# " COMPARATIVE STUDY OF MIFEPRISTONE AND VAGINAL MISOPROSTOL COMBINATION OVER VAGINAL MISOPROSTOL ALONE IN FIRST TRIMESTER ABORTION "

*Dissertation submitted to*

**THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY**

**In partial fulfillment for the award of the Degree of**

**M. D. OBSTETRICS AND GYNAECOLOGY**

**BRANCH II**


**K.A.P. VISWANATHAM GOVERNMENT MEDICAL COLLEGE**

**THIRUCHIRAPALLI**

**MARCH 2012**

# DECLARATION CERTIFICATE

This is to certify that the work embodied in the dissertation exhibited **COMPARATIVE STUDY OF MIFEPRISTONE AND VAGINAL MISOPROSTOL COMBINATION OVER VAGINAL MISOPROSTOL ALONE IN FIRST TRIMESTER ABORTION** has been carried out by **DR.V.JAYASUDHA** during the period April 2010 – April 2012 in **K.A.P VISHWANATHAM GOVERNMENT MEDICAL COLLEGE, THIRUCHIRAPALLI**, for the partial fulfillment of **MD BRANCH II OBSTETRICS AND GYNAECOLOGY DEGREE.**

The work has been carried out with care and precision.

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This is to certify that the dissertation titled**"Comparative study of combined oral mifepristone and vaginal misoprostol versus vaginal misoprostol alone in first trimester abortion"** as part of the fulfillment of M.D( Obstetrics & Gynaecology ) course 2010-2012 by Dr.V.Jayasudha of K.A.P.Vishwanatham Govt. medical college, Tiruchy, has been cleared by the ethical committee.

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ABSTRACT

" comparative study of mifepristone and vaginal misoprostol combination over vaginal misoprostol alone in first trimester abortion "

To assess the efficacy of mifepristone vaginal misoprostol in first trimester abortion.

To compare this combination with vaginal misoprostol alone for first trimester MTP.

To compare the various parameters involved in MTP in both the methods and asses the most suitable methods for first trimester MTP.

I. 50 mifepristone + misoprostol group

II. 50misoprostol group

Mifepristone + misoprostol

Day 1 – 200 mg mifepristone was given orally

Day 3 – 400 microgram of misoprostol kept vaginally and observe 4 hours in op department.

Misoprostol group

400 microgram of misoprostol in posterior fornix repeated 4 to 6 hours apart after admission of patient in ward. Maximum of 3 doses

Following were the observations of this study.

1. Most of the patients were in the age group 21-30 and parous
2. 4% of patients were unmarried who responded well for medical methods.

3. Almost all patients had various symtoms in both groups.

4. Expulsion was complete in the Mifepristone+Misoprostol group with only 2 woman needing check curettage for confirmation of complete abortion. However in one women, there was no response and their pregnancy was terminated by MVA. On the other hand 48% of women in the Misoprostol alone group had to have curettage for completing the abortion process, and 10% of patients there was no response.

5. Induction-abortion time is less in patients with Mifepristone +Misoprostol than Misoprostol alone (4-5 hours vs 20-22 hrs. respectively).

6. None of the patients needed blood transfusion or volume expanders.

7. None of the patients had delayed bleeding after 45 days. On an average Bleeding stopped within 2 to5 days of expelling products.

8. Misoprostol is less expensive and efficacious. However induction abortion interval is prolonged than Mifepristone +Misoprostol combination.

9. Though Mifepristone is more expensive, the high complete abortion rate and expulsion withing 4-5 hrs of Misoprostol administration makes it a preferred method where cost is not a restraining factor.

1. Mifepristone-Misoprostol combination is an effective out-patient procedure for early MTP and is ideal for home management.

2. Complete abortion rate is high with this combination.

3. Similarly the induction abortion interval with this method is also less.

4. Other associated complications are less.

   The only confounding factor is the cost involved which is about 20 times that of Misoprostol alone.

This makes the routine use of Mifepristone-Misoprostol combination for first trimester abortion an effective option where cost is not a consideration or in situations where and early abortion is required.

Keywords

First trimester abortion

Mifepristone

Vaginal misoprostone

Comparison

Complete abortion

Post – aortal complications

# INTRODUCTION

MTP act can have an impact on reduction of maternal mortality and morbidity through safe abortion.

Where abortion is legal, it is generally reasonably safe, where it is illegal, complications are common, and about 78,000 women die every year from these complications.

Regardless of personal feelings about the ethics of interrupting pregnancy professionals have duty to know the medical facts about abortion and share them with their patients.

Worldwide, about 46 million women have abortions each year, and about half of these procedures are illegal and considered “unsafe” by the World Health Organization.

Unsafe abortion is a “procedure for terminating an unwanted pregnancy either by person lacking the necessary skills or in an environment lacking the minimal medical standards or both.”

## GLOBAL ABORTION SCENARIO

Globally out of 210 million pregnancies, that occur each year, about 46 million (22%) end in induced abortion of which 20 million is estimated to be unsafe.

Majority of women are likely to have at least one abortion by the time they are 45 years. It is unfortunate and disheartening to note that in spite of liberalized abortion rules there is still one unsafe abortion for every 7 live birth.

**INDIAN ABORTION SCENARIO**

3.1 lakh legal abortions are being performed every year with an abortion rate of 2.3 / 1000 pregnancy.

4.6 million Illegal abortions are being performed every year with an illegal abortion rate of 130-200 / 1000 pregnancy.

**MATERNAL MORTALITY**

Due to legal abortion – 0.7/100,000

Due to criminal abortion – 500 / 100,000.

In developing countries, risk of death following complication of unsafe abortion procedure is much higher than when the abortion was performed professionally under safe condition. Complication of unsafe abortions may lead to sequel such as infertility, chronic PID, TO mass etc. Hence safe and simple abortion procedures and techniques for early-induced abortion are the need of the hour. When performed by trained health care providers with proper equipment, correct techniques and scrutinizing standard, abortion is one of the safest medical procedures.

Safe abortion services as provided by law should be:

- Easily available
- By well trained health care providers
- Regulation of health systems.
- Infrastructure including equipments and supplies

**METHODS AVILABLE FOR FIRST AND SECOND TRIMESTER MTP**

**FIRST TRIMESTER**

1. Menstrual regulation
2. Manual / Electrical vacuum aspiration
3. Dilatation and curettage.
4. Laminaria tent and prostaglandins for cervical dilatation.
5. Medical methods.

**SECOND TRIMESTER**

1. Extra amniotic instillation of ethacridine lactate 1% or 2%
2. Intra amniotic instillation of various agents.
3. Prostaglandins in various combination.
4. Mechanical devices like laminaria tents, catheters.
5. Aspirotomy.
6. Hysterotomy.

Many surgical methods of first trimester MTP have been associated with complications like

- Excessive Bleeding
- Uterine perforation.
- Syncopal attacks.
- Shock.
- Infection.
- Incompetence of os.
- Cervical Stenosis.
- Ashermann syndrome.
- Chronic Pelvic Inflammatory disease.
- Infertility.

Abortion in the first trimester is safe compared to that in the second trimester and medical methods are still safer than surgical techniques.

Medical methods are safe, efficient, simple and results usually in complete abortion of the various medical methods. Mifepristone and Misoprostol have largely replaced other procedures. Both Mifepristone and Misoprostol have been used singly in various doses and also in combination dosage schedule. There are many studies for both and each study claims its schedule to be superior and safer than others.

This study is taken to compare the efficacy, complications and complete abortion rate of Mifepristone and Misoprostol combination and Misoprostol alone in first trimester MTP.

# REVIEW OF LITERATURE

In India the MTP act was passed by parliament in 1971 and came into force on 1st April 1972.

## HISTORY

To reduce high maternal mortality associated with abortion, Govt. of India set up.

- Shantilal Shah committee in 1964, which recommended liberalization of abortion law to decrease MMR.
- Bill presented in Rajya Sabha, and Lok Sabha, in 1969.
- Act passed by parliament in August 1971, Implemented in April 1972 all over India.
- Revised in 1975.
- The act was amended in December 2002, and rules in June 2003.

## I CONDITIONS UNDER WHICH PREGNANCY CAN BE TERMINATED

### (a) Medical Grounds

Continuing of pregnancy might endanger the life of pregnant women.

Can cause grave injury to physical and mental health like, cardiac, renal diseases, diabetes, psychiatric illness.

**(b) Eugenic Grounds**

Risk of child being born with serious physical and mental handicap, hereditary disorder, viral infection.

**(c) Humanitarian Grounds**

Pregnancy due to rape or incest.

**(d) Social Grounds**

Risk or injury to mental health of pregnant women.

Failure of any contraceptive method.

**PROTECTIVE UMBRELLA OF MTP ACT**

Even today voluntarily "Causing miscarriage to a woman with child other than in good faith for the purpose of saving her life" is a crime under section 312 of IPC. Punishable with fine and/or imprisonment.

**II WHO CAN PERFORM MTP**

Any Registered medical practitioner with the following qualifications and/ or experience,

~Who has completed six months of 'House Surgeoncy' in Obstetrics and Gynaecology.

~ Who had experience at any hospital for a period not less than one year in the practice of Obstetrics and Gynaecology.

~ Who has assisted a RMP in the performance of 25 cases of MTP out of which at least five have been performed independently, in a hospital established or maintained, or

A training institute approved by the Government (enabling to do only up to 12 wks of gestation).

~Who holds a PG Diploma or Degree in Obstetrics and Gynaecology.

## III. WHERE CAN BE PERFORMED?

(a) A hospital established or maintained by government, or

(b) At places approved by 'District Level Committee'

These rules in existence since 1972 were amended in 2002 and 2003 to incorporate some newer requirements to MTP and also to plug the lacunae and loopholes in the existing act.

**HIGHLIGHTS OF NEW RULES ARE**

Composition and tenure of District level committee( 3-5 members)

1. One member of District level committee shall be gynaecologist / surgeon/ anesthetist.

2. Other members from the local medical profession, non-governmental organization and panchayat institution.

3. One member of the committee should be a woman.

The tenure of the committee would be for two calendar years and the tenure of the NGO member shall not be for more than two terms.

**APPROVED PLACE**

- ❖ up to 7 weeks – conservative with RU-486 by RMP at his clinic with access to approved place.
- ❖ up to 12 weeks – place approved with the following facilities,
  - Gynaecology examination table/ labour table.
  - Resuscitation and sterilization equipments.
  - Drugs and Parenteral fluids.
  - Backup facilities for treatment of shock and facilities for transportation.
- ❖ Up to 20 weeks -approved place with the following facilities:
  - An operation table and instruments for performing abdominal or Gynaecological surgery,

- Anaesthetic equipments, Resuscitation and sterilization equipments; and

- Drugs and parenteral fluids for emergency use, as notified by government of India from time to time.

**FOR MEDICAL ABORTION**

The clinic where an approved registered medical practitioner prescribes medical drugs does not need a approval.

**EXPERIENCES**

**Up to 20 weeks**

A practitioner should hold PG degree / diploma in obstetrics and gynaecology.

A practitioner who has completed 6 months of house surgency in obstetrics and gynaecology.

A practitioner who has at least one year experience in practice of obstertrics and gynaecology.

**Up to 12 Weeks**

Practitioner who has assisted registered medical practitioner in the performance of 25 cases of MTP, of which at least five has been performed independently in hospital established or maintained by the Govt.

## RCOG GUIDELINES FOR MEDICAL ABORTION

## INFORMATION FOR WOMEN

Verbal advice and printed information has to be given to women

Information to women about procedure

Confidentiality

Informed consent

## GESTATION AGE < 7 WEEKS

- Medical abortion using Mifepristone –Misoprostol is an appropriate method
- Conventional suction termination should be avoided at gestation of < 7 weeks.
- Surgical abortion using rigorous protocol may also be an appropriate method for early termination of pregnancy.

## RIGOROUS PROTOCOL CONSISTS OF

Pregnancy testing

USG before procedure

Inspection of products of conception aspirated using magnification

Follow up with β HCG if gestational sac is not clearly seen.

**RECOMMENDED REGIMENS FOR EARLY MEDICAL ABORTION**

a. 200 mg Mifepristone orally followed by prostaglandin is adequate.

b. Misoprostol, a PG analogue given vaginally is a cost effective alternative for all abortion procedures.

200 mg of Mifepristone is as effective as 600 mg and evidence shows that Mifepristone given vaginally is a cost effective alternate to Gemeprost. (Crenin and Edwards)[1]

Combining Mifepristone with Misoprostol produce higher rate of complete abortion, than when Misoprostol alone is used for this indication. Complete abortion rate for Mifepristone – Misoprostol at < 49 days was 96% and it decreases to 85% at > 57 days. The incomplete abortion rate increases from 2.9 to 10% and method failure rise from 1.1 to 7.2 % with this regimen as gestational age increases.

The addition of more doses of Misoprostol to the Mifepristone - Misoprostol regimen did increase the success rate and reduce both incomplete abortion rate and method failure rate. However incomplete abortion is less with vaginal misoprostol.

- Meta analysis. Kahn et al.2000.[2]

**COMPLICATION AND SEQUELAE (ROYAL COLLEGE OF OBSTETRICS AND GYNAECOLOGY)**

**Hemorrhage** Around 1.5 / 1000 abortions

Rate is less in early abortion

< 13 weeks 1.2 /1000 abortions

>20 weeks 8.5 / 1000 abortions

**Failed or continuation of pregnancy**

Medical abortion 6.0/1000

**Post abortion sequel**

PID upto 10%

Rate is decreased when prophylactic antibiotics are used.

**Future reproductive performance**

No proven association between induced abortion and subsequent preterm delivery or infertility.

**Psychological Sequel**

Only a small percentage of women experience a feeling of guilt.

## METHODS OF FIRST TRIMESTER ABORTION

### Medical methods

- Prostaglandins
- Methotrexate
- Mifepristone (RU 486)
- Mifepristone with PG analogues. [Ashok Et al 1998 and other studies][3,9]

## PROSTAGLANDINS

Blanchard K et al feels that Misoprostol when used alone hold promise for early termination of pregnancy. ( Blanchard K et al 2000).[10]

Various studies using 800 microgram of Misoprostol administered 24 to 48 hrs apart shows success rates between 85% and 92% percentage-- Ngai SW et al., 2000.[11]

Tang and Ho tried 400 microgram of Misoprostol up to maximum of 5 doses sublingually for second trimester abortion with success rate of 100%.[12]

The prostaglandins other than Misoprostol like Gemeprost – was tried in various regimens. (Kuldipsingh et al BJOG, Feb – 2003).[13]

Misoprostol is effective, less expensive than Gemeprost and it does not need refrigeration – ( RCOG 2004).[14]

**METHOTREXATE**

Methotrexate (both oral and intra muscular) combined with Misoprostol have been under investigation since 1993 with complete abortion rates similar to Mifepristone regimens for pregnancies up to 49 days gestation.(CreninMd, et. al 2000).[15]

50 mg/m body surface area of Methotrexate followed by 800 microgram of Misoprostol from day 3 to day 7, have shown to result in complete abortions in 83 to 96% of cases.(Crenin Md, 2000 and other studies)[15-19]

It was observed that abortion using Methotrexate and Misoprostol takes longer and may take up to 5 weeks in 20 to 30% of women.

Use of Methotrexate for first trimester abortion is only of academic interest since WHO toxicity panel recommended against Methotrexate use due to its teratogenicity.

**MIFEPRISTONE**

Mifepristone an antiprogestin currently being used extensively for first trimester MTP. It acts by binding with progesterone receptor and inhibits the action of progestin, hence interface with the continuation of pregnancy.

After confirming the eligibility to undergo medical abortion, 600 mg of Mifepristone is administered orally or day 1.

On day 3, the patent is assessed for the possibility of pregnancy expulsion, which occurs in 2 to 5% of patients with Mifepristone alone.

**MIFEPRISTONE WITH PG ANALOGUES**

This is the most widely accepted method of early medical abortion.

Original protocol is 600 mg of Mifepristone orally on day 1 followed by prostaglandin analogues on day 3. This has been associated with a success rate of 95% (Trussell and Ellertson 1989).[7]

In order to reduce the cost of 600 mg of Mifepristone lower dose was tried.

Later it was thought that 200 mg of Mifepristone is as efficacious as 600 mg of Mifepristone –(MC Kinley et. al 1993).[20]

Then Mifepristone in the doses of 200, 400 & 600 were tried followed by a vaginal Gemeprost 48 hrs later. The success rate of above dosage regimens was found to be 93.8%, 94.1% and 94.3% respectively. The overall continuation of pregnancy rate was 0.4% in all the regimens.(WHO task force on post-ovulatory method of fertility, BMI, 1993)[21].

Two large trials with 2000 clients also confirmed the efficacy of 200 milligram of oral Mifepristone with Misoprostol vaginally (Ashok PW[3], Schaff EA[22], CContraception1999).

There was a randomized trial conducted in order to reduce the doses of Mifepristone to 50 mg orally followed 48 hrs later by Gemeprost for early medical abortion. However the relative risk of failure with lower dose was calculated to be 1.6 times the higher dose. (WHO task force on postovulatory method for fertility regulation, BJOG,2001).[23]

A large randomized study as to the most effective route of administration of Misoprostol following Mifepristone was conducted in which 800 microgram of Misoprostol was administered vaginally or orally. The study found the vaginal route to be more efficacious with a complete abortion rate of 93%. The same after oral route was 78%. The failure rates were also higher in the oral route (7%) compared to the vaginal administration of Misoprostol (1%) (EL Refaey, 1995).[24]

Many do not prefer Mifepristone and Sulprostone combination as there is a high rate of MI follows Sulprostone use.( Meta analysis, Kahn et at. 2000).[2]

The following combined regimen is recommended by RCOG for MTP with a pregnancy up to 9 completed weeks since LMO (2000).[14]

200 mg Mifepristone followed by 36 – 48 hrs by 1.0 mg of vaginal Gemeprost.

OR

800 mcg vaginal Misoprostol

OR

400 mcg oral Misoprostol up to 7 weeks.

All these were found to result in 98 % complete abortion

(*Trussell – Ellertson 1989)*[7]

**Parity and success rates of early medical abortion**

| Gestation | Nulliparous % | Parous % |
|---|---|---|
| < 7 weeks | 98.6 | 96.2 |
| 7-8 weeks | 98.3 | 93.1 |
| 8-9 weeks | 96.4 | 91.0 |
| > 9 weeks | 73.3 | 83.0 |

1. In Nulliparous women gestational age have no influence on the outcome of pregnancy termination in early weeks.

2. However after 9 weeks of pregnancy, there was a significantly lower rate of complete abortion.

3. In parous women the complete abortion rate was lower after 7 weeks.

(*Bartely et at, contraception ,2000*)[25]

Three regimens of Mifepristone + Misoprostol combination for early medical abortion was advocated by Helene et al.

| REGIMEN I | REGIMEN II | REGIMEN III |
|---|---|---|
| Ru 486 200 mg PO day 1<br>+<br>800 mcg miso PO day 3<br>+<br>400 mcg miso PO Bd 7 days | Ru 486 200 mg PO. day 1<br>+<br>800 mcg miso PV day 3<br>+<br>400 mcg miso PO Bd 7 days | Ru 486 200 mg PO day 1<br>+<br>800 mcg miso PV day 3 |
| Complete abortion rate 92% | Complete abortion rate 94.7% | Complete abortion rate 93.5% |

*Helene et al BJOG, Sept 2003*[26]

However studies from ICMR has shown 200 mg of Mifepristione followed 36-48 hrs by 400 meg of oral or vaginal Misoprostol to be equally efficient with a Complete abortion rate of 95 % - 99% - ICMR 1994[27], Aubeny B. Baulieu 1991.[28]

**On Going Trials**

A large multicentric trial by WHO on Mifepristone and Misoprostol as an abortificient in women with amenorrhoea up to 63 days is being conducted. The results may reveal more useful information on the efficacy of these drugs as a medical method of termination of early pregnancy.**(WHO 1994)**[29]

**CONTRA INDICATION FOR MIFEPRISTIONE – MISOPROSTOL REGIMEN**

1. Severe anemia
2. Adrenal failure
3. Medical disease that preclude use of Misoprostol
4. Suspected ectopic pregnancy
5. Bleeding disorders (WHO, 2000)[30]

**SURGICAL METHODS OF FIRST TRIMESTER MTP**

1. Menstrual regulator (MR)
2. Vacuum aspiration
3. Suction evacuation / curettage

**IMMEDIATE COMPLICATIONS OF SURGICAL METHODS**

1. Excessive Bleeding
   - (a) Uterine atony
   - (b) Retained products of conception
   - (c) Uterine perforation
   - (d) Cervical laceration
   - (e) Post abortal syndrome
2. Syncopal attacks

3. Shock

4. Infection

**DELAYED COMPLICATION**

1. Incompetence of os

2. Cervical Stenosis

3. Ashermann Syndrome

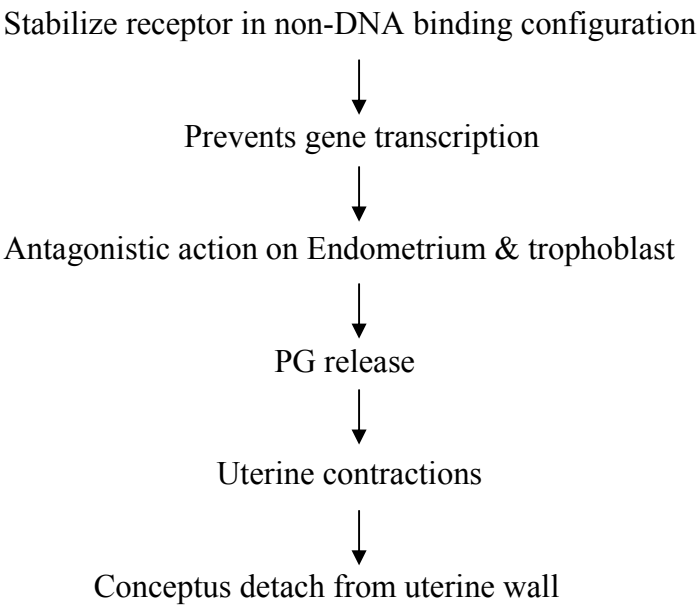
4. Chronic Pelvic Inflammatory Disease

5. Infertility

**MIFEPRISTONE (RU -486)**

Discovered by French biochemist Dr.Etienne-Emile Baulieu consultant to Roussel Uclaf company. Mifepristone is a 19 Nor-testosterone derivative [17beta-hydroxy-11beta-(4-dimethylaminophenyl)-17alpha-(1-propynyl)-estra-4,9-dien-3-one] which is an antiprogestin. Due to its high affinity for progesterone receptor it competitively binds them.

The postulated mechanism of action is:




**USES**

**I ABORTIFACIENT**

- It acts on target cells of endometrium & decidua[31]
- Affects the pituitary gonadotrophic cells producing remarkable decrease in LH level which results in leuteolysis and shedding of endometrium.[31]
- Softens and ripens the cervix and produce increased release of myometrial prostaglandin resulting in expulsion of products of conception.[32]
- It also increases the sensitivity of uterus to exogenous prostaglandins.
- Anti glucocorticoid agent.
- Weakly antiestrogenic[34]

Rodger, Baird B.J.O.G, Baulieu EE. 1989 Medline, Henshaw RC, TempletonAA, Johnstudd, 1993. Baird 1993.

## II CONTRACEPTIVE

- Continuous administration of the drug in a dose of 20 mg from day1to30 days inhibits ovulation and delays menstruation.[35]
- Administration of 100 mg Mifepriston, 5 and 8 days after LH surge results in defective secretory endometrium.[35]
- Each month, administration of the drug in late luteal phase induces menstruation whether or not pregnant.[34]
- As an emergency contraceptive – 600 mg of Mifepristone within 72 hrs of unprotected coitus has 100% success rate.

  (Wolf JP.Contr.- Barid DT. Contraception 1993, Van Sankon and Haspel 1987 / IPPF Med Bull 1988).[35-37]

## III. CERVICAL DILATATION

To ripen the cervix prior to surgical method of MTP

Reduce the induction – abortion interval in medical method

- Urquahat DL. Templeton AF Contraception 1990.[38]

## OTHER SYNERGISTIC USES

❖ Endometriosis - Continuous use up to 3 months

- Kettle LM – Fertility – Sterility[39]/99/56

- ❖ Uterine leiomyoma - 49% reduction of tumor size with 3-month use.

  - Howitz KB, Murphy Clinical Endocrin.[40]

- ❖ Cushing's syndrome - For unresectable humour

  - Grun Berg Neuro Surgery 1991[41]

  - Neiman LK et. al, J. Clinical Endo 1985[42]

- ❖ For unruptured ectopic - Mifepristone instilled results in resolution of sac-trophoblast.

- ❖ Glaucoma

- ❖ Viral infections

**PHARMACOKINETICS**

Following oral administration of Mifepristone it rapidly gets absorbed with peak plasma level of 1.89 in 90 minutes.

98% bound to plasma proteins – albumin an acid glycoprotein.

Following distribution phase, elimination of Mifepristone is slow, the first 50% being eliminated in 12-17hrs followed by a more rapid elimination.

T ½ -18hrs.

Metabolism via hepatic microsomal enzyme – iso enzyme cytP450-3A4

By 11 days after 600mg of drug 80% is excreted in faeces & 9% in urine.

Serum levels are undetectable after 11 days.

**CONTRAINDICATIONS FOR MIFEPRISTONE**

1. Confirmed or suspected ectopic pregnancy.
2. Undiagnosed adnexal mass
3. IUD in place
4. Hemorrhagic disorder or concurrent anticoagulant treatment
5. Inherited porphyrias
6. Chronic adrenal failure
7. H/o allergy to Mifepristone or to other prostaglandins
8. Concurrent steroid treatment.

-WHO 2002[30]

**DRUG INTERACTIONS**

**Drugs that increase the serum level of Mifepristone (through CytP-450-3A4):**

Ketoconazole

Itraconazole

Erythromycin and

Grape Juice

**Drugs that decrease the serum level of Mifepristone**

Rifampicin

Dexamethasone

Phenytoin

Carbamazepine

Phenobarbitone.

**Drug side effects**

Abdominal pain

Uterine cramping

Diarrhoea

Headache

Dyspepsia

Pelvic pain

Hypertension

Hashimoto’s thyroiditis

**MISOPROSTOL ($C_{22}H_{38}O_5$)**

It is a 11-alpha,16-Dihydroxy-16-methy1-9-oxoprost –13E –en-1- oic acid methyl ester. It is a synthetic prostaglandin structurally related to $PGE_1$

Available as 100 mcg and 200-mcg tablet

**Each tablet has**

- Hydrogenated castor oil
- Hydroxy propyl methylcellulose.
- Microcrystalline cellulose
- Sodium starch glycolate

Misprostol inhibits gastric acid secretion & promotes bicarbonate secretion. It is mucoprotective and is used in drug-induced gastric and in duodenal ulcer. Misoprostol softens the cervix, produce uterine contractions without exerting any adverse effect on mother and fetus.

It is also used in second trimester abortion

No evidence of fetotoxic, teratogenic, carcinogenic effect in animal studies.

- Oriole IM Br.J.Obst.gy. 2000[43]

**PHARMACOKINETICS**

- Rapidly absorbed orally
- Rapid de-esterification to its acid which is responsible for clinical activity
- Reaches peak serum level in 15-30 minutes
- Half-life 20- 40 minutes.
- Can be stored in ordinary temperature
- Vaginal application is better than oral route for MTP.

**Dosage**

1. First trimester MTP along with mifepristone 600 mg orally followed 48 hrs later by 800 mcg of oral or vaginal misoprostol.
2. Second trimester along with mifepristone in various doses in various regimens

**Side effects**

- Nausea
- Vomiting
- Headache
- Diarrhea
- Hypotension
- Excessive Bleeding
- Abdominal / Uterine cramps

# AIMS AND OBJECTIVES

- **To assess the efficacy of Mifeprostone & Misoprostol combination in first trimester abortion**
- **To compare this combination with vaginal Misoprostol alone for first trimester MTP**
- **To compare the various parameters involved in MTP in both the methods & assess the most suitable method for first trimester MTP.**

# MATERIALS AND METHODS

The present study was carried out at K.A.P.VISWANATHAM MEDICAL COLLEGE, TRICHY during academic year 2010-2012.

The purpose of study is to compare the efficacy of Mifeprostone – vaginal Misoprostol combination with vaginal Misoprostol as a method of first trimester abortion.

**Study design** : Comparative Study

**Study place** : K.A.P.VISWANATHAM medical college,Trichy.

**Study Population** : Patients requesting MTP who attended family welfare/ Planning Dept. at K.A.P.VISWANATHAM medical college, Trichy

**Sample size** : 100 (Random Allocation to either of groups)

50 – Mifepristone + Misoprostol Group

50 – Misoprostol Group

**Year of Study** : July 2010 – July 2011.

**INCLUSION CRITERIA**

1. Confirmed pregnancy upto 9 weeks
2. Single intra uterine live gestation
3. No other medical or surgical contra-indication for the procedure.

4. Contraceptive failure.

5. MTP for social & eugenic causes.

**EXCLUSION CRITERIA**

- ❖ Gestation age > 9 weeks
- ❖ Women smoke >10 cigarettes abortion
- ❖ Missed / incomplete / inevitable abortion
- ❖ Suspected ectopic pregnancy
- ❖ Any previous attempts at terminating the present pregnancy
- ❖ Pregnancies with IUD in situ.

**METHODOLOGY**

All these women were thoroughly investigated before MTP. The work up included;

- ❖ Details of patient
- ❖ Investigations
- ❖ Examination of vital signs
- ❖ Abdominal and pelvic examination
- ❖ USG only on Indication
- ❖ Counseling

Such of those women who were willing to adhere to the protocol were include for the study, provided they fulfilled the inclusion criteria.

**DETAILS OF PATIENT**

Name

Age, address

Socio economic status

Obstetric Formula

Menstrual history

Marital history

Obstetric history

Medical history

Surgical history

Examination of patient

General Examination

Abdominal Examination

Bi-manual pelvic examination

Routine Investigations like

Urine - Albumin

Sugar

Hb%

ABO, Rh typing (if not done early)

VDRL

HIV [with patient consent]

All these women are informed about the procedure.

An informed consent was obtained from these selected women.

**MIFERISTONE – MISOPROSTOL GROUP**

The Mifeprostone – Misoprostol protocol is an out-patient procedure. Very few women who will not be in a position to reach the hospital in time, if there is bleeding, severe pain, vomiting etc. were admitted on humanitarian and medical grounds.

**Dosage schedule**

**Day 1** - 200 mg of Mifepristone was given orally. They were informed about symptoms and were asked to return to the hospital if the symptoms are severe.

**Day 3** - 400 µg of Misoprostol kept vaginally and observed for 4 hrs in OP dept. 90% expelled within 4 hrs.

Such of these women who did not expel within 4-6 hrs after vaginal Misoprostol were given the option of either going home and coming back on

day 15 or admission in the hospital. Such of those women who preferred admission were admitted till the abortion is complete.

If evacuation is not complete even after 15 days it was considered as failure and the patients were offered other methods of termination.

**MISOPROSTOL GROUP**

50 patients were selected for vaginal Misoprostol method of first trimester MTP.

**Procedure**

Patient was asked to empty the bladder and was asked to lie down in the dorsal position with knee semi flexed and hip abducted. After cleaning and draping, a Sim's speculum was introduced into vagina and posterior lip of cervix was caught with volsellum.

400 µg Misoprostol was kept in posterior fornix and repeated 4 to 6 hrs apart depending on response (maximum 3 doses).

5 ml of distilled water instilled to dissolve the tablet and facilitate the absorption through mucosa.

Patient kept in the ward till expulsion is complete – wherever necessary, check curettage was performed.

If no expulsion occurred after 20 – 24 hrs it is considered as a failure and other interventions offered.

Advised about the symptoms like,

Nausea / vomiting / diarrhoea

Abdominal Cramps

Headache

Bleeding

# RESULTS AND ANALYSIS

## TABLE 1: AGE

| S.NO | AGE | Mifepristone + Misoprostol | | Misoprostol | |
|---|---|---|---|---|---|
| | | No. of cases | % | No. of cases | % |
| 1 | 18-20 | 4 | 8 | 3 | 6 |
| 2 | 21-25 | 20 | 40 | 22 | 44 |
| 3 | 26-30 | 18 | 36 | 15 | 30 |
| 4 | >30 | 8 | 16 | 10 | 20 |

Most of patients in both the groups were in age group of 20-30 years(75%).

In our study 16% of women from Mifepristone+Misoprostol combination belongs to age group of above 30 and only 8% in the above combination group were below 20 years. The difference is of minimal significance ($p = 0.001$).

**DISTRIBUTION OF AGE (18-30 AND ABOVE)**

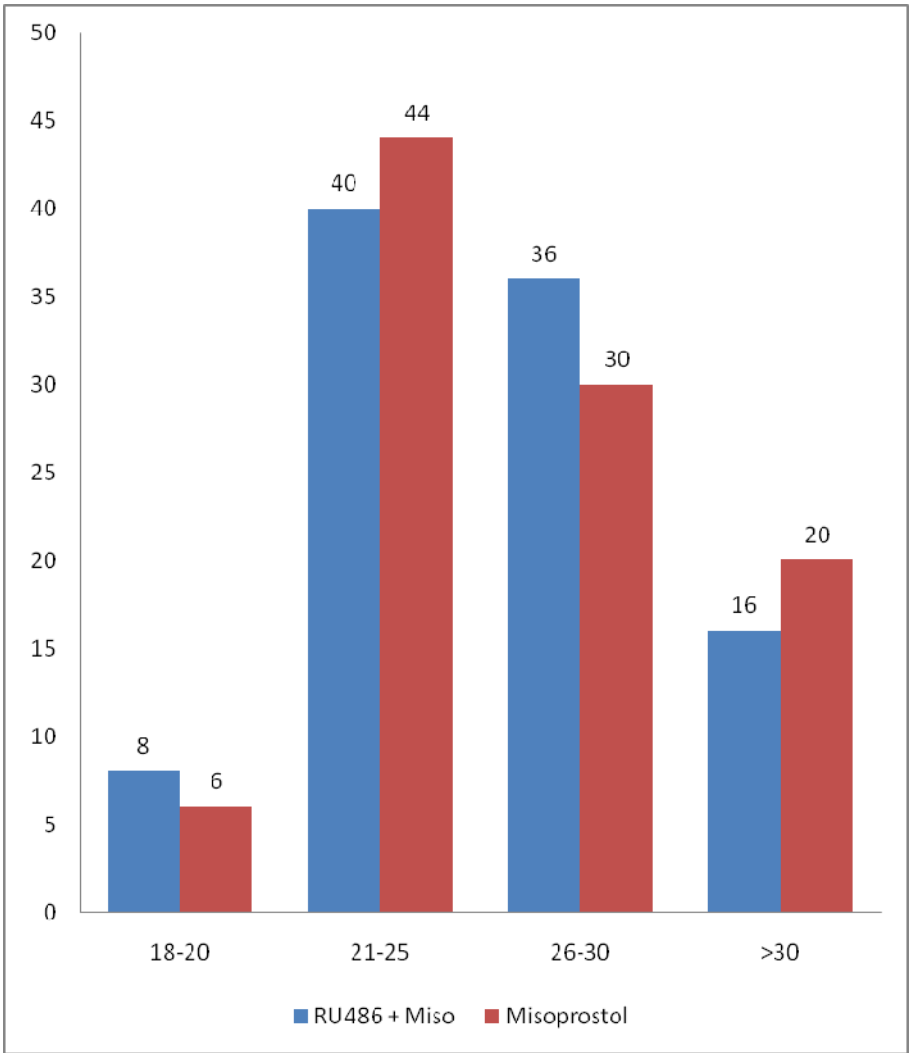


**TABLE 2: PARITY**

| S.No | Parity | Mifepristone + Misoprostol | | Misoprostol | |
|---|---|---|---|---|---|
| | | No. of cases | % | No. of cases | % |
| 1 | UMP | 2 | 4 | - | 0 |
| 2 | Primi | 4 | 8 | 4 | 8 |
| 3 | $G_2$ | 36 | 72 | 38 | 76 |
| 4 | $G_3$ | 8 | 16 | 8 | 16 |

80% of women is both groups were parous whereas only 4% unmarried pregnancy noted in Mifespristone + Misoprostol group. None of them were unmarried in Misoprostol group.

**DISTRIBUTION OF PARITY**

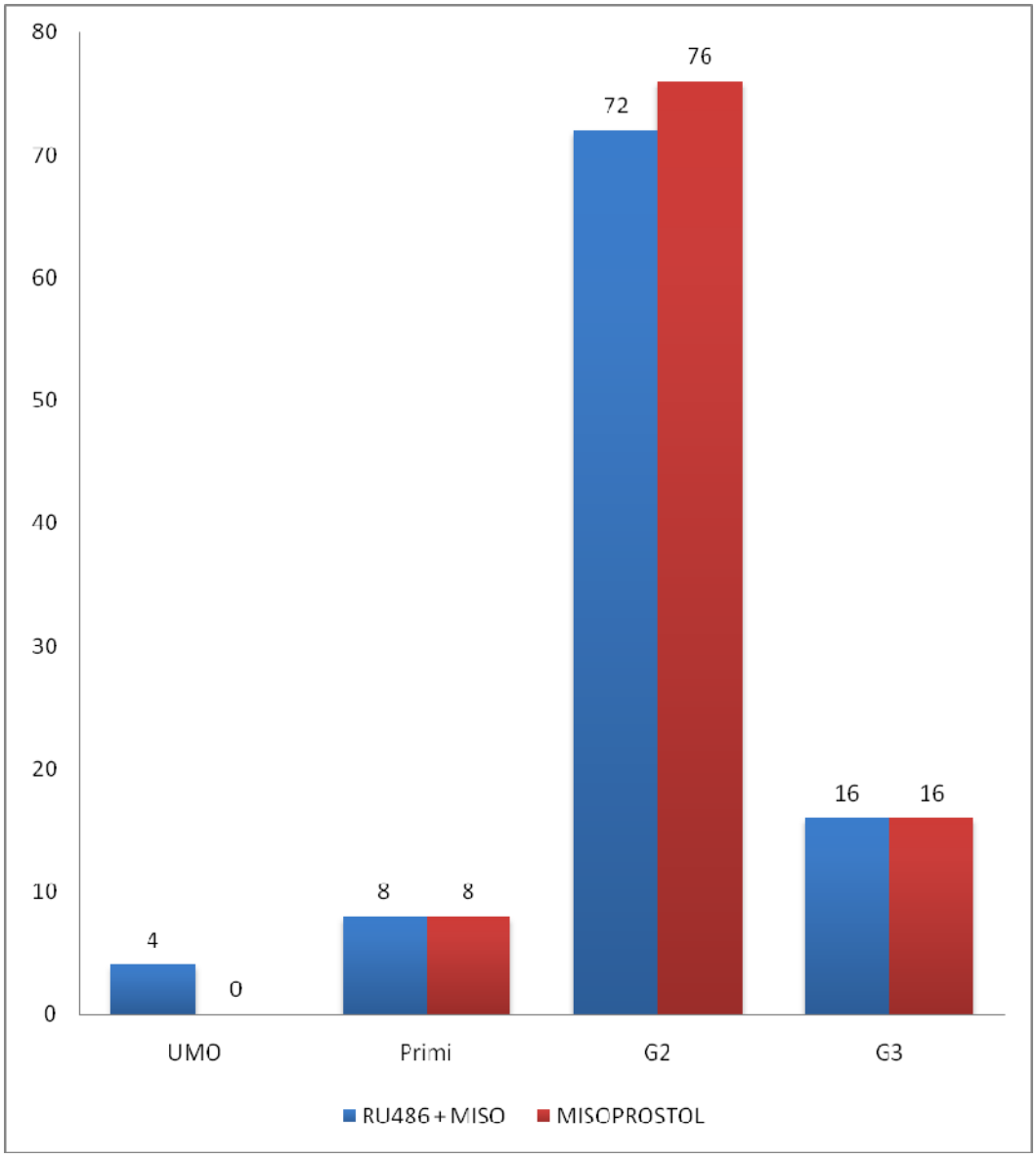


**TABLE 3 : ANALYSIS OF SOCIO ECONOMIC STATUS**

| S.NO | Status | Mifepristone + Misoprostol | | Misoprostol | |
|---|---|---|---|---|---|
| | | No. of cases | % | No. of cases | % |
| 1 | Class I / II | 2 | 4 | 0 | 0 |
| 2 | Class III | 8 | 16 | 6 | 12 |
| 3 | ClassIV/V | 40 | 80 | 44 | 88 |

≥ 80% of women in both groups belong to Socio-economic status of IV / V.

## DISTRIBUTION OF SOCIO ECONOMIC STATUS

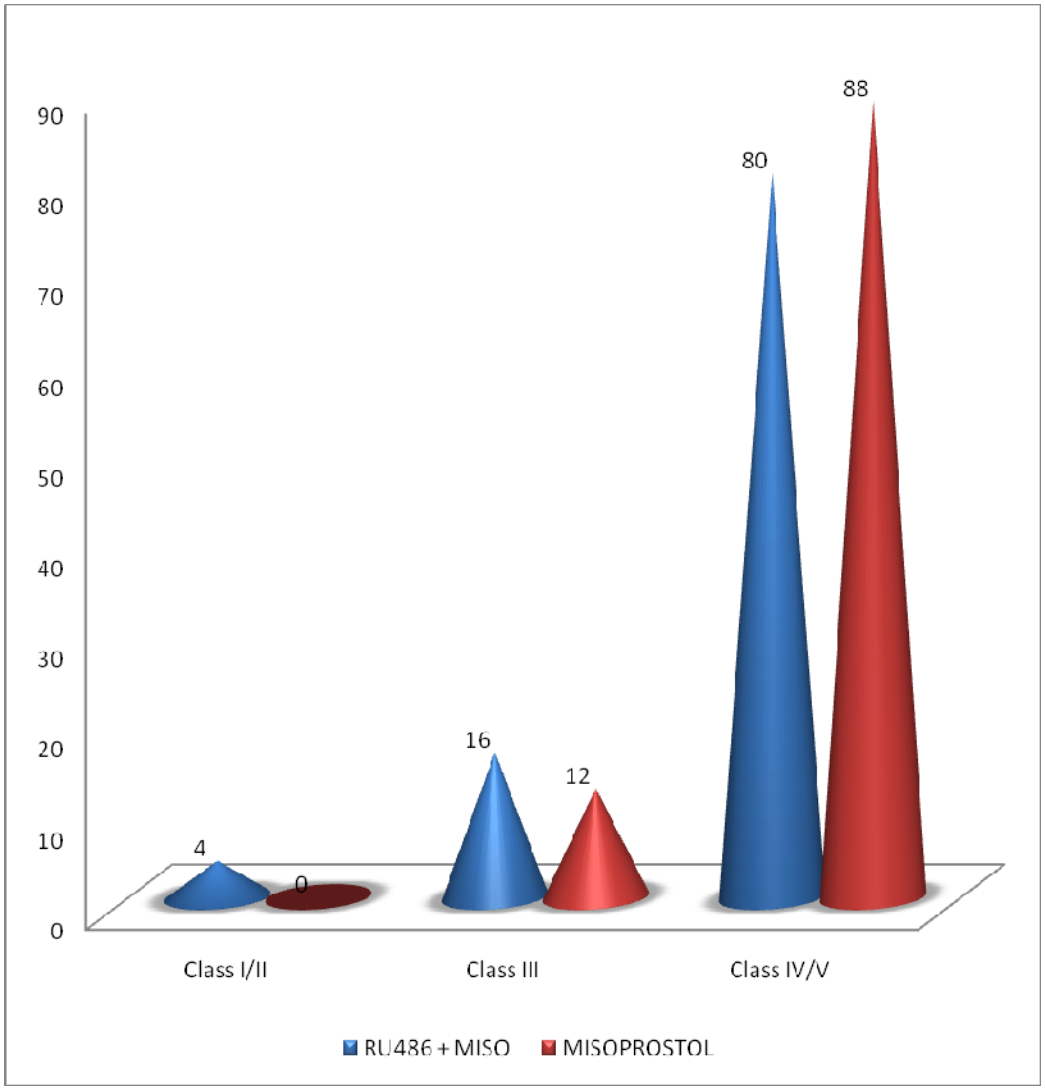


**TABLE 4 : GESTATIONAL AGE**

| S.NO | Gestational Age | Mifepristone + Misoprostol | | Misoprostol | |
|---|---|---|---|---|---|
| | | No. of cases | % | No. of Cases | % |
| 1 | <45 Days | 30 | 60 | 18 | 36 |
| 2 | 45-56 Days | 15 | 30 | 28 | 56 |
| 3 | >56 Days | 5 | 10 | 4 | 8 |

60% of women in Mifepristone + Misoprostol group where in the gestational age of < 45 days whereas only 10% of women where in gestational age of above 56 days, on the contrary 56% of women in Misoprostol group belong to gestational age of 45-56 days.

## DISTRIBUTION OF GESTATIONAL AGE

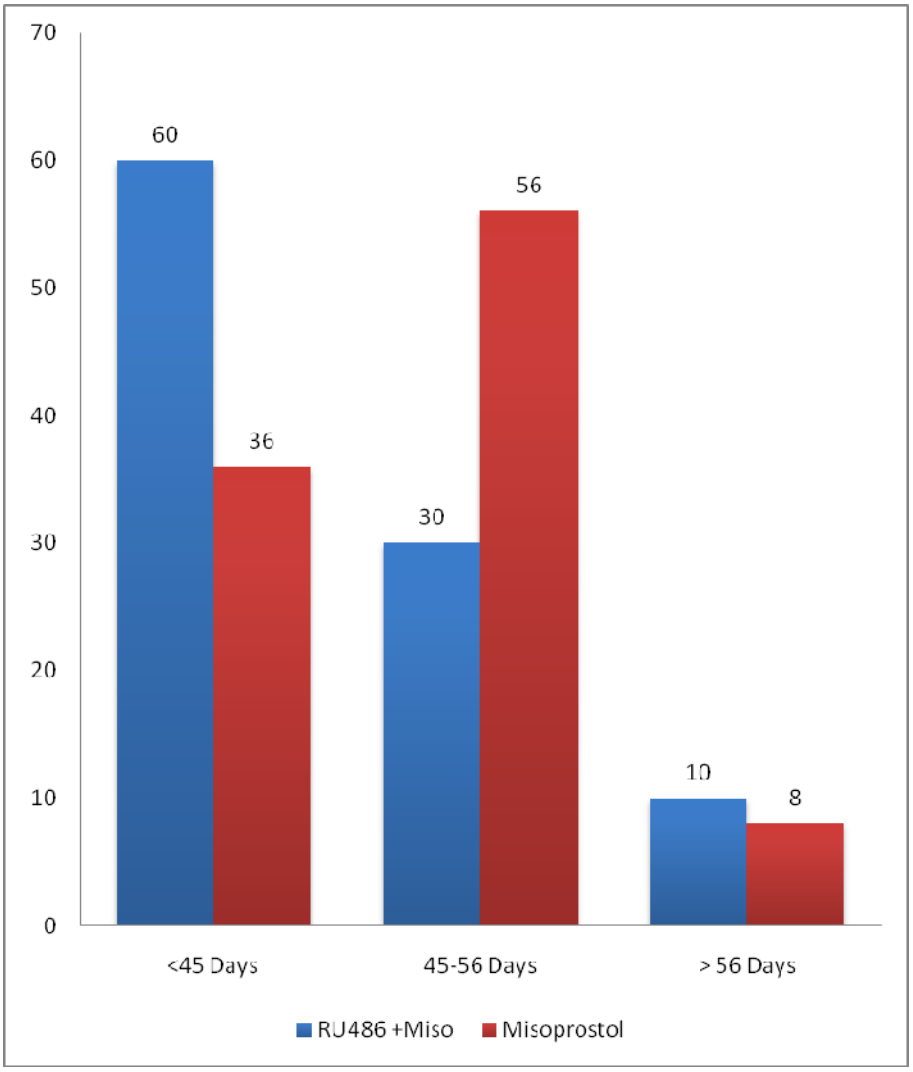
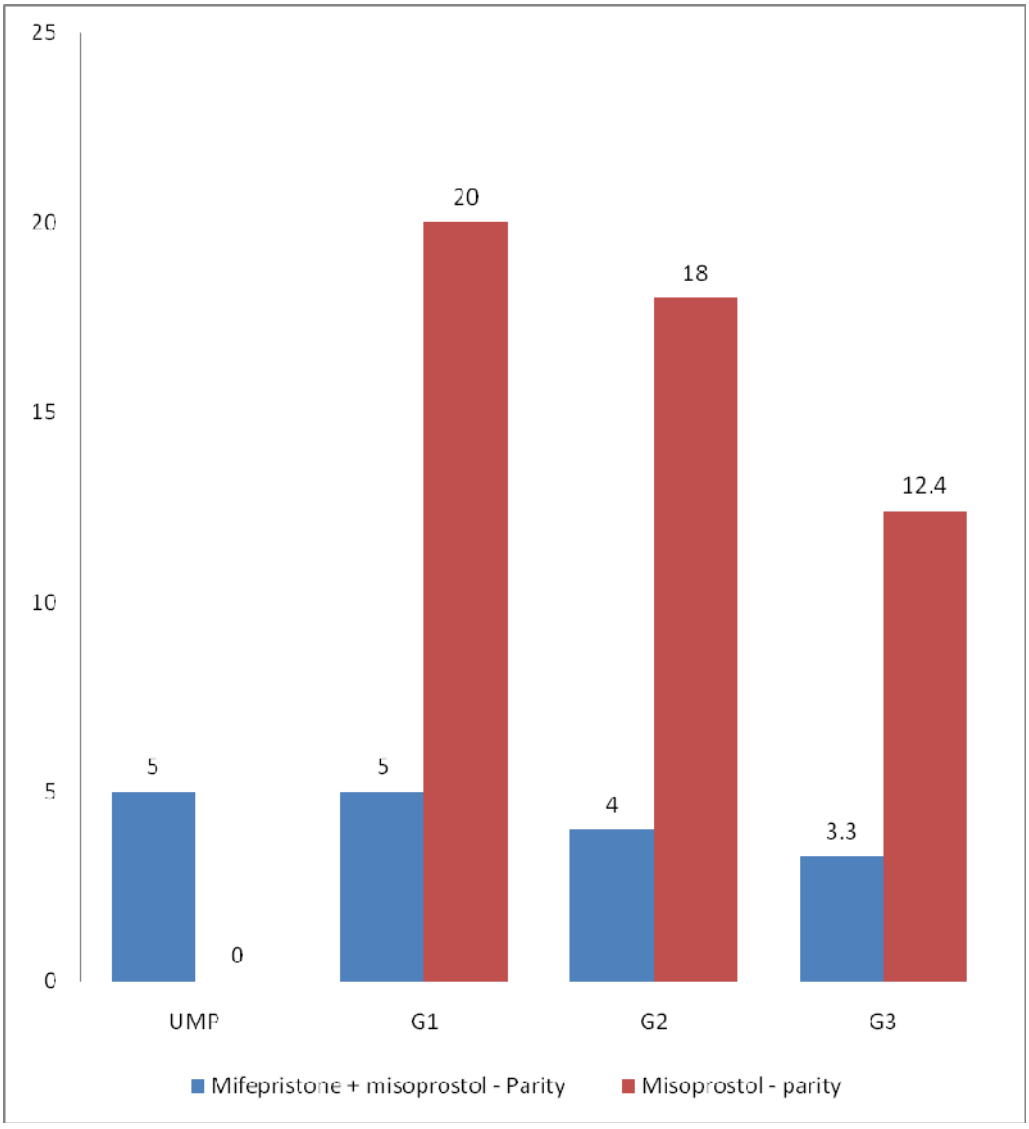


**TABLE 5: INDUCTION ABORTION INTERVAL**

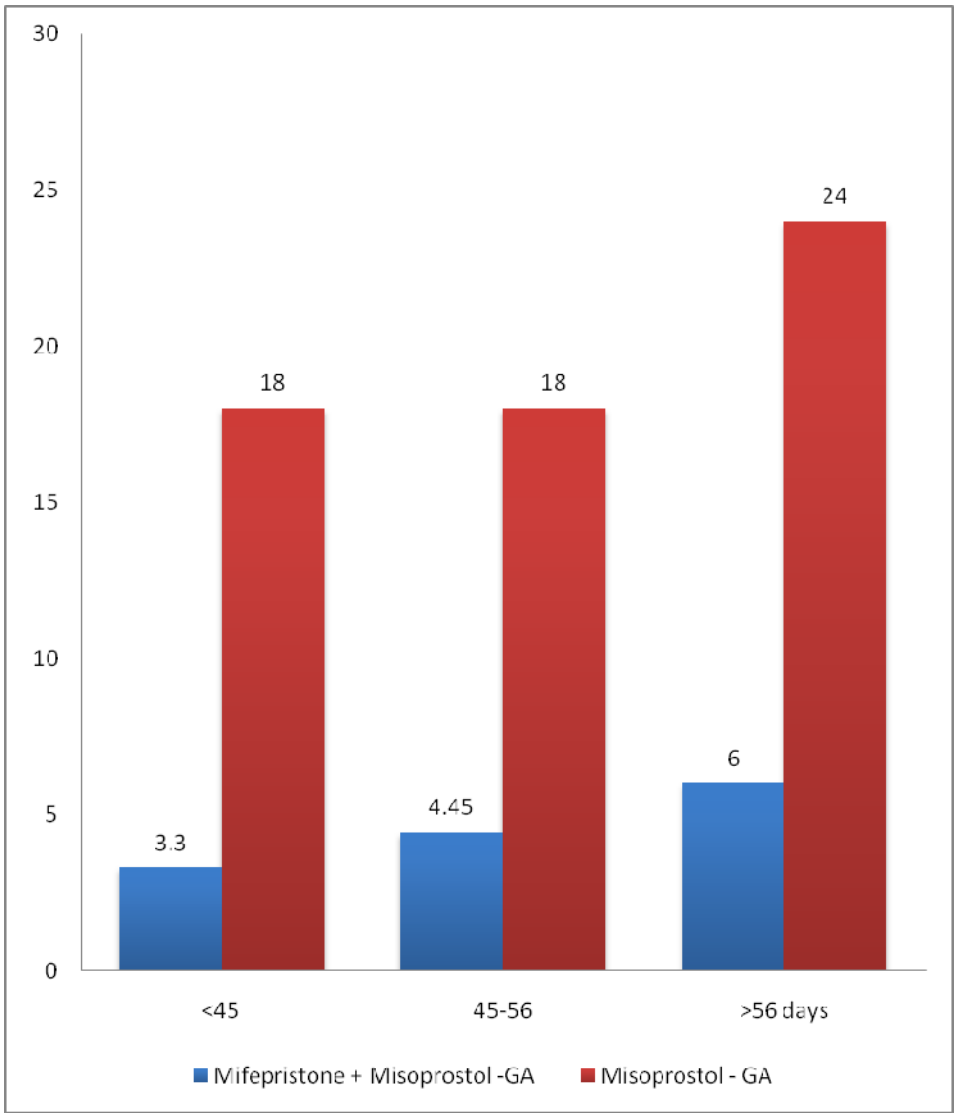
| **Characters** | | **Mifepristone + Misoprostol (in Hrs).** | **Misoprostol** |
|---|---|---|---|
| Parity | UMP | 5.00 | - |
| | G1 | 5.00 | 20 |
| | G2 | 4.00 | 18 |
| | G3 | 3.30 | 12.40 |
| GA | <45 | 3.30-4.00 | 18 |
| | 45-56 | 4-4.30 | 18 |
| | >56 days | 6.00 | 24 |

When the induction abortion interval between Mifeprostone and Misoprotol combination is compared with that of Misoprostol alone it showed a 'p' value of 0.000 there by indicating that the reduced interval in the Mifepristone+ Misoprostol group is significant.

## INDUCTION – ABORTION INTERVAL



## INDUCTION – ABORTION INTERVAL



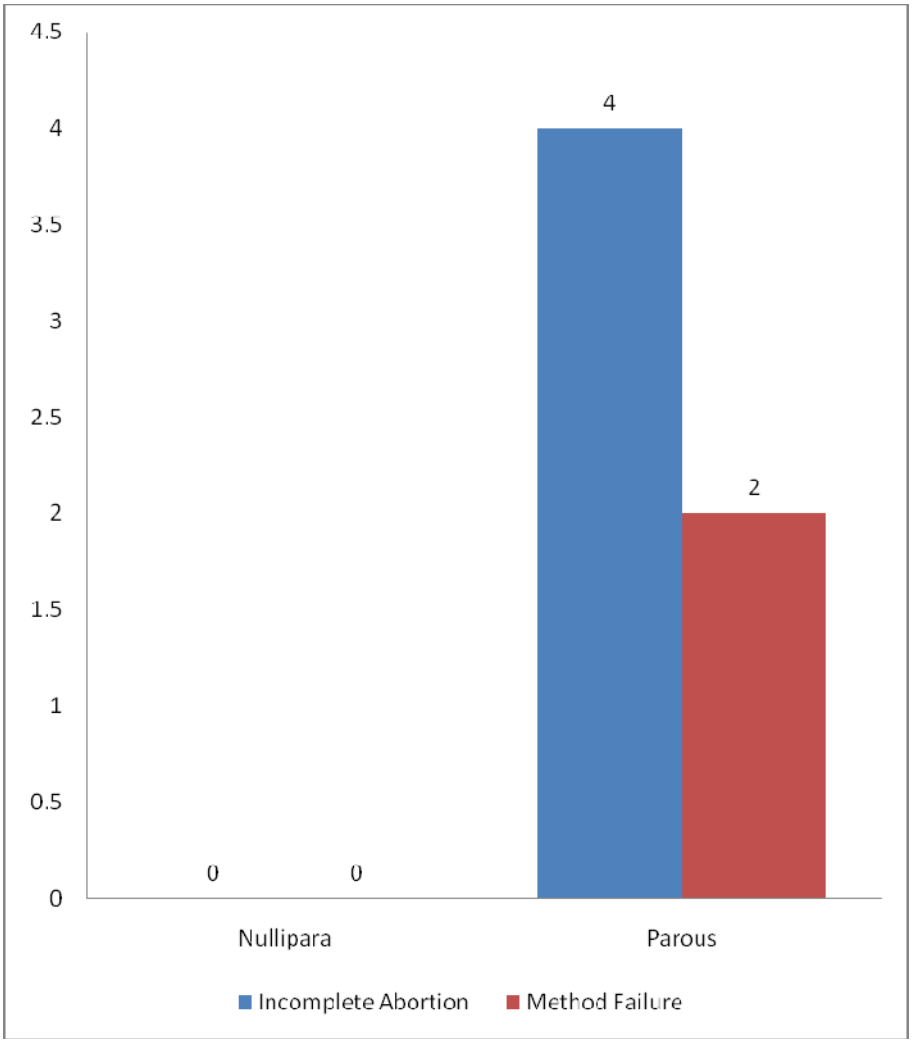
## TABLE 6: ANALYSIS OF COMPLETE ABORTION

| SI. No | Characters | Mifepristone + Misoprostol | | | | Misoprostol | | | | P value |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Incomplete Abortion | | Method Failure | | Incomplete Abortion | | Method Failure | | |
| | | No. Of Cases | No. Of % | No. Of Cases | No. Of % | No. Of Cases | No. Of % | No. Of Cases | No. Of % | |
| 1 | Nullipara | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.000 |
| 2 | Parous | 2 | 4 | 1 | 2 | 24 | 48 | 5 | 10 | |

Complete abortion rates in the two groups showed a significant variation in favour of Mifepristone – Misoprostol combination.

**ANALYSIS OF MIFEPRISTONE +**

**MISOPROSTOL RESUTS**



## ANALYSIS OF MSOPROSTOL RESULTS

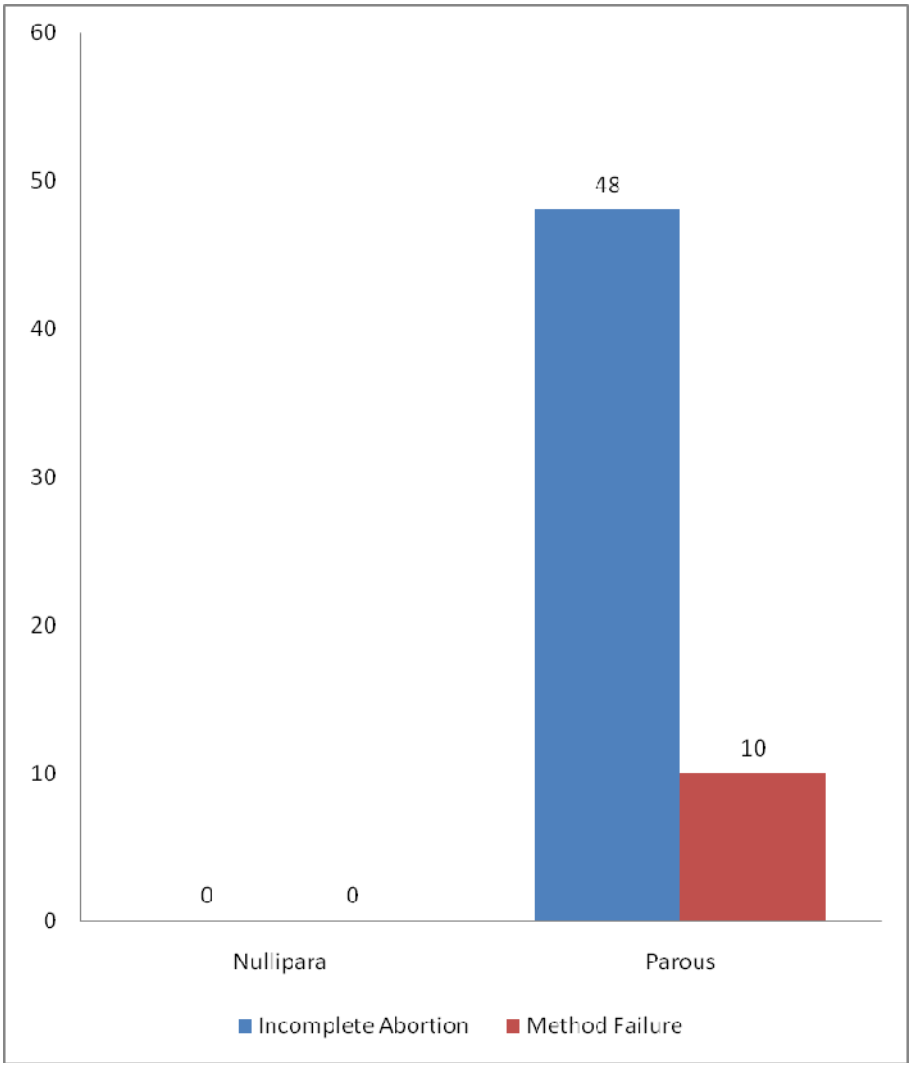


**TABLE 7 : ANALYSIS OF SYMPTOMS**

| SI. No | Symptoms | Mifepistone + Misoprostol | | Misoprostol | |
|---|---|---|---|---|---|
| | | No. of Cases | % | No. of Cases | % |
| 1. | Symptom free | 0 | 0 | 0 | 0 |
| 2. | Abd / Ut. cramps | 30 | 60 | 16 | 32 |
| 3. | Excessive bleeding | 14 | 28 | 22 | 44 |
| 4. | Vomiting | 4 | 8 | 12 | 24 |
| 5. | Dizziness | 2 | 4 | 0 | 0 |

Comparing the significance of variables in the symptoms, both groups showed statistically incidence of side effects. However a larger study will be required to confirm the results ( $p = 0.0001$).

**ANALYSIS OF SYMPTOMS**

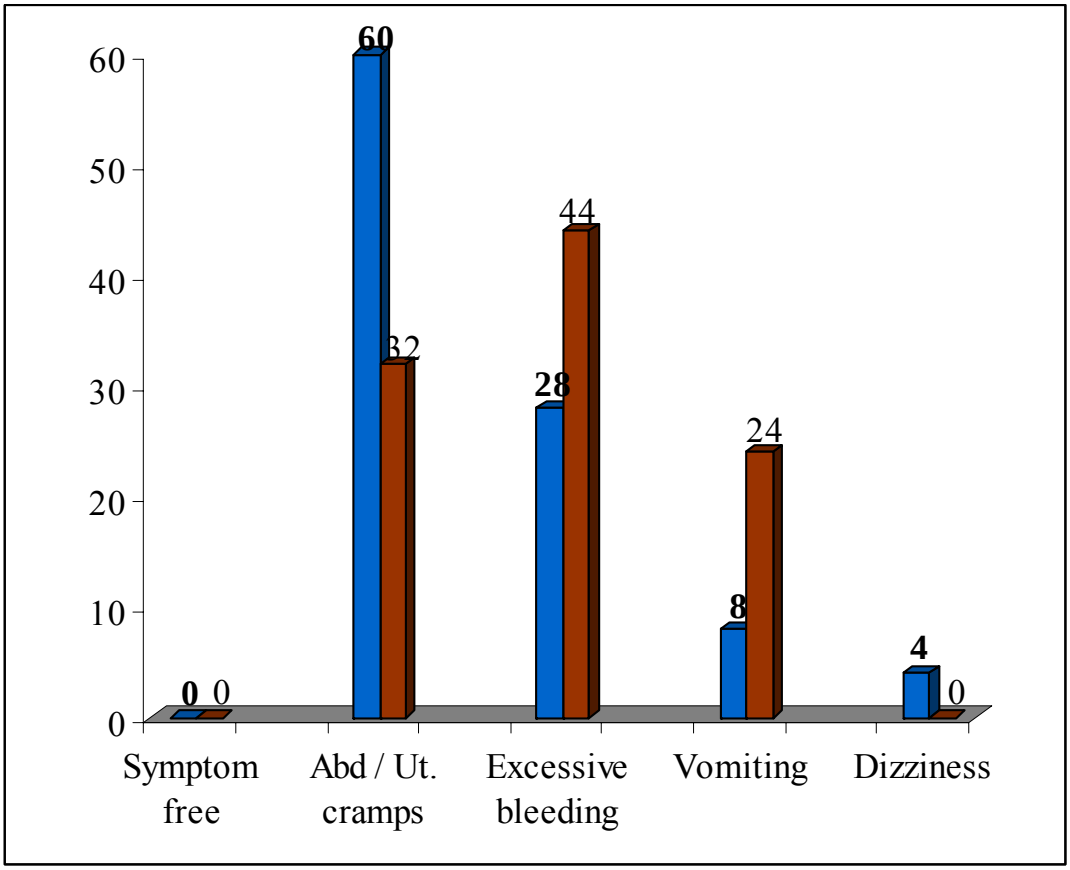
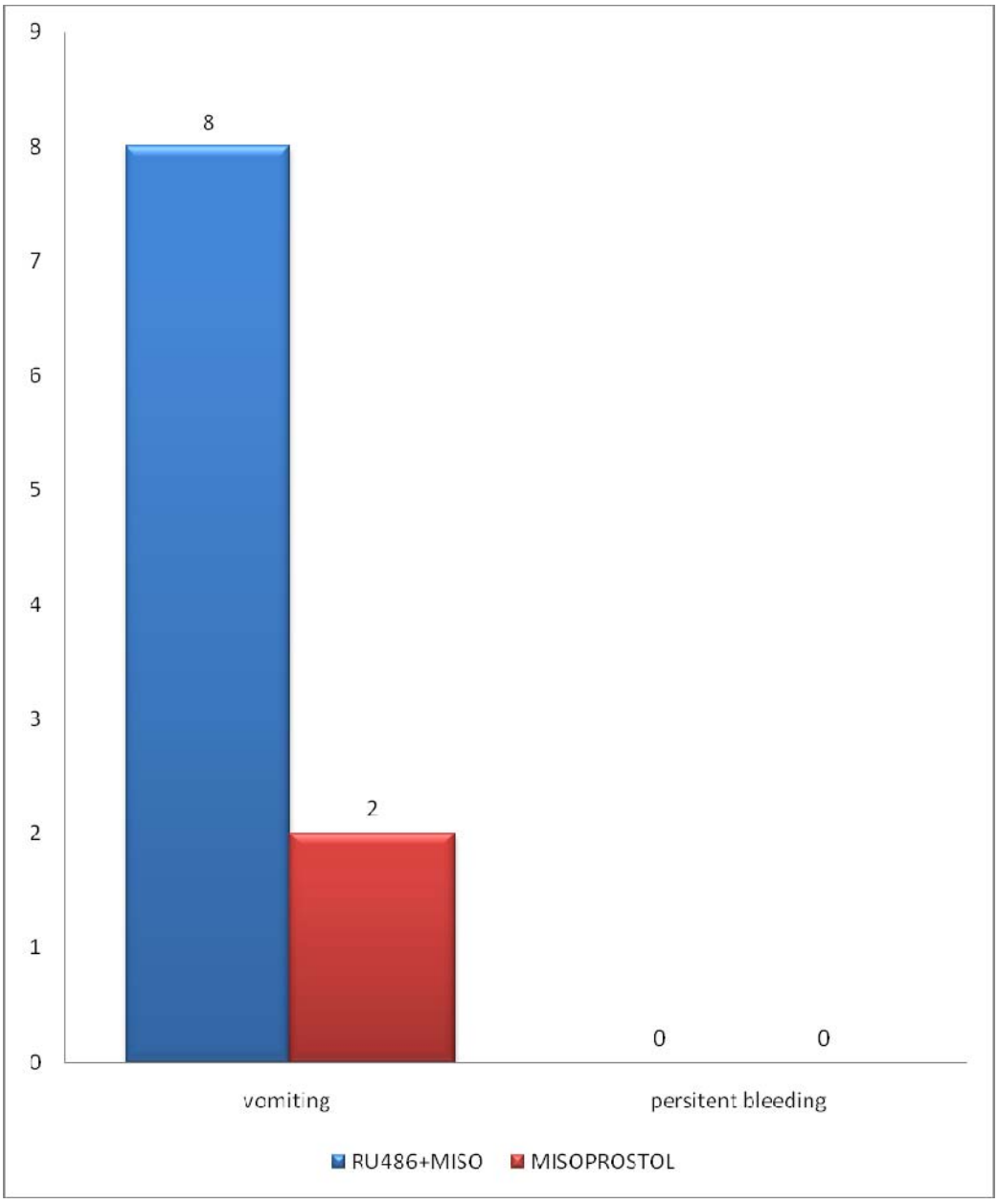


**TABLE 8 : ANALYSIS OF POST ABORTIVE COMPLICATIONS**

| SI. No. | Conditions | Mifepristone + Misoprostol | | Misoprostol | |
|---|---|---|---|---|---|
| | | No. of Cases | % | No. of Cases | % |
| 1. | Vomiting | 4 | 8 | 1 | 2 |
| 2. | Persistent Bleeding | 0 | 0 | 0 | 0 |

8% of women in Mifepriston + Misoprostol had vomiting whereas 2% of women in Misoprotol had vomiting, No women had persistent bleeding in both the groups.

# ANALYSIS OF POST ABORTIVE COMPLICATIONS



# DISCUSSION

This study was conducted at K.A.P.VISWANATHAM MEDICAL COLLEGE TRICHY during the period of 2010 – 2012. 100 Women were included in this study and the outcome analyzed using various parameters. The results were subjected to statistical analysis using the T – test -2 tailed one sample test and chi-square test.

**Age (Table – 1)**

Most of the patients in both the groups were in the age group of 20-30 years(75%).Women aged 35 years and above were not included in the original French study.

-WHO-1994[29]

In our study 16% of women from Mifepristone – Misoprostol combination belongs to the age group of above 30 and only 8% in the above combination group were below 20 years. The difference is of minimal significance (p=0.001).

**Parity (Table – 2)**

Looking at the parity of women seeking MTP in the first trimester it was found that more than 80% patient were second gravid, while 4% were unmarried. Parity is a major determinant of success rate in medical abortion.

In nulliparous women gestational age has no influence on the outcome of pregnancy termination in early weeks. However there was significantly lower rates of compete abortion in nulliparous women when age of gestation was> 7 weeks.

| | Gestational Age In Days | Complete Abortion |
|---|---|---|
| | **<49** | **98.6%** |
| **Nulliparous** | **50-56** | **98.3%** |
| | **57-63** | **96.4%** |
| | **>63** | **11%** |

Whereas in parous women the rate of complete abortion was lower after 7 weeks.

| | Gestational Age In Days | Complete Abortion |
|---|---|---|
| | **<49** | **96.2%** |
| **Parous** | **50-56** | **93.1%** |
| | **57-63** | **91.8%** |
| | **>63** | **10%** |

This is a retrospective analysis of 3161 cases by Bartley et al[25].

In the present study also 83% of women from both the group were parous.

Rational for this varied observation in different gestational age still remains unexplained. There is no variable significance in parity

**Analysis of Socio-Economic Status (table-3)**

Most of the women attending our hospital belongs to the marginalized group. Hence between 75 and 80% of women in both the groups were from socio-economic class of IV and V. Socio-economic status has no influence on the outcome.

**Gestational Age (table-4)**

Gestational age is the most important parameter that determines the successful outcome.

The influence of duration of pregnancy on successful MTP has been extensively studied. Kahn in his meta analysis finds the rate of complete abortion to be 96% when period of amenorrhea is <49 days, which declines to 85% when the gestational age is > 57 days.

Though initially medical abortion was used only up to 7 weeks, it has been extended to cover even those seeking abortion after 63 days. The rate of complete abortion in late MTPs was found to be 94.5% and the same increased

to 95.7% when additional dose of 800 μg of Misoprostol was introduced vaginally.

- Gouk EV, Lincoln K [44]

Spitz[6] also concur with other studies where it has been established that lesser the gestational age more is the success rate. Our study also compare well these studies; complete abortion rate being 94% when the period of amenorrhea is <49 days.

**Induction-Abortion interval (table-5)**

In EL.Refaey et al[24], 93% of abortion occurred within 4 hrs of vaginal Misoprostol administration in Mifepristone + Misoprostol and 78% occurred within 4 hrs if Misoprostol was administered orally.

Present study also shows the induction-abortion interval to be only 4 to 5 hrs following vaginal administration of Misoprostol, which is similar to the results of EL. Refaey et al[24].

The induction abortion interval in this study when vaginal Misoprostol alone was used for early MTP was found to be 23 to 24 hrs both in nulliparous and parous women.

Moreover, the expulsion rate was more in parous women than nulliparous women. The study thus has findings similar to the study by Blanchard[10], Velozco[45], and Carbonell et al.[18]

In our study none of the women were Rh negative. Hence there was no need for administering anti D immunoglobulin. If the client is Rh negative, 50 mcg of anti D immunoglobulin should be administered at the time of induction.

Thus the combined regimen has more rate of complete abortion with less induction-abortion interval than when Misoprostol alone was used.

**Analysis of complete abortion (Table-6)**

The present study had 2 cases of incomplete abortion in Mifepristone-Misoprostol group, the method failure rate was 2%, which indicates that additional methods like MVA were used in these patients. These results were similar to that of E1 Refaey et al who reported complete abortion rate to be 95% in vaginal instillation and 87% in oral administration of Misoprostol for first trimester MTP. This again shows complete abortion is more with vaginal administration than oral route. Peyron et al[4] in a 1993 study with Mifepristone–Misoprostol combination reported 96.9% complete abortion with 0.8% incomplete abortion.

When Misoprostol was used alone for first trimester MTP, the complete abortion rate was found to be only 50% with high rate of incomplete abortion

and method failure that made this regime unpopular. Peyron et al[4] has shown in a study that success rate of Misoprostol when it is used alone is 85% to 95%. This concludes that Misoprostol is more effective when it is used in combination with Mifepristone than when used alone for medical abortion.

All these studies including the present one reaffirms the fact that complete abortion rates are more in early pregnancy either with Mifepristone+Misoprostol or Misoprostol alone. Similarly, a meta analysis of 2000 patients reveal that the rate of incomplete abortion is more in parous women in Misoprostol group. This difference is statistically significant.

**Analysis of symptoms (Table-7)**

The symptoms were analyzed and the outcome of the study is interpreted as follows:

Vomiting was seen in 8% of our patients unlike the study by Cabezas et al[46] in 1998 where it was 15%. Though Spitz[6] reports 100% bleeding in his study, only 28% of our patients had excessive bleeding. Both vomiting and bleeding were more when Misoprostol alone was used for MTP (24 and 44% respectively).

Though blood transfusion was an option if bleeding is prolonged or excessive, no such necessity arouse in our study. However blood loss was not a common side effect in the WHO, 2000[30] study also.

60% of women from our study experienced pain that was similar to the rate of pain reported by Cabazes et al.[46] though pain was noted in many patients, it was not very severe. Pain and bleeding increase with increasing gestational age in Henshaw et al.[33]

**Analysis of post-abortive complications (Table-8)**

In our study 8% of women from Mifepristone + Misoprostol group had vomiting whereas only 2% of women from Misoprostol group had vomiting. No patient had persistent bleeding in both the groups.

# SUMMARY

This is a comparative study of medical methods for first trimester abortion conducted at K.A.P.VISWANATHAM MEDICAL COLLEGE, TRICHY.

Total no. of patients – 100

No. of women who were given Mifepristone & Misoprostol combination -50

No. of women received Misoprostol alone -50

Following were the observations of this study.

1. Most of the patients were in the age group 21-30 and parous
2. 4% of patients were unmarried who responded well for medical methods.
3. Almost all patients had various symtoms in both groups.
4. Expulsion was complete in the Mifepristone+Misoprostol group with only 2 woman needing check curettage for confirmation of complete abortion. However in one women, there was no response and their pregnancy was terminated by MVA. On the other hand 48% of women

in the Misoprostol alone group had to have curettage for completing the abortion process, and 10% of patients there was no response.

5. Induction-abortion time is less in patients with Mifepristone +Misoprostol than Misoprostol alone (4-5 hours vs 20-22 hrs. respectively).

6. None of the patients needed blood transfusion or volume expanders.

7. None of the patients had delayed bleeding after 45 days. On an average Bleeding stopped within 2 to5 days of expelling products.

8. Misoprostol is less expensive and efficacious. However induction abortion interval is prolonged than Mifepristone +Misoprostol combination.

9. Though Mifepristone is more expensive, the high complete abortion rate and expulsion withing 4-5 hrs of Misoprostol administration makes it a preferred method where cost is not a restraining factor.

# CONCLUSION

1. Mifepristone-Misoprostol combination is an effective out-patient procedure for early MTP and is ideal for home management.

2. Complete abortion rate is high with this combination.

3. Similarly the induction abortion interval with this method is also less.

4. Other associated complications are less.

   The only confounding factor is the cost involved which is about 20 times that of Misoprostol alone.

This makes the routine use of Mifepristone-Misoprostol combination for first trimester abortion an effective option where cost is not a consideration or in situations where and early abortion is required.

# MASTER CHART

| Sl. No | Age | SES | Marital Status | OB. For | GA | Method | | Ind-Abo. Interval | | Results | | Sideeffects | | Alternate method | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | RU486+ Miso | Miso | RU486+ Miso | Miso | RU486+ Miso | Miso | RU486+ Miso | Miso | RU486+ Miso | Miso |
| 1. | 19 | 3 | UM | UMP | <45 | 1 | | 5.00 | | 1 | | 3 | | | |
| 2. | 21 | 3 | M | P | <45 | | 2 | | 20.00 | | 2 | | 3 | | D/C |
| 3. | 23 | 4 | M | $G_2$ | 45-56 | 1 | | 4.00 | | 1 | | 2 | | | |
| 4. | 27 | 4 | M | $G_2$ | >56 | 1 | | 4.00 | | 1 | | 4 | | | |
| 5. | 24 | 1 | M | $G_2$ | <45 | | 2 | | 18.00 | | 1 | | 1 | | |
| 6. | 22 | 5 | M | $G_2$ | 45-56 | 1 | | 4.00 | | 1 | | 2 | | | |
| 7. | 26 | 4 | M | $G_2$ | 45-56 | | 2 | | 18.20 | | 2 | | 3 | | D/C |
| 8. | 22 | 3 | M | P | <45 | | 2 | | 20.20 | | 1 | | 1 | | |
| 9. | 25 | 4 | M | $G_2$ | 45-56 | 1 | | 4.30 | | 1 | | 4 | | | |
| 10. | 28 | 5 | M | $G_2$ | 45-56 | | 2 | | 18.10 | | 2 | | 1 | | D/C |
| 11. | 31 | 4 | M | $G_3$ | >56 | 1 | | 3.30 | | 2 | | 2 | | D/C | |
| 12. | 28 | 5 | M | $G_2$ | 45-56 | 1 | | 4.00 | | 1 | | 2 | | | |
| 13. | 20 | 3 | M | $G_2$ | <45 | | 2 | | 18.30 | | 2 | | 1 | | D/C |
| 14. | 35 | 5 | M | $G_3$ | 45-56 | 1 | | 6.00 | | 2 | | 1 | | D/C | |
| 15. | 21 | 5 | M | $G_2$ | 45-56 | 1 | | 4.30 | | 1 | | 1 | | | |
| 16. | 22 | 4 | M | P | 45-56 | 1 | | 5.00 | | 1 | | 1 | | | |
| 17. | 27 | 5 | M | $G_2$ | <45 | 1 | | 4.00 | | 1 | | 3 | | | |

| Sl. No | Age | SES | Marital Status | OB. For | GA | Method | | Ind-Abo. Interval | | Results | | Sideeffects | | Alternate method | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso |
| 18. | 33 | 4 | M | $G_3$ | 45-56 | | 2 | | 12.35 | | 3 | | 3 | | MVA |
| 19. | 33 | 4 | M | $G_3$ | 45-56 | | 2 | | 12.30 | | 1 | | 1 | | |
| 20. | 18 | 4 | UM | UMP | >56 | 1 | | 5.00 | | 1 | | 2 | | | |
| 21. | 23 | 4 | M | $G_2$ | 45-56 | | 2 | | 18.00 | | 3 | | 1 | | MVA |
| 22. | 26 | 3 | M | $G_2$ | 45-56 | 1 | | 4.00 | | 1 | | 1 | | | |
| 23. | 26 | 4 | M | $G_2$ | >56 | 1 | | 6.00 | | 3 | | 3 | | | MVA |
| 24. | 23 | 1 | M | $G_2$ | 45-56 | 1 | | 4.30 | | 1 | | 1 | | | |
| 25. | 30 | 4 | M | $G_3$ | <45 | 1 | | 3.30 | | 1 | | 1 | | | |
| 26. | 28 | 4 | M | $G_2$ | <45 | | 2 | | 18.00 | | 2 | | 1 | | D/C |
| 27. | 26 | 3 | M | $G_2$ | <45 | | 2 | | 18.00 | | 2 | | 3 | | D/C |
| 28. | 18 | 4 | M | P | 45-56 | 1 | | 5.00 | | 1 | | 1 | | | |
| 29. | 27 | 4 | M | $G_2$ | >56 | 1 | | 4.30 | | 1 | | 2 | | | |
| 30. | 25 | 5 | M | $G_2$ | >56 | 1 | | 4.30 | | 1 | | 2 | | | |
| 31. | 24 | 5 | M | $G_2$ | 45-56 | 1 | | 4.30 | | 1 | | 2 | | | |
| 32. | 24 | 3 | M | $G_2$ | <45 | 1 | | 5.00 | | 1 | | 2 | | | |
| 33. | 21 | 4 | M | P | <45 | | 2 | | 24.00 | | 3 | | 2 | | MVA |
| 34. | 22 | 4 | M | $G_2$ | <45 | | 2 | | 22.30 | | 2 | | 3 | | D/C |
| 35. | 32 | 4 | M | $G_2$ | <45 | 1 | | 4.00 | | 1 | | 1 | | | |
| 36. | 27 | 5 | M | $G_3$ | 45-56 | 1 | | 4.15 | | 1 | | 1 | | | |

| Sl. No | Age | SES | Marital Status | OB. For | GA | Method | | Ind-Abo. Interval | | Results | | Sideeffects | | Alternate method | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso |
| 37. | 31 | 5 | M | $G_2$ | 45-56 | 1 | | 4.30 | | 1 | | 1 | | | |
| 38. | 29 | 4 | M | $G_2$ | 45-56 | 1 | | 4.10 | | 1 | | 1 | | | |
| 39. | 21 | 4 | M | $G_2$ | <45 | 1 | | 3.30 | | 1 | | 1 | | | |
| 40. | 22 | 5 | M | $G_2$ | <45 | 1 | | 3.30 | | 1 | | 1 | | | |
| 41. | 23 | 5 | M | $G_2$ | <45 | 1 | | 4.00 | | 1 | | 2 | | | |
| 42. | 21 | 5 | M | P | <45 | 1 | | 3.30 | | 1 | | 1 | | | |
| 43. | 23 | 4 | M | $G_2$ | 45-56 | | 2 | | 18.20 | | 2 | | 2 | | D/C |
| 44. | 21 | 4 | M | $G_2$ | <45 | | 2 | | 18.10 | | 3 | | 2 | | MVA |
| 45. | 23 | 5 | M | $G_2$ | <45 | 1 | | 3.30 | | 1 | | 1 | | | |
| 46. | 31 | 4 | M | $G_2$ | <45 | 1 | | 3.30 | | 1 | | 1 | | | |
| 47. | 29 | 5 | M | $G_2$ | <45 | | 2 | | 18.45 | | 1 | | 3 | | |
| 48. | 18 | 4 | M | P | 45-56 | 1 | | 5.00 | | 1 | | 1 | | | |
| 49. | 32 | 5 | M | $G_3$ | 45-56 | | 2 | | 12.40 | | 2 | | 3 | | D/C |
| 50. | 26 | 4 | M | $G_2$ | <45 | | 2 | | 18.00 | | 1 | | 3 | | |
| 51. | 21 | 5 | M | $G_2$ | 45-56 | 1 | | 4.00 | | 1 | | 2 | | | |
| 52. | 21 | 5 | M | $G_2$ | 45-56 | 1 | | 4.00 | | 1 | | 1 | | | |
| 53. | 21 | 5 | M | $G_2$ | 45-56 | 1 | | 4.00 | | 1 | | 1 | | | |
| 54. | 33 | 5 | M | $G_2$ | <45 | | 2 | | 18.00 | | 2 | | 2 | | D/C |
| 55. | 27 | 5 | M | $G_2$ | <45 | | 2 | | 18.00 | | 2 | | 2 | | D/C |

| Sl. No | Age | SES | Marital Status | OB. For | GA | Method | | Ind-Abo. Interval | | Results | | Sideeffects | | Alternate method | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso |
| 56. | 33 | 4 | M | $G_3$ | 45-56 | 1 | | 3.30 | | 1 | | 2 | | | |
| 57. | 24 | 4 | M | $G_2$ | <45 | | 2 | | 18.30 | | 2 | | 2 | | D/C |
| 58. | 25 | 5 | M | $G_2$ | 45-56 | 1 | | 4.00 | | 1 | | 1 | | | |
| 59. | 24 | 5 | M | $G_2$ | <45 | 1 | | 3.30 | | 1 | | 1 | | | |
| 60. | 23 | 5 | M | $G_2$ | <45 | 1 | | 3.30 | | 1 | | 1 | | | |
| 61. | 28 | 5 | M | $G_2$ | 45-56 | 1 | | 4.00 | | 1 | | 2 | | | |
| 62. | 31 | 4 | M | $G_2$ | <45 | | 2 | | 18.00 | | 2 | | 3 | | D/C |
| 63. | 29 | 5 | M | $G_2$ | <45 | | 2 | | 18.00 | | 1 | | 2 | | |
| 64. | 21 | 5 | M | $G_2$ | <45 | | 2 | | 18.00 | | 1 | | 2 | | |
| 65. | 29 | 3 | M | $G_2$ | 45-56 | 1 | | 4.00 | | 1 | | 1 | | | |
| 66. | 23 | 4 | M | $G_2$ | 45-56 | | 2 | | 18.00 | | 1 | | 2 | | |
| 67. | 31 | 4 | M | $G_2$ | <56 | | 2 | | 24.00 | | 2 | | 2 | | D/C |
| 68. | 30 | 3 | M | $G_3$ | 45-56 | | 2 | | 18.30 | | 1 | | 2 | | |
| 69. | 19 | 4 | M | P | <45 | | 2 | | 18.00 | | 2 | | 2 | | D/C |
| 70. | 29 | 4 | M | $G_2$ | <45 | | 2 | | 18.40 | | 1 | | 1 | | |
| 71. | 24 | 2 | M | $G_2$ | <45 | | 2 | | 18.00 | | 1 | | 1 | | |
| 72. | 24 | 3 | M | $G_2$ | <45 | | 2 | | 18.00 | | 2 | | 3 | | D/C |
| 73. | 25 | 4 | M | $G_2$ | 45-56 | | 2 | | 18.30 | | 2 | | 2 | | D/C |
| 74. | 23 | 4 | M | $G_2$ | 45-56 | | 2 | | 18.30 | | 1 | | 2 | | |
| 75. | 34 | 4 | M | $G_3$ | 45-56 | 1 | | 3.30 | | 1 | | 2 | | | |

| Sl. No | Age | SES | Marital Status | OB. For | GA | Method | | Ind-Abo. Interval | | Results | | Sideeffects | | Alternate method | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso |
| 76. | 27 | 3 | M | $G_2$ | <45 | | 2 | | 18.00 | | 1 | | 3 | | |
| 77. | 22 | 4 | M | $G_2$ | <45 | | 2 | | 18.00 | | 1 | | 2 | | |
| 78. | 35 | 5 | M | $G_2$ | <45 | 1 | | 3.30 | | 1 | | 3 | | | |
| 79. | 28 | 4 | M | $G_2$ | <56 | | 2 | | 24.00 | | 2 | | 2 | | D/C |
| 80. | 40 | 4 | M | $G_3$ | <45 | | 2 | | 12.00 | | 3 | | 1 | | MVA |
| 81. | 27 | 4 | M | $G_2$ | 45-56 | 1 | | 4.30 | | 1 | | 1 | | | |
| 82. | 19 | 5 | M | $G_2$ | 45-56 | | 2 | | 18.00 | | 1 | | 3 | | |
| 83. | 26 | 3 | M | $G_3$ | <45 | | 2 | | 12.40 | | 2 | | 2 | | D/C |
| 84. | 22 | 4 | M | $G_2$ | 45-56 | 1 | | 4.30 | | 1 | | 1 | | | |
| 85. | 30 | 4 | M | $G_2$ | 45-56 | 1 | | 4.00 | | 1 | | 1 | | | |
| 86. | 22 | 4 | M | $G_3$ | <45 | | 2 | | 12.00 | | 2 | | 2 | | D/C |
| 87. | 31 | 4 | M | $G_2$ | >56 | 1 | | 6.00 | | 1 | | 1 | | | |
| 88. | 23 | 4 | M | $G_2$ | 45-56 | | 2 | | 18.40 | | 2 | | 1 | | D/C |
| 89. | 29 | 5 | M | $G_3$ | <45 | | 2 | | 12.00 | | 1 | | 2 | | |
| 90. | 25 | 5 | M | $G_2$ | 45-56 | | 2 | | 18.30 | | 1 | | 1 | | |
| 91. | 29 | 5 | M | $G_2$ | <45 | 1 | | 4.00 | | 1 | | 1 | | | |
| 92. | 24 | 4 | M | $G_2$ | <45 | | 2 | | 18.00 | | 2 | | 1 | | D/C |
| 93. | 29 | 5 | M | $G_2$ | >56 | | 2 | | 24.00 | | 1 | | 1 | | |
| 94. | 28 | 4 | M | $G_2$ | 45-56 | | 2 | | 18.30 | | 2 | | 2 | | D/C |
| 95. | 23 | 4 | M | $G_3$ | <45 | 1 | | 3.30 | | 1 | | 1 | | | |

| Sl. No | Age | SES | Marital Status | OB. For | GA | Method | | Ind-Abo. Interval | | Results | | Sideeffects | | Alternate method | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso | RU486+ | Miso |
| 96. | 21 | 5 | M | $G_2$ | 45-56 | | 2 | | 18.00 | | 1 | | 1 | | |
| 97. | 26 | 3 | M | $G_2$ | <45 | | 2 | | 18.10 | | 2 | | 2 | | D/C |
| 98. | 36 | 4 | M | $G_3$ | 45-56 | 1 | | 3.30 | | 1 | | 1 | | | |
| 99. | 31 | 5 | M | $G_2$ | <45 | | 2 | | 18.00 | | 1 | | 1 | | |
| 100. | 22 | 5 | M | $G_2$ | <45 | | 2 | | 18.00 | | 1 | | 2 | | |

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