	5	10	8	16	0.371
6.	Excessive bleeding PV	2	4	3	6	0.650
7.	Diarrhoea	1	2	2	4	0.557

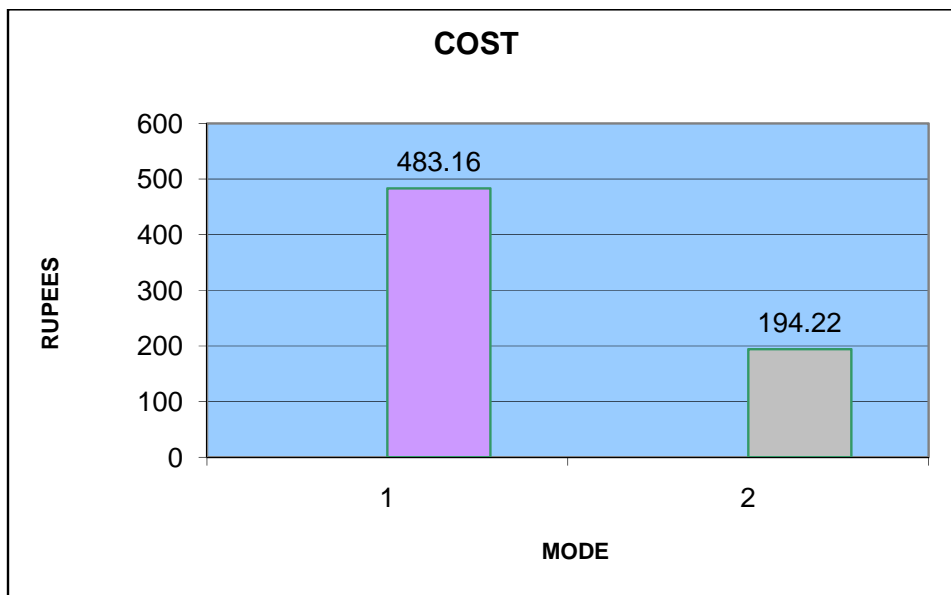
There was no statistically significant side effects between two groups. Side effects were treated symptomatically and no major complications were found in both groups.

**TABLE 14: COST INCURRED IN BOTH GROUPS**

	<b>Method group</b>	<b>Min cost per dose</b>	<b>Avg. cost</b>	<b>Mean</b>	<b>Std. Deviation</b>	<b>Std. Error mean</b>
Cost Rupees	Mife+miso	427	483.16	483.1600	49.93194	7.06144
	Miso only	117	194.22	194.2200	42.78770	6.05109

In this study, the minimum cost per dose of Mife + Miso group was Rs.427 while that of misoprostol group was Rs.117.

The average cost in this study in Mife + Miso group was Rs.483.16 and Rs.194.22 in miso group





## DISCUSSION

The various methods used for second trimester termination of pregnancy are undergoing critical appraisal worldwide. Misoprostol, although being used routinely for second trimester MTP has the disadvantages of long induction-abortion interval, more chances of incomplete abortion and high failure rate. Recently, Mifepristone and Misoprostol combination has been found to be very effective in the termination of second trimester pregnancy with short induction-abortion interval and high success rate inspite of its high cost. The present study evaluated the time-trusted method of instilling Vaginal Misoprostol with Mifepristone versus vaginal administration of Misoprostol alone in second trimester pregnancy termination.

The present study done at Institute of Obstetrics and Gynaecology, Egmore, was a randomized comparative study of 100 patients with gestational age between 14-20wks admitted for unwanted pregnancy or anomalous fetus. Group I (50 patients) received 200 mg of Mifepristone and 800 mcg vaginal misoprostol after 36 hours, followed by 400 mcg vaginal misoprostol every three hours (maximum of four doses) or until delivery and Group II (50 patients) received 800 mcg

vaginal misoprostol followed by 400 mcg vaginal misoprostol every three hours (maximum of four doses) or until delivery for induction of abortion.

## **Patient Characteristics**

### **Age:**

In this study, the mean age of patients in mifepristone + misoprostol group was 24.9 years with a range of 16-35 years and the mean age of patients in misoprostol group was 25.1 years with a range of 18-36 years. There was no association between advancing maternal age and induction abortion rates or complete abortion rates in our study.

This was comparable to the study of KAPP, NATHALIE MD, MPH<sup>45</sup> the mean age of mifepristone + misoprostol was 25.7 years and that in misotropol was 25.5 years.

In the study of JAN E DICKINSON<sup>46</sup> the mean age of mifepristone + misoprostol was 32 years and that of misoprostol was 32 years.

**Gravida:**

In the present study at least one prior delivery accounted for 24% in the mifepristone + misoprostol group and 34% in the misoprostol group.

In the study of JAN E DICKINSON<sup>46</sup> mifepristone + misoprostol group was 57.8% and misoprostol group was 60.3%.

**Gestational age:**

In the present study, the mean gestational age in mifepristone + misoprostol group was 18.08 weeks while that in misoprostol group was 18.44 weeks.

In the study of JAN E DICKINSON<sup>46</sup> the mean gestational age was 19.1 weeks in mifepristone + misoprostol group and 19.6 weeks in misoprostol group.

**Indication:**

In this study, the most common indication for pregnancy termination was unwanted pregnancy and it accounts for 66% in both groups and it is comparable with other studies.

## Parameters Studied :

### Induction abortion:

In the present study the mean induction abortion interval was 8.2 hrs for mifepristone + misoprostol group and 12.8hrs for misoprostol group which was statistically significant (<0.000)

In the study of JAN E DICKINSON<sup>46</sup> the mean induction abortion interval was 8.6hrs for mifepristone + misoprostol group and 15.5hrs for misoprostol group.

**TABLE 15: I-A INTERVAL AND SUCCESS RATES IN VARIOUS STUDIES**

Study	Induction – Abortion interval (hours)		Success rate (%)	
	Mifepristone + Misoprostol	Misoprostol	Mifepristone + misoprostol	Misoprostol
JAN E DICKINSON <sup>46</sup>	8.6	15.5	98%	96.3%
KAPP NATHALIE <sup>45</sup> MD, MPH	10	18	99%	97%
PRESENT STUDY 2010	8.2	12.8	100%	96%

It is known that induction of labour is easily accomplished in multiparous compared with primiparous<sup>51,52</sup> women, in our study also the induction abortion interval is shortened in multiparous compared to primiparous woman in mife + miso group.

**TABLE 16: I-A INTERVAL IN PARITY**

Study	Nulli parous		Multiparous	
	Mifepristone + Misoprostol (hrs)	Misoprostol (hrs)	Mifepristone + Misoprostol (hrs)	Misoprostol (hrs)
JAN E DICKINSON <sup>46</sup>	11	16.8	6.9	14.1
PRESENT STUDY 2010	11	14.4	7.4	11.6

In the study of JAN E DICKINSON<sup>46</sup> with increasing gestational age the induction abortion interval was prolonged. In our study with increasing gestational age the induction abortion interval was prolonged in Misoprostol group but it was not statistically significant.

**TABLE 17: I-A INTERVAL IN VARIOUS STUDIES**

<b>STUDY</b>	<b>Dose(mcg)</b>	<b>Dosage Interval (hours)</b>	<b>I-A Int (hours)</b>
Jain et al <sup>14</sup>	200	12	12
Bebbington et al <sup>11</sup>	600 - 400	4	19.6
Jain et al <sup>14</sup>	200	6	13.8
Herabutya et al <sup>15</sup>	600	12	15.2
Herabutya. et al <sup>15</sup>	800	12	15.3
Blumenthal et al <sup>21</sup>	200	3	9.5
Nuutila et al <sup>22</sup>	100	6	23.1
Nuutila et al <sup>22</sup>	200	12	27.8
Tang et al <sup>12</sup>	400	3	10.5
Dickinson <sup>26</sup>	400	6	15.1
Present study 2010	800-400	3	12.8

**Table 2 : Mean dosage of Drug required (Misoprostol)****Mean dose of drug required**

In our study, the mean dose of misoprostol required in pretreatment with mifepristone was 1376 mcg while in misoprostol group was 1992 mcg . In the study of JAN E DICKINSON<sup>46</sup> the dose required in both groups were 1600mcg.

**TABLE 18: DOSAGE OF MISOPROSTOL IN MISOPROSTOL ALONE GROUP**

<b>Study</b>	<b>Misoprostol Mean (mcg) dose</b>	<b>Induction – Abortion Interval</b>
Snehamy Chaudhri et al <sup>18</sup>	760	15.5
C.S,W,Ngai et al <sup>23</sup>	2000	16.3
Jan E Dickinson <sup>46</sup>	1600	15.5
Present Study 2010	1992	12.8

**TABLE 19: DOSE OF VAGINAL MISOPROSTOL USED IN VARIOUS STUDIES IN MIFEPRISTONE + MISOPROSTOL GROUP**

<b>S. No</b>	<b>Study</b>	<b>Mife pristone Dose (mg)</b>	<b>Inerval between mife pristone – misoprosto l (hrs)</b>	<b>Misoprostol (Mean dose) (Mcg)</b>	<b>Induction - Abortion Interval (hrs)</b>
1	WEBSTER D <sup>9</sup>	200 mg – 600 mg	36-48	1600	6.9
2	SUKWAI NGAI OI SHAN TANG AND PAK CHANG <sup>39</sup>	200 mg	36-48	812	10
3	ROSE SB, SHANG C, SIMMONS A <sup>43</sup>	200 mg	36-48	1200	6
4	JAN E DICKINSON <sup>46</sup>	200 mg	36-48	1600	8.6
5	HAMODA ET – AL <sup>42</sup>	200 mg	36-48	1600	5.4
6	E1 – REFAEY AND TEMPLETON <sup>40</sup>	600 mg	36-48	2200mcg over 12 hr well towarted	6.4
7	ASHOK AND TEMPLETON <sup>41</sup> (1999)	200 mg	36-48	1200 mcg	6.5
8	HAMMOND (RCOG) <sup>48</sup>	200 mg	36-48	1200 mcg	7.4
9	PRESENT STUDY	200 mg	36 hrs	1376 mcg	8.2

Studies have shown that pretreatment with mifepristone results in shorter induction – abortion intervals compared to misoprostol group alone and also dose of misoprostol required is reduced. In the study of El. Refaey and Templeton<sup>40</sup> 2200mcg over 12 hrs and 4000mg over 48 hrs were well tolerated.

### **OUTCOME:**

The success rate at less than 12 hrs was 76% with in mifepristone + misoprostol group and 36% with in misoprostol group which is greater than most of the observations in other studies probably because of the high dose and shorter dosing interval<sup>41</sup>. But the final success rate at 24hrs and 48 hrs in the present study was 100% with mifepristone + misoprostol group and 96% in misoprostol group which is comparable to other studies.



**TABLE 20 : OUTCOME IN VARIOUS STUDIES  
(MISOPROSTOL)**

Study	Success rates of misoprostol-n(%)				Failure - N (%) and mode of Termination
	12 hrs	24hrs	36 hrs	48 hrs	
CHAUDURI ET AL <sup>18</sup>	21 (35%)	45 (75%)	53 (88%)	(57) 95%	3(5%) - 2 received PGF2 $\alpha$ 1 hysterotomy was done
BISWAS ET AL <sup>27</sup>	(5) 20%	21 (84%)	23 (92%)	-	2(8%) Not mentioned
YAPAR ET AL <sup>19</sup>	-	-	-	38 (77.5%)	11(22.5%)
TANG ET AL <sup>12</sup>		96 (86%)		106 (95%)	6(5%) 1 expelled spontaneously remaining 5 aborted with intra vaginal gemeprost
JAIN ET AL <sup>20</sup>	-	81 (81%)	100 (100%)		-
ENG ET AL <sup>24</sup>	15(60 %)	21 (84%)	-	-	4 (16%) 1- sulprostone; remaining 3 underwent suction evacuation
PRESENT STUDY 2010	36%	94%	-	94%	Mifepristone + misoprostol

**TABLE 20 : OUTCOME IN VARIOUS STUDIES  
(MIFEPRISTONE WITH MISOPROSTOL)**

Study	SUCCESS RATES OF MIFEPRISTONE + MISOPROSTOL IN VARIOUS STUDIES			
	12 hrs	24 hrs	36 hrs	48 hrs
Sukwai Ngai Shan Tang and Pak Chang <sup>39</sup>	70.4%	81.4%	99.5%	97%
Elrefaey et al <sup>40</sup>		97%	98.3%	99%
Ashok et al <sup>41</sup>		97.1%		99.2%
ROSE SB Shand c <sup>43</sup>		95.9%		
SIN Ee GOh, KokJoo Thong <sup>44</sup>		97.9%	99.5%	99.5%
JAN E DICKINSON <sup>46</sup>	70.4%	91.5%	98%	
Present study 2010		100%		100%

**Additional Intervention:**

Additional intervention needed more in misoprostol group compared to mife + miso group and most of the Patients required

surgical evacuation in both both group which was comparable with other studies.

**TABLE 22: INTERVENTIONS USED FOR INCOMPLETE ABORTIONS**

<b>Study</b>	<b>Mode</b>	<b>n%</b>	<b>Intervention</b>
KAPP NATHAL IE, MD, MPH <sup>45</sup>	Mifepristone + Misoprostol	3.1%	Surgical Evacuation
	----- Misoprostol	6.3%	
JAN E DICKINSON <sup>46</sup>	Mifepristone + Misoprostol	24.5%	Surgical Evacuation
	----- Misoprostol	25.6%	
SIN, EE, GOH, KOK, JOO THONG <sup>44</sup>	Mifepristone + Misoprostol	5%	Surgical Evacuation
	----- Misoprostol	6.5%	
PRESENT STUDY 2010	Mifepristone + Misoprostol	10%	Surgical Evacuation oxytocin infusion
	----- Misoprostol	24%	Surgical Evacuation oxytocin infusion ,miso prostol <sup>53</sup>

**Side effects:**

There was no major side effects like uterine rupture, infection, sepsis, hypersensitivity reactions or maternal deaths in either group. Two patients in mifepristone plus misoprostol group and three patients in misoprostol group had bleeding more than 300ml which in all cases

this was due to incomplete abortion which was controlled by surgical evacuation. However no transfusion were required in either group.

In the study of Tang et al<sup>12</sup> and HO et al<sup>23</sup> where dosing interval was frequent the incidence of side effects were more, but in the present study it is comparable with other studies.

**Other Complications:** In the present study there was no post procedural genital infections or cervical tears which was comparable to others studies also.

**TABLE 23: SIDE EFFECTS IN VARIOUS STUDIES n(%)**

Study	Mode	Nausea	Vomiting	Diarrhoea	Fever	Excess Bleeding	Rigor	Cx Tear
Chauduri et al <sup>18</sup>	PGE1	-	9(15%)	-	8 (13.3%)	-	-	-
Biswas et al <sup>27</sup>	PGE1	1(4%)	-	-	-	-	4 (16%)	-
Bebbington et al <sup>11</sup>	PGE1	-	-	-	12 (24%)	-	-	-
Jain at al <sup>14</sup>	PGE1	-	11 (4%)	11(4%)	30 (11%)	-	-	-
Nuutila et al <sup>22</sup>	PGE1 100mcg	-	6 (22%)	0	-	-	-	-
Nuutila et al <sup>22</sup>	PGE1 200mcg	-	3 (11%)	2(8%)	-	-	-	-
Tang et Al <sup>12</sup>	PGE1	53 (48%)	-	29 (26%)	66 (59%)	-	72 (64%)	-
Ho et al <sup>23</sup>	PGE1	20 (40.8%)	14 (28.6%)	9 (18.6%)	-	-	-	-

**TABLE 24: SIDE EFFECTS IN VARIOUS METHODS**

Study	Mode	Nausea	Vomiting	Diarrhoea	Fever	Excessive bleeding	Rigor
Sukwai Ngai o Shan Tang and PAK Chung <sup>39</sup>	Mifepristone + Misoprostol			40% oral 23.2% vaginal			
Haitham Homoda <sup>42</sup>	Mifepristone + Misoprostol	26%	25%	25%	-	-	28%
ROSE SB Shang C Simmon A <sup>43</sup>						8.1%	
Jan E Dickinson <sup>46</sup>	Mife + Miso Miso				43.7% 51.3%		
Present Study 2010 <sup>29</sup>	Mifepristone + Misoprostol	22%	14%	2%		12%	
	Miso	26%	26%	4%		22%	

**Cost incurred:**

Average cost in misoprostol group was rupees 194.22 while in mifepristone + misoprostol group was rupees 483.16 So Misoprostol group is very economical as mentioned in various studies.

## SUMMARY

1. One hundred Patients opting for second trimester pregnancy termination or diagnosed to have anomalous fetus were considered for the study. Fifty patients received 200mg Mifepristone ,followed by 800mcg vaginal misoprostol 36 hours later, followed by 400mcg vaginal misoprostol every 3 hours interval of maximum 4 doses or until delivery. In another fifty women, 800mcg vaginal misoprostol followed by 400 mcg vaginal misoprostol every 3 hrs interval of maximum 4 doses or until delivery.
2. The two groups were comparable with respect to maternal age, parity and gestational age at the time of induction of abortion. Majority of patients in either group were in the age group of 21-25 years. The commonest gestational age in both group was between 17-18 weeks.
3. There were more multigravida than primigravida in both the groups. Induction abortion interval in primigravida is more compared to multigravida in both group and it was statistically

significant in Mifepristone and misoprostol combination (pvalue.01).

4. The most common indication for pregnancy termination in both group was unwanted pregnancy due to social reasons.
5. Induction abortion interval in Mifepristone and misoprostol group was 8.2 hours and that in misoprostol alone group was 12.8 hours. The difference between them was found to be statistically significant (p value 0.000).
6. According to the gestational age, induction abortion interval was not statistically significant in both groups
7. The percentage of complete abortion in Mifepristone and misoprostol group was 90% and in misoprostol group was 72% but the difference was not statistically significant. The percentage of incomplete abortion was 10% in Mifepristone and misoprostol group and was 24% in misoprostol alone group which did not reach statistical significance
8. There was no failure in Mifepristone and misoprostol group and 4% in misoprostol alone group, but it was not statistically

significant. The complete abortion rate within 12 hours was 76% in Mifepristone and misoprostol group and 36% in misoprostol alone group and in 24 hrs it was 100% and 96% respectively. Additional intervention needed in Mifepristone and misoprostol combination group was 10% and in misoprostol alone group was 28% and most common being instrumental evacuation.

9. The mean dose of misoprostol used was 1376 mcg and that of misoprostol group was 1992 mcg.
10. The average cost in misoprostol alone group was rupees 194.2 and Mifepristone and Misoprostol combination group was rupees 483.1, which is two times higher.
11. There was no statistically significant side effects between two groups and no major maternal complications found in both groups.
12. It was observed that no bleeding (or) abdominal pain (or) any adverse reactions were not reported after administration of Mifepristone prior to vaginal Misoprostol administration (36 hrs). so Mifepristone could be administered safely prior to hospital admission for termination.



## CONCLUSION

Comparing Mifepristone and Vaginal misoprostol combination with vaginal misoprostol alone for second trimester pregnancy termination, it was observed that

- ✚ Mifepristone with vaginal misoprostol combination group is associated with shorter induction abortion interval and 100% success rate. The complete abortion rate, success rate and side effects were comparable in both group.
- ✚ Vaginal misoprostol alone group also doesn't have the 36 hours anxiety/unease from the time of mifepristone administration.
- ✚ Vaginal misoprostol alone group is cost effective.
- ✚ Hence vaginal misoprostol alone group can also be considered as an effective alternative for Mifepristone and vaginal misoprostol combination group.

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## ABBREVIATIONS

ACTH	-	Adrenocorticotrophic Hormone
COX	-	Cyclo-Oxygenase
CX	-	Cervix
EAE	-	Extra Amniotic Ethacridine Lactate
GA	-	Gestational age
HRS	-	Hours
hCG	-	Human Chorionic Gonadotropin
I-A Int	-	Induction Abortion Interval
IAPG	-	Intra Amniotic Prostaglandin
LT	-	Leukotriene
mcg	-	Microgram
mg	-	milligram
MTP	-	Medical Termination of Pregnancy
Mife+Miso	-	mifepristone+misoprostol
Miso	-	Misoprostol
NS	-	Not Significant
PG	-	Prostaglandin
PO	-	Per Oral
PV	-	Per Vaginal
S	-	Significant
SD	-	Standard Deviation
WK	-	Week



BP  
 RR  
 PER ABDOMEN EXAMINATION:  
 SPECULUM EXAMINATION:  
 PER VAGINAL EXAMINATION:  
 INVESTIGATIONS:

URINE ALBUMIN  
 SUGAR  
 HB%  
 BLOOD GROUPING/RH TYPING  
 HIV(WITH CONSENT)  
 VDRL  
 BLOOD SUGAR,UREA,ECG,USG.  
 DATE/TIME OF ADMINISTRATION OF  
 MIFEPRISTONE;  
 DATE/TIME OF ADMINISTRATION OF VAGINAL  
 MISOPROSTOL:  
 NUMBER OF DOSES:  
 DATE/TIME OF EXPULSION OF FOETUS:  
 DATE/TIME OF EXPULSION OF PLACENTA:

OUTCOME

COMPLETE:	
INCOMPLETE:	
FAILED:	

IF INCOMPLETE ADDITIONAL METHODS USED FOR  
 COMPLETING THE ABORTION:  
 ADDITIONAL INTERVENTIONS IF NEEDED:  
 INDUCTION-ABORTION INTERVAL IN HOURS:  
 SIDE EFFECTS:

NAUSEA		RIGOR	
VOMITING		FEVER	
DIARRHOEA		HAEMORRHAGE	
HEADACHE		PAIN	

ADDITIONAL PROCEDURES: CUT/TUBECTOMY

S. NO	NAME	AGE in Years	InPatient No	PARITY	GA	INDICATION	METHOD	INITIAL DOSAGE Initial dosage 800 Mcg	REPEAT DOSAGE 400 Mcg	TOTAL DOSAGE	IND-ABO INTERVAL in Hours	RESULT	ADD INT	Side Effects	COST(RS)	Addl Pro	FAILURE EXPULSION TIME
1	ANANDHI	19	2879	G1	17	Unwed	MIFE+MISO	1	3	2000	12	Complete			544		
2	CHRISTINA	20	12100	G1	16	Unwed	MIFE+MISO	1	3	2000	12	Complete		Rigor,Fever	544		
3	AGNES	19	11386	G1	20	Unwed	MIFE+MISO	1	3	2000	12.3	Complete			544		
4	REVATHY	19	11502	G1	17	Unwed	MIFE+MISO	1	1	1200	7	Complete		Nausea,Vomiting,Pain	466		
5	SUBHA	20	8517	G1	17	Unwed	MIFE+MISO	1	3	2000	13	Complete		Rigor,Fever	544		
6	YASODHA	16	8113	G1	17	Unwed	MIFE+MISO	1	1	1200	6.4	Complete			466		
7	PARAMESWARI	19	18239	G1	18	Unwed	MIFE+MISO	1	1	1200	7	Complete		Nausea,Vomiting,Pain	466		
8	CHELLAMAL	20	23849	G1	16	Unwed	MIFE+MISO	1	4	2400	16.1	Incomplete	IE	Fever,Vomiting	583		
9	PUSPA	18	19988	G1	16	Unwed	MIFE+MISO	1	4	2400	16	Incomplete	IE	Pain	583		
10	UMA	19	12609	G2A1	18	ANOMALOUS	MISO ONLY	1	4	2400	23.3	Complete		Rigor,Vomiting	234		
11	ELLANA	18	10349	G1	16	Unwed	MISO ONLY	1	3	2000	11	Complete		Fever	195		
12	USHA	18	10972	G1	19	Unwed	MISO ONLY	1	3	2000	12	Complete		Rigor,Fever,	195		
13	NISHA	19	11009	G1	20	Unwed	MISO ONLY	1	4	2400	16.3	Incomplete	IE	Rigor,Diarrhoea,Bleeding	234		
14	BOMMUKUTTY	20	11505	G1	17	Unwed	MISO ONLY	1	4	2400	14.4	Complete		Vomiting	234		
15	SEETA	20	23208	G1	20	Unwed	MISO ONLY	1	3	2000	13	Complete			195		
16	Nathiya	23	2195	G3P1L1A1	20	Unwanted	MIFE+MISO	1	2	1600	10	Complete			505	CUT	
17	AMUDHA	23	2910	G1	18	Unwed	MIFE+MISO	1	2	1600	10	Complete			505		
18	ANANDAVALI	25	8292	G2P1L1	17	ANOMALOUS	MIFE+MISO	1	3	2000	13	Complete		Vomiting,Diarrhoea	544	CUT	
19	PRIYA	25	7564	G1	17	Unwed	MIFE+MISO	1	4	2400	16.4	Incomplete	IE	Rigor,Fever,Bleeding	583		
20	MANJULA	25	8180	G3P2L2	18	Unwanted	MIFE+MISO	1	0	800	4.2	Complete		Nausea,Pain	427	TAT	
21	BHAVANI	22	18764	G2P1L1	18	Unwanted	MIFE+MISO	1	1	1200	7	Complete		Vomiting	466	CUT	
22	NEETHUSINGH	23	18872	G1	19	Unwed	MIFE+MISO	1	1	1200	7	Complete			466		
23	DEVI	23	19294	G1	16	Unwed	MIFE+MISO	1	3	2000	13	Incomplete	IE	Rigor,Fever	544		
24	CHITRA	23	22594	G1	16	Unwed	MIFE+MISO	1	0	800	4	Complete		Fever	427		
25	ROJAVATHY	22	22271	G1	18	Unwed	MIFE+MISO	1	3	2000	13	Complete			544		
26	SATHYA	22	22278	G2P1L0	18	ANOMALOUS	MIFE+MISO	1	1	1200	10	Complete			466		
27	AMBIGA	24	13953	G2P1L1	17	Unwanted	MIFE+MISO	1	2	1600	9.2	Complete			505	CUT	
28	MAHESWARI	24	14000	G2P1L1	20	Unwanted	MIFE+MISO	1	2	1600	10	Complete			505	CUT	
29	NIRMALA	24	13949	G2P1L1	18	Unwanted	MIFE+MISO	1	0	800	4	Complete		Nausea,Pain	427	CUT	
30	PARVATHY	24	14146	G3P2L2	17	Unwanted	MIFE+MISO	1	0	800	4.3	Complete			427	TAT	
31	SUDHA	24	17193	G2P1L1	17	Unwanted	MIFE+MISO	1	2	1600	10	Complete			505	CUT	
32	REKA	23	18018	G2P1L1	20	Unwanted	MIFE+MISO	1	3	2000	11	Complete			544	CUT	
33	SILAMBARASI	23	20394	G2P1L1	19	Unwanted	MIFE+MISO	1	2	1600	10	Complete			505	CUT	
34	PRIYADARSHNI	25	18130	G3P2L2	20	Unwanted	MIFE+MISO	1	1	1200	7	Complete			466	TAT	
35	VALARMATHY	22	4567	G1	20	Unwed	MISO ONLY	1	4	2400	17.1	Incomplete	IE		234		
36	REVATHY	22	10784	G1	20	Unwed	MISO ONLY	1	4	2400	14.3	Complete			234		

S. NO	NAME	AGE in Years	InPatient No	PARITY	GA	INDICATION	METHOD	INITIAL DOSAGE Initial dosage 800 Mcg	REPEAT DOSAGE 400 Mcg	TOTAL DOSAGE	IND-ABO INTERVAL in Hours	RESULT	ADD INT	Side Effects	COST(RS)	Addl Pro	FAILURE EXPULSION TIME
37	INDRANI	22	10699	G1	18	Unwed	MISO ONLY	1	4	2400	14	Complete			234		
38	KALA	21	10778	G1	16	Unwed	MISO ONLY	1	4	2400	13.2	Incomplete	IE	Vomiting,Bleeding	234		
39	ADHILAKSHMI	24	11006	G2P1L1	18	Unwanted	MISO ONLY	1	3	2000	13	Complete		Rigor,Fever	195	CUT	
40	THABASAM	25	11109	G2P1L1	18	UNWAnted	MISO ONLY	1	3	2000	13.1	Complete		Vomiting,Diarrhoea	195	CUT	
41	REKHA	23	11527	G2P1L1	17	Unwanted	MISO ONLY	1	3	2000	11	Complete		Rigor,Fever	195	CUT	
42	ARULSELVI	23	23009	G2P1L1	18	Unwanted	MISO ONLY	1	1	1200	7	Complete		Nausea,Vomiting,Pain	117	CUT	
43	MEGALA	22	24219	G4P3L3	18	Unwanted	MISO ONLY		1	1200	7	Complete		Nausea,Fever	117		
44	VASANTHI	21	24819	G4P3L3	18	ANOMALOUS	MISO ONLY	1	1	1200	6.5	Incomplete	IE	Nausea,Vomiting,Pain	117		
45	VIOLA	25	11708	G3P2L2	18	Unwanted	MISO ONLY	1	4	2400	19.3	Incomplete	IE	Bleeding	234		
46	SASIKALA	22	11248	G2P1L1	17	Unwanted	MISO ONLY	1	4	2400	18.1	Complete		Rigor,Vomiting	234	CUT	
47	MEENA	21	12313	G2P1L1	19	Unwanted	MISO ONLY	1	4	2400	16	Complete			234	CUT	
48	PODUMPONNU	24	12452	G2P1L1	17	Unwanted	MISO ONLY	1	2	1600	9	Complete		Nausea,Pain	156	CUT	
49	DHANALAKSHMI	24	12624	G1	20	Unwed	MISO ONLY	1	4	2400	18.1	Complete		Vomiting	234		
50	VALARMATHY	22	12770	G2P1L1	18	Unwanted	MISO ONLY	1	4	2400	16.3	Incomplete	IE	Rigor,Vomiting	234	CUT	
51	KALAVANI	21	12885	G2P1L1	17	Unwanted	MISO ONLY	1	4	2400	15	Complete			234	CUT	
52	MARY	24	12917	G2P1L1	16	Unwanted	MISO ONLY	1	2	1600	10	Complete		Nausea,Pain	156		
53	VIJAYALAKSHMI	22	13015	G3P2L2	20	Unwanted	MISO ONLY	1	4	2400	16.2	Incomplete	IE	Vomiting	234		
54	ARULMOZHI	24	13270	G3P2L2	20	Unwanted	MISO ONLY	1	2	1600	10	Complete		Nausea,Pain	156	TAT	
55	SARANYA	22	13280	G3P2L2	20	Unwanted	MISO ONLY	1	2	1600	10	Complete		Nausea,Pain	156	TAT	
56	Vanitha	26	2040	G2P1L1	20	Anamolous Baby	MIFE+MISO	1	2	1600	9.5	Complete		Pain	505	CUT	
57	Chinakka	30	2137	G4P3L3	18	Unwanted	MIFE+MISO	1	1	1200	6.4	Complete		Nausea,Pain	466	TAT	
58	Jayabarunisha	28	2136	G4P3L3	19	Unwanted	MIFE+MISO	1	1	1200	6.3	Complete		Nausea,Vomiting,Pain	466	TAT	
59	Manju	27	2677	G5P2L2A2	20	Unwanted	MIFE+MISO	1	0	800	5	Complete		Nausea,Pain	427	TAT	
60	RAMESWARI	28	12108	G3P2L2	16	Unwanted	MIFE+MISO	1	0	800	5	Complete		Nausea	427	TAT	
61	JAYALAKSHMI	27	18414	G4P3L2	18	Unwanted	MIFE+MISO	1	0	800	4	Complete			427		
62	KAVITHA	28	19086	G2P1L1	18	ANOMALOUS	MIFE+MISO	1	0	800	4	Complete		Nausea	427	CUT	
63	ADHILAKSHMI	28	18724	G3P2L2	18	Unwanted	MIFE+MISO	1	1	1200	7.3	Complete			466	TAT	
64	VANITHA	28	14078	G2P1L0	18	ANOMALOUS	MIFE+MISO	1	2	1600	10	Complete			505		
65	GEETHA	26	16619	G3P2L2	19	Unwanted	MIFE+MISO	1	3	2000	13	Complete		Rigor,Fever	544	TAT	
66	LAKSHMI	27	19038	G3P2L2	18	Unwanted	MIFE+MISO	1	0	800	4.15	Complete			427	TAT	
67	GAYATHRI	28	20654	G3P2L2	17	Unwanted	MIFE+MISO	1	3	2000	13	Complete		Rigor,Fever	544	TAT	
68	DHANALAKSHMI	28	21490	G3P2L2	20	Unwanted	MIFE+MISO	1	0	800	4.2	Complete			427	TAT	
69	BHUVANESWARI	29	23279	G3P2L2	19	Unwanted	MIFE+MISO	1	0	800	4.3	Complete		Vomiting	427	TAT	
70	LILLY	26	22117	G3P2L2	20	Unwanted	MIFE+MISO	1	1	1200	7.2	Complete			466	TAT	
71	DEVIKA	28	21961	G3P2L2	19	Unwanted	MIFE+MISO	1	1	1200	7.3	Complete			466	TAT	
72	SARUMATHI	30	19962	G3P2L2	20	Unwanted	MIFE+MISO	1	0	800	4.5	Complete			427	TAT	



S. NO	NAME	AGE in Years	InPatient No	PARITY	GA	INDICATION	METHOD	INITIAL DOSAGE Initial dosage 800 Mcg	REPEAT DOSAGE 400 Mcg	TOTAL DOSAGE	IND-ABO INTERVAL in Hours	RESULT	ADD INT	Side Effects	COST(RS)	Addl Pro	FAILURE EXPULSION TIME
73	PREMA	29	19562	G3P2L2	20	Unwanted	MIFE+MISO	1	1	1200	7.3	Complete			466		
74	SUSEELA	28	11701	G3P2L2	18	Unwanted	MISO ONLY	1	4	2400	19.3	Complete		Rigor,Fever	234		
75	JAYALAKSHMI	27	180317	G4P3L2	20	Unwanted	MISO ONLY	1	4	2400		FAILURE	MIFE+MISO		234	72hrs	
76	PONNI	29	11150	G3P2L2	18	Unwanted	MISO ONLY	1	1	1200	8.2	Complete		Nausea,Vomiting,Pain	117		
77	SARGUNAVALLI	28	10992	G3P2L2	18	Unwanted	MISO ONLY	1	1	1200	7	Complete		Nausea,Pain,Vomiting	117	TAT	
78	RUKMANI	28	10956	G3P2L2	18	Unwanted	MISO ONLY	1	1	1200	8.3	Complete		Nausea,Pain,Fever	117		
79	BARATHI	27	11526	G3P2L2	18	Unwanted	MISO ONLY	1	2	1600	10	Incomplete	IE	Nausea,Pain	156		
80	SASIKALA	28	11599	G2P1L1	18	Unwanted	MISO ONLY	1	3	2000	13	Complete		Pain	195	CUT	
81	SERUMIRA	26	11967	G3P2L2	18	ANOMALOUS	MISO ONLY	1	3	2000	12.1	Complete		Rigor,Fever	195	TAT	
82	LAKSHMI	28	23709	G3P2L2	18	Unwanted	MISO ONLY	1	2	1600	10	Complete		Nausea,Pain	156	TAT	
83	ESAKIAMAL	28	12501	G3P2L2	20	Unwanted	MISO ONLY	1	3	2000	13	Complete		Nausea,Pain	195	TAT	
84	UMA	29	12609	G2P1L1	17	Unwanted	MISO ONLY	1	1	1200	7	Complete		Nausea,Pain	117	CUT	
85	RAMEELA	26	12108	G3P2L2	20	Unwanted	MISO ONLY	1	3	2000	13	Incomplete	IE	Rigor,Fever	195		
86	EMARALDMARY	29	13908	G2P1L1	18	Unwanted	MISO ONLY	1	4	2400	17	Complete		Fever	234		
87	RAJESWARI	26	13761	G3P2L2	19	Unwanted	MISO ONLY	1	4	2400	12.1	Complete		Pain	234	TAT	
88	ASWINI	27	13783	G3P2L2	18	Unwanted	MISO ONLY	1	4	2400		FAILURE	MIFE+MISO		234		69 HOURS
89	BARISHA	28	13860	G2P1L1	20	Unwanted	MISO ONLY	1	2	1600	10	Incomplete	IE	Nausea,Pain	156		
90	VIJAYALAKSHMI	26	13756	G3P2L2	20	Unwanted	MISO ONLY	1	2	1600	10	Complete		Nausea,Pain	156		
91	KAMATCHI	31	5602	G3P2L2	18	Unwanted	MIFE+MISO	1	0	800	4.1	Complete			427	TAT	
92	KUTTI	35	17283	G5P4L4	18	Unwanted	MIFE+MISO	1	0	800	4.1	Complete		Nausea	427		
93	CHITRA	32	10194	G3P2L2	18	Unwanted	MIFE+MISO	1	1	1200	7	Incomplete	IE		466		
94	KANCHANA	31	22281	G3P2L2	17	Unwanted	MIFE+MISO	1	0	800	4.3	Complete		Nausea,Pain	427	TAT	
95	RAJESWARI	32	10618	G3P2L2	20	Unwanted	MISO ONLY	1	4	2400	20.3	Complete		Rigor	234	TAT	
96	TAMILARASI	36	10718	G2P1L0	18	ANOMALOUS	MISO ONLY	1	3	2000	13	Complete		Vomiting	195		
97	SWEETYMALAR	32	10586	G3P2L2	20	Unwanted	MISO ONLY	1	2	1600	9.2	Complete		Nausea,Pain	156		
98	KALA	32	12142	G4P3L3	17	Unwanted	MISO ONLY	1	3	2000	13	Incomplete	IE		195		
99	USHA	32	13301	G2P1L2	18	Unwanted	MISO ONLY	1	4	2400	16.5	Incomplete	IE		234		
100	SHYAMALADEVI	33	13788	G3P2L2	19	Unwanted	MISO ONLY	1	4	2400	13.2	Complete		Pain	234		

Key to Master chart

- GA Gestational Age
- Add Int Additional Intervention
- Addl Pro Additional procedure
- IE Instrumental evacuation
- TAT Transabdominal tubectomy