

“COMPARATIVE STUDY OF MIFEPRISTONE AND VAGINAL MISOPROSTOL COMBINATION OVER VAGINAL MISOPROSTOL ALONE IN FIRST TRIMESTER ABORTION”

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BRANCH II



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CERTIFICATE

This is to certify that this dissertation entitled "**COMPARATIVE STUDY OF MIFEPRISTONE AND VAGINAL MISOPROSTOL COMBINATION OVER VAGINAL MISOPROSTOL ALONE IN FIRST TRIMESTER ABORTION**" is a bonafide work done by **Dr. N.REENU SINDHUJA**, postgraduate student in M.D (Obstetrics and Gynaecology) under my overall supervision and guidance at the Institute of Obstetrics and Gynaecology, Madras Medical College, Chennai in partial fulfillment of the regulations of Tamilnadu Dr. M.G.R. medical university for the award of M.D degree in Obstetrics and Gynaecology.

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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 a 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 Organisation.

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 are 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 AVAILABLE 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 ERMINATED

(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 / imprisonment.

II WHO CAN PERFORM MTP

Registered medical practitioner with obstetrics and gynaecology qualification.

Registered medical practitioner with postgraduate qualification in obstetrics and gynaecology.

Registered medical practitioner who has MTP certificate with training of 6 months in obstetrics and gynaecology.

III. WHERE CAN BE PERFORMED?

(a) All government hospitals where facilities for MTP exist.

(b) At places recognized and approved by govt under the MTP act.

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

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. At least 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

- ❖ A place for MTP up to 12 weeks - routine gynaecology clinic.
- ❖ A place for MTP up to 20 weeks - should have operation table to perform major surgical techniques.

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 obstetrics 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 a hospital established or maintained by the Govt.

RCOG GUIDELINES FOR MEDICAL ABORTION

INFORMATION FOR WOMEN

Verbal advise and printed information has to be given to women

Information to women about procedure

Confidentially

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. E

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.

COMPLICATION AND SEQUAE BY 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]³⁹

PROSTAGLANDINS

Blanchard K et al feels that misoprostol when used alone hold promise for early termination of pregnancy /Blanchard K et al 2000¹⁰

Various studies using 800 - micro gram of misoprostol administered 24 to 48 hrs apart shows success rates between 85% and 92% percentage.

Ngai Sw et al., 2000¹¹

Tang¹² and Ho tried 400 microgram of misoprostol up to maximum of 5 doses sublingually for second trimester abortion with success rate of 100%.

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 2000)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 interfere with the continuation of pregnancy.

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

On day 3, the patient 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% *-(Trusell elterson 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 Kinky 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, BMJ, 1993)²¹.

Two large trials with 2000 clients also confirmed the efficacy of 200 milligram of oral mifepristone with misoprostol vaginally (Ashok PW³, Schaff EA²², Contraception, 1999).

There was a randomized trial conducted in order to reduce the dose 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%) (ELRefacy, 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 LMP¹⁴ (2000).

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

(Trusell - Elterson 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 had 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.

(Bartley et al 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	Ru 486 200 mg PO. day 1	Ru 486 200 mg PO day 1
+	+	+
800 mcg miso PO day 3	800 mcg miso PV day 3	800 mcg miso PV day 3
+	+	
400 mcg miso PO Bd 7 days	400 mcg miso PO Bd 7 days	
Complete abortion rate 92%	Complete abortion rate 94.7 %	Complete abortion rate 93.5 %

Helene et al BJOG, Sept 2003²⁶

However studies from ICMR has shown 200 mg of mifepristone followed 36-48 hrs by 400 meg of oral or vaginal misoprostol to be equally efficient with a Complete abortion rate of 95% - 99% - ICMR²⁷ 1994. Aubency and Bauilieu²⁸1991.

On Going Trials

A large multicentric trial by WHO on mifepristone and misoprostol as an abortifacient 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 MIFEPRISTONE - 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 MVA / EVA
3. Suction evacuation / curettage

IMMEDIATE COMPLICATIONS OF SURGICAL METHODS

- Excessive Bleeding** - (a) Uterine atony
- (b) Retained products of conception
- (c) Uterine perforation
- (d) Cervical laceration
- (e) Post abortal syndrome

1.Syncopal attacks

2.Shock

3.Infection

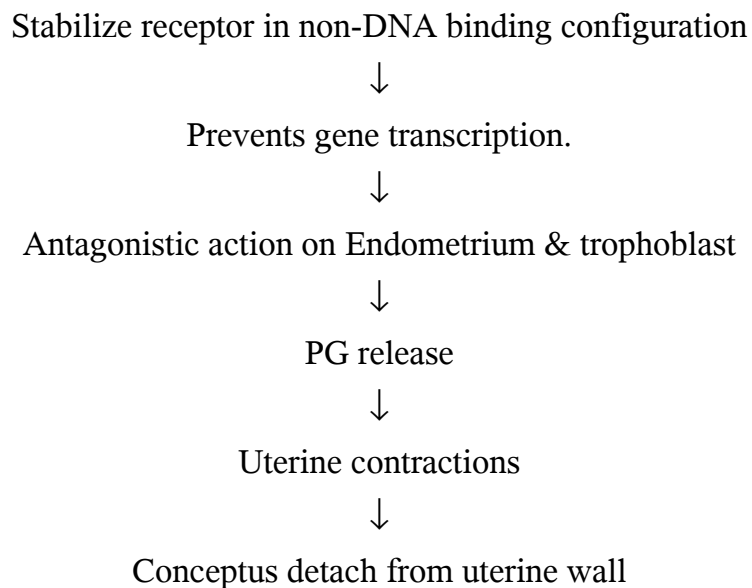
DELAYED COMPLICATION

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.E.E. Baulieu working Roussel Uclaf Mifepristone is a 19 Nor testosterone derivative 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 & decidua³¹
- 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 antiestrogenic³⁴

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

II AS A CONTRACEPTIVE

- Continuous administration of the drug in a dose of 20 mg from day1 - 30 days inhibits ovulation and delays menstruation.³⁵
- Administration of 100 mg of mifepristone, 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 a emergency contraceptive - 600 mg of mifepristone within 72 hrs of unprotected coitus

has 100% success rate.³⁶⁻³⁷

(Wolf JP. Contr. - Baird DT. Contraception 1993, Van Sankon and Haspel 1987 / IPPF Med Bull 1988).

III. CERVICAL DILATATION

To ripen the cervix prior to surgical method of MTP

Reduce the induction - abortion interval in medical method

- Urquhart DL. Templeton AF Contraception 1990³⁸

OTHER SYNERGISTIC USES

- ❖ Endometriosis - Continuous use up to 3 months
 - Kettle LM - Fertility - Sterility³⁹ /99/56
- ❖ Uterine leiomyoma - 49% reduction of tumor size with 3-month use.
 - Howitz KB, Murphy Clinical Endocrin.⁴⁰
- ❖ Meningioma - For unresectable tumour
 - Grun Berg Neuro Surgery 1991⁴¹
- ❖ Cushing's syndrome - Neiman LK et. al, J. Clinical Endo 1985⁴²
- ❖ For unruptured ectopic sac- - Mifepristone instilled results in resolution of 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 & 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_{1/2} -18 hrs.

Metabolism via hepatic microsomal enzyme - iso enzyme cyp 3 A4

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 2002³⁰

DRUG INTERACTIONS

Drugs that increase the serum level of mifepristone (through Cy P3 A4) :

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

Diarrhea

Dizziness

Headache

Dyspepsia

Pelvic pain

Hypertension

Hashimoto's thyroiditis

MISOPROSTOL

It is a 11 alpha 16 dehydroxy 16 methyl 19 isoprost - 13E - en - coate. It is a synthetic prostaglandin structurally related to PGE!

Available as 100 mcg and 200-mcg tablet

Each tablet has

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

Misoprostol inhibits gastric acid secretion & promotes bicarbonate secretion. It is mucoprotective and is used in drug-induced gastric ulcer and also 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.

- Oridi Im Br. J. Obst. gy.s 2000⁴³

PHARMACOKINETICS

- Rapidly absorbed orally
- Rapid deesterification 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 meg of oral or vaginal misoprostol.
- 2.Second trimester along with mifepristone in various doses in various regimens

Side effects

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

AIMS AND OBJECTIVES

- ❖ To assess the efficacy of mifepristone & 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 Institute of Obstetrics and Gynaecology, Chennai - 8 during 2007 - 2008.

The purpose of study is to compare the efficacy of mifepristone - vaginal misoprostol combination with vaginal misoprostol as a method of first trimester abortion.

Study design	:	Comparative Study
Study place	:	Institute of Obstetrics and Gynaecology, Chennai - 600 008.
Study Population	:	Patients requesting MTP who attended family planning Dept. IOG, Chennai.
Sample size	:	100 (Random Allocation to either of groups) 50 - Mifepristone + Misoprostol Group 50 - Misoprostol Group
Year of Study	:	Jan 2007 - July 2008

INCLUSION CRITERIA

1. Confirmed pregnancy up to 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 / day
- ❖ 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 included 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

Bimanual 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.

MIFEPRISTONE - MISOPROSTOL GROUP

The mifepristone - 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 grounds.

Dosage schedule

Day 1 - 200mg 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 ug 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 to 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

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)

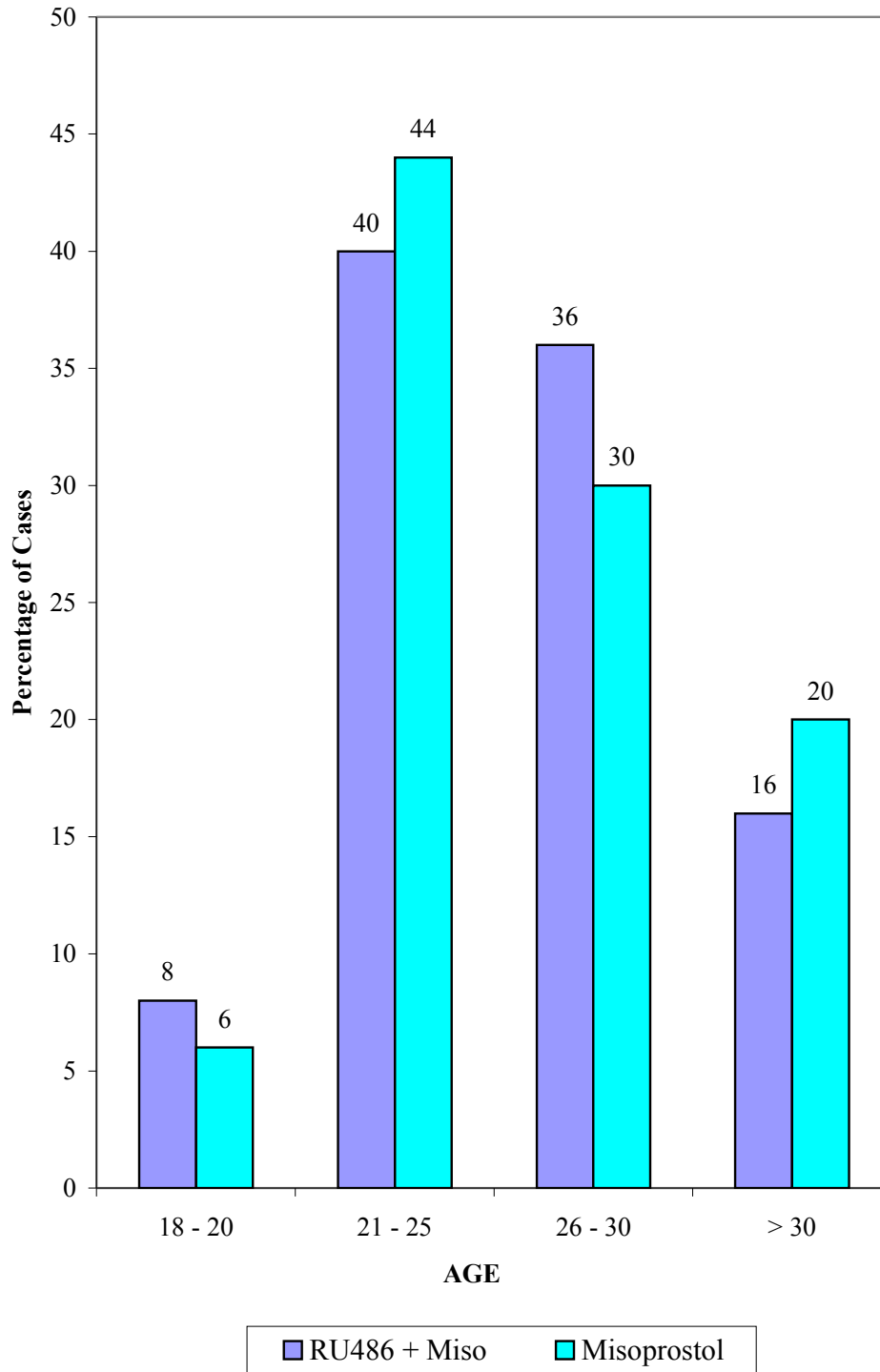


TABLE 2: PARITY

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 in both groups were parous whereas only 4% unmarried pregnancy noted in mifepristone + misoprostol group. None of them were unmarried in misoprostol group.

DISTRIBUTION OF PARITY

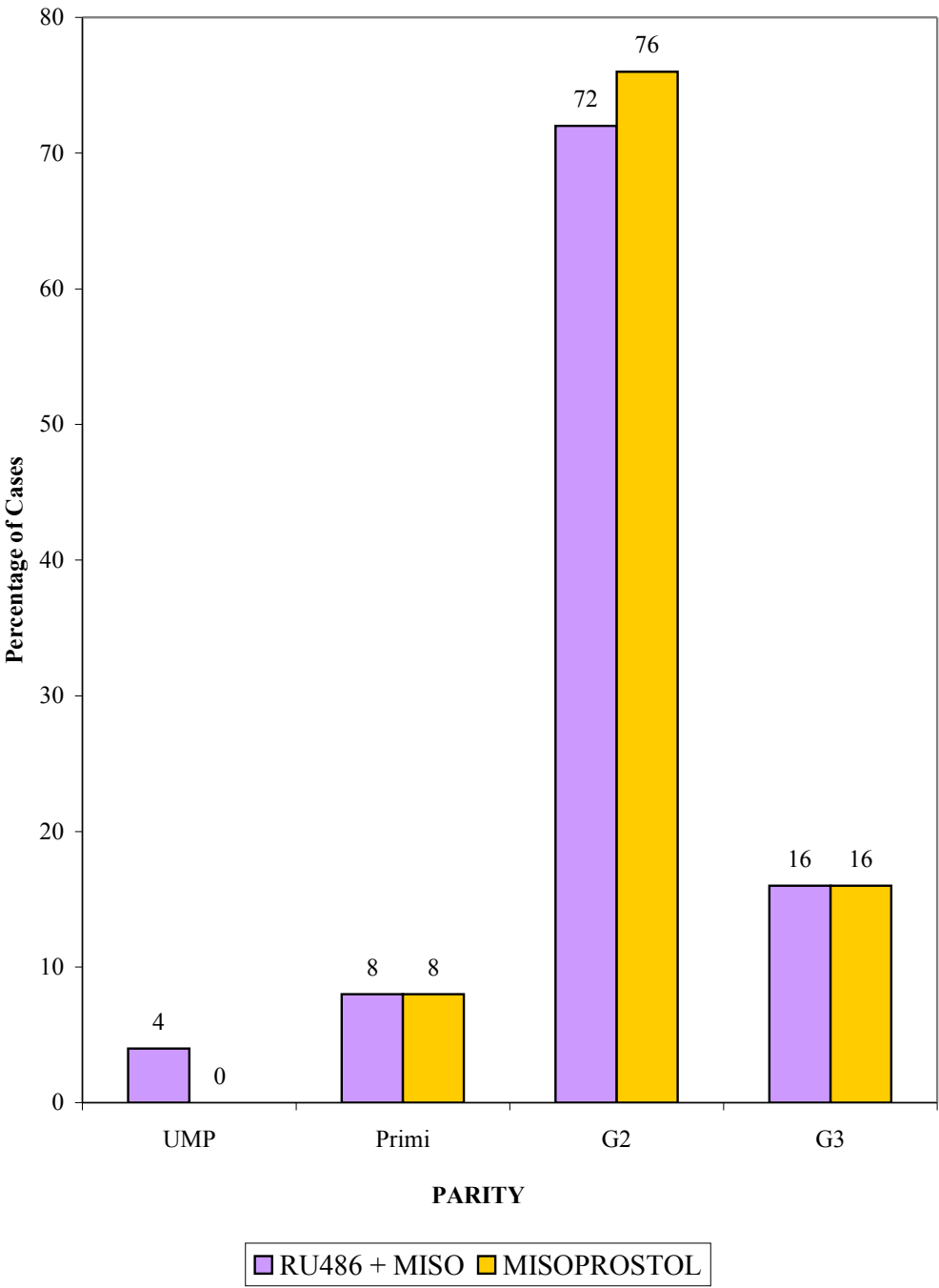


TABLE 3 : ANALYSIS OF SOCIO ECONOMIC STATUS

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.	Class IV/V	40	80	44	88

80% of women in both groups belong to Socioeconomic status of IV / V.

DISTRIBUTION OF SOCIO ECONOMIC STATUS

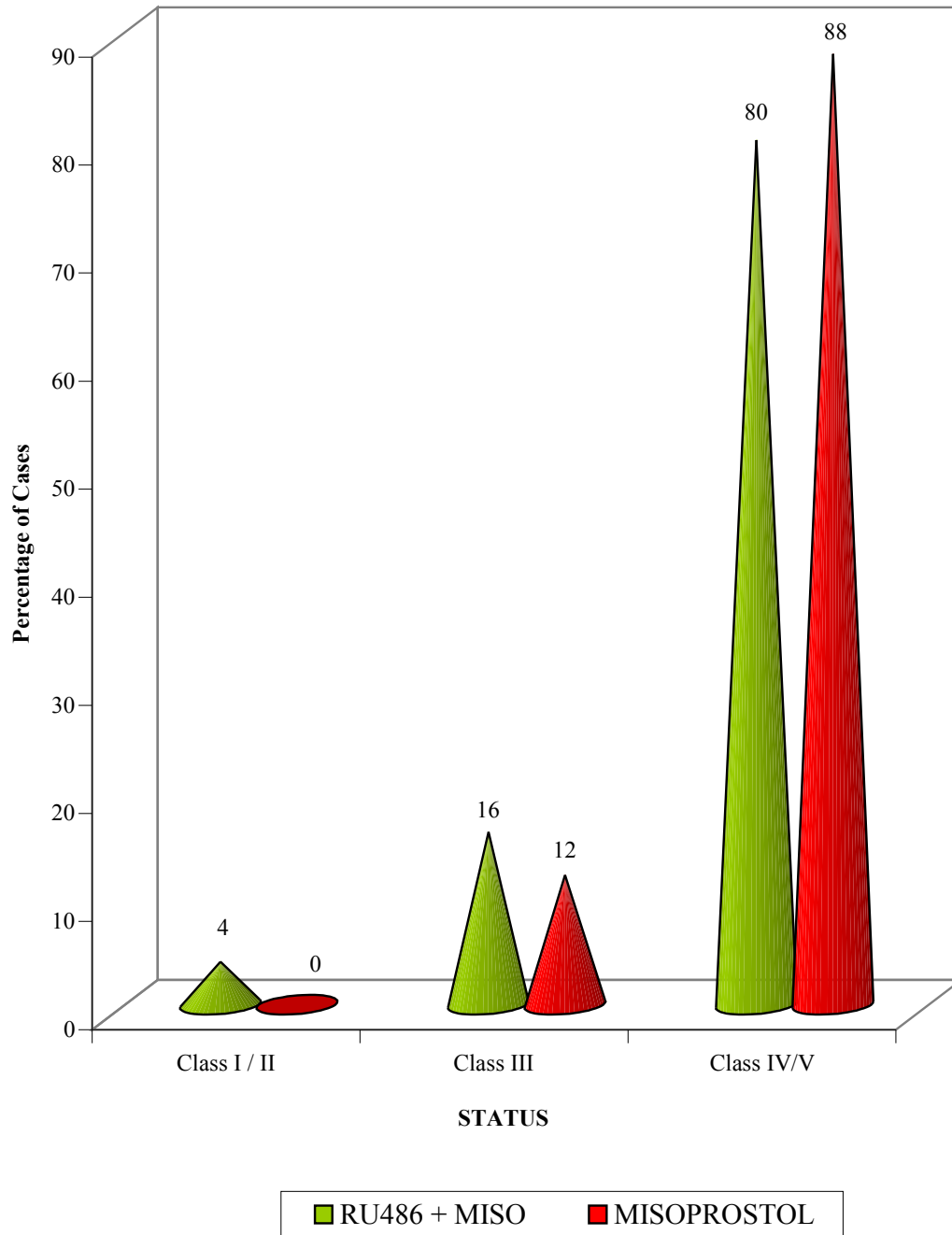
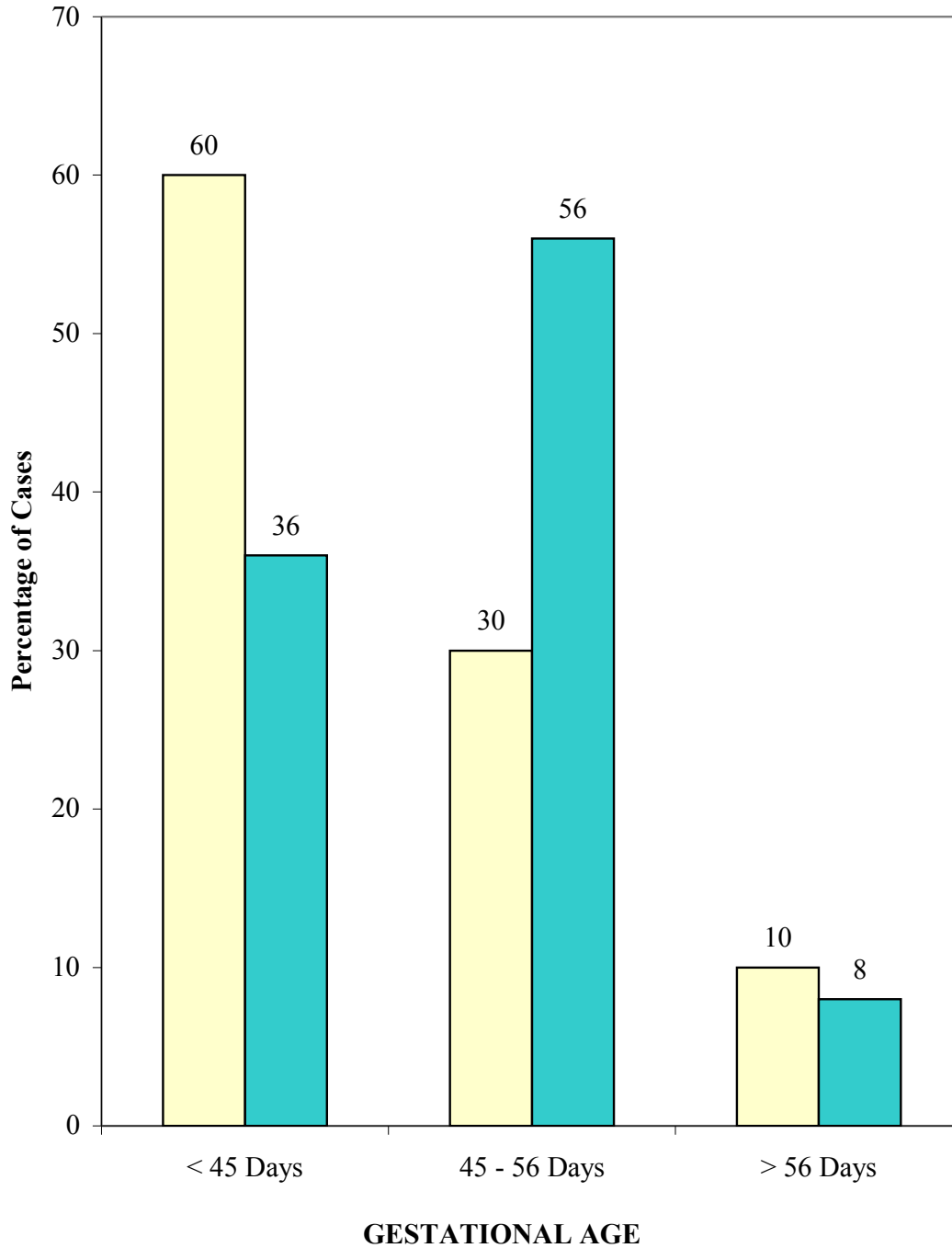


TABLE 4 : GESTATIONAL AGE

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



RU486 + Miso

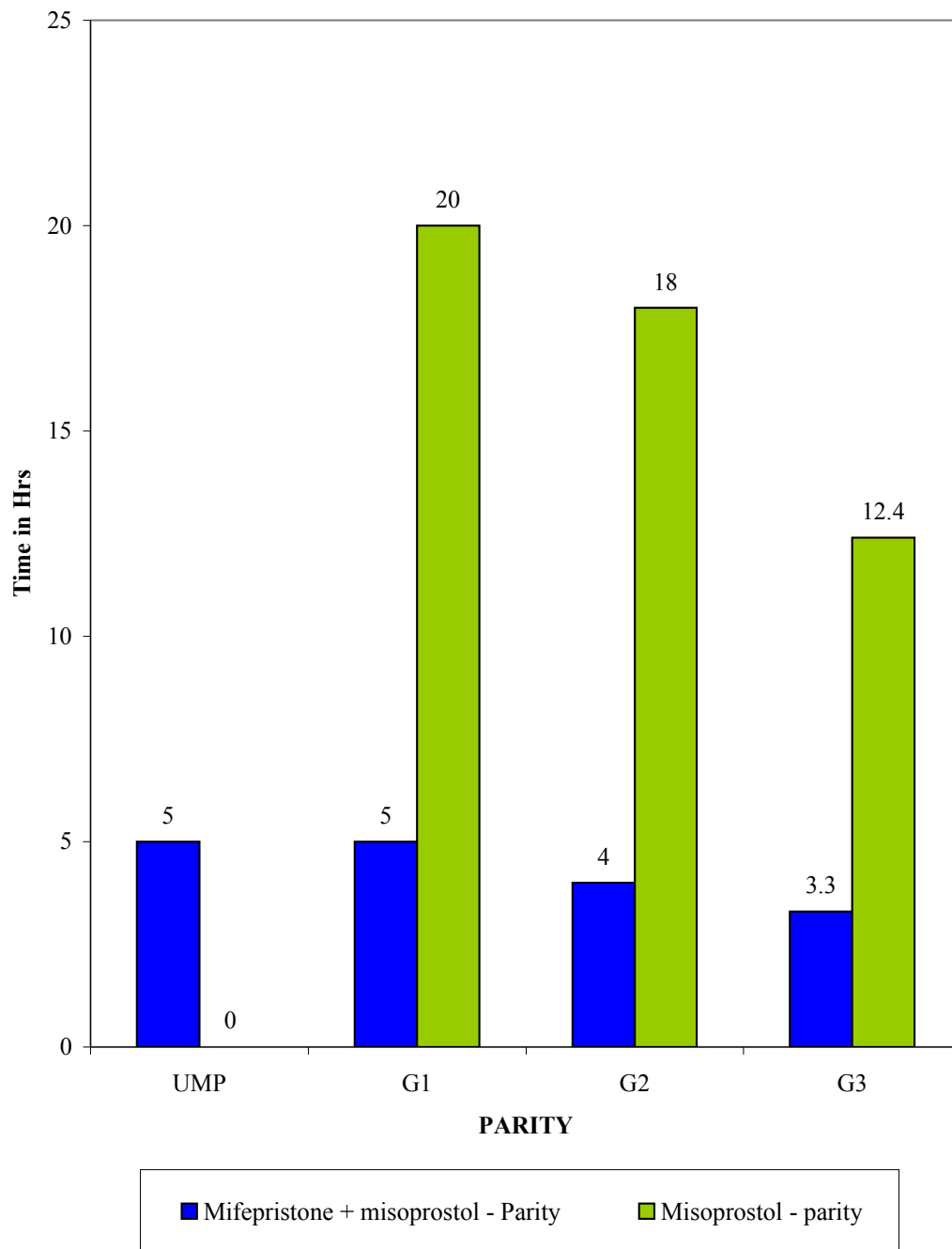
Misoprostol

TABLE 5 : INDUCTION ABORTION INTERVAL

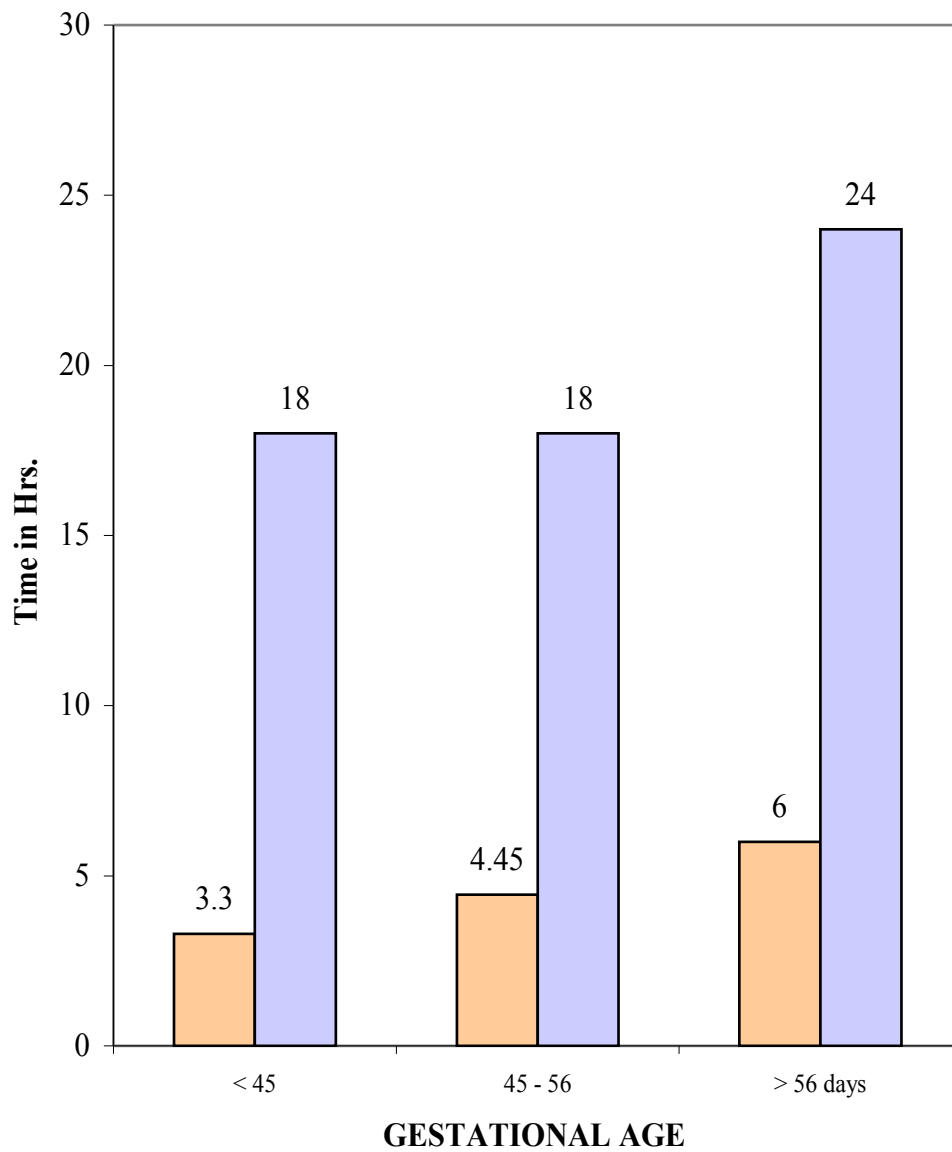
Characters		Mifepristone + Misoprostol (in Hrs).	Misoprostol
Parity	UMP	5.00	-
	G1	5.00	20
	G2	4.00	18
	G3	3.30	12.40
GA	< 45	3.30 - 4.00	18
	45 - 56	4 - 4.30	18
	> 56 days	6.00	24

When the induction abortion interval between mifepristone and misoprostol combination is compared with that of misoprostol alone it showed a p value of 0.000 thereby indicating that the reduced interval in the mifepristone - misoprostol group is significant.

INDUCTION - ABORTION INTERVAL



INDUCTION -ABORTION INTERVAL



■ Mifepristone + Misoprostol - GA

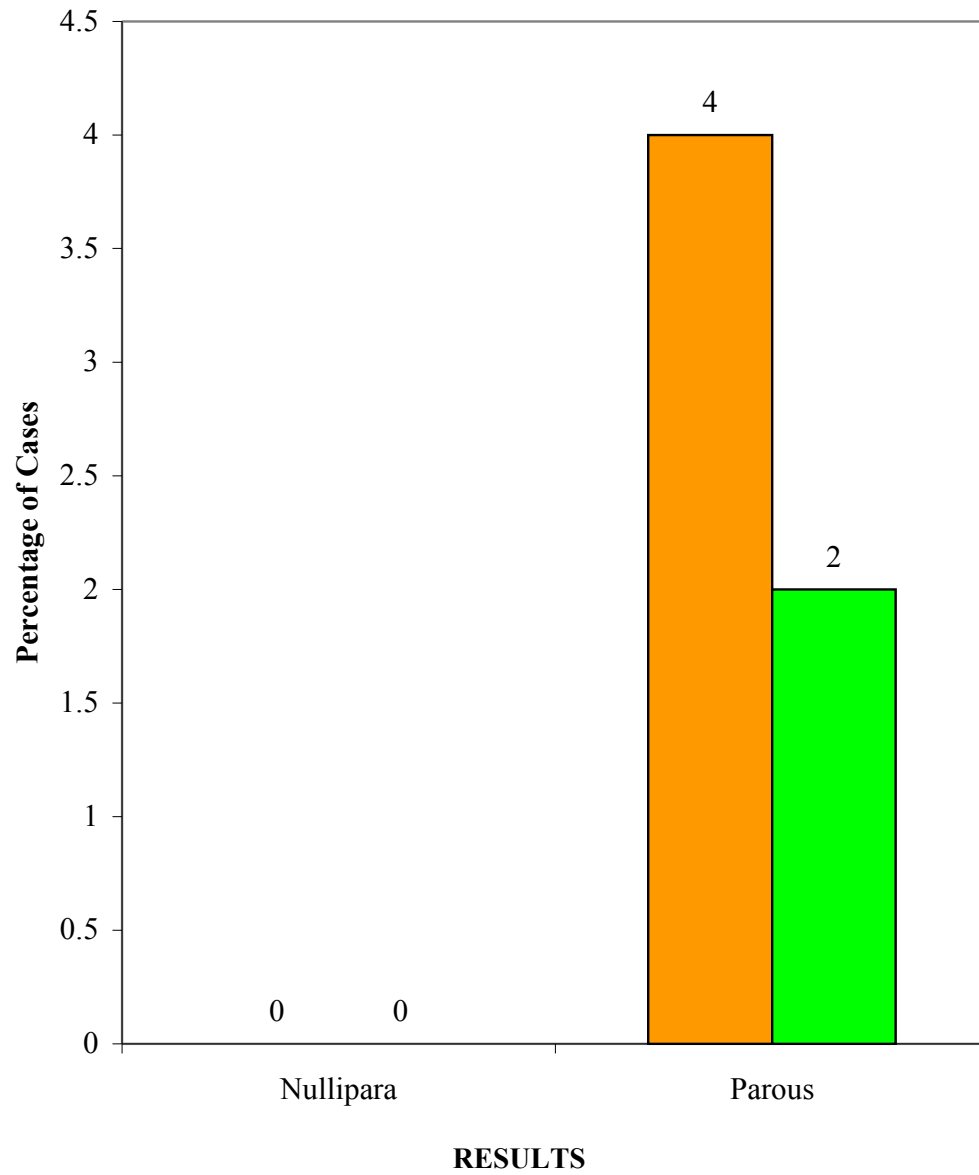
■ Misoprostol - GA

TABLE 6 : ANALYSIS OF COMPLETE ABORTION

Sl. 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 MIFERPRISTONE + MISOPROSTOL RESULTS



■ Incomplete Abortion ■ Method Failure

ANALYSIS OF MISOPROSTOL RESULTS

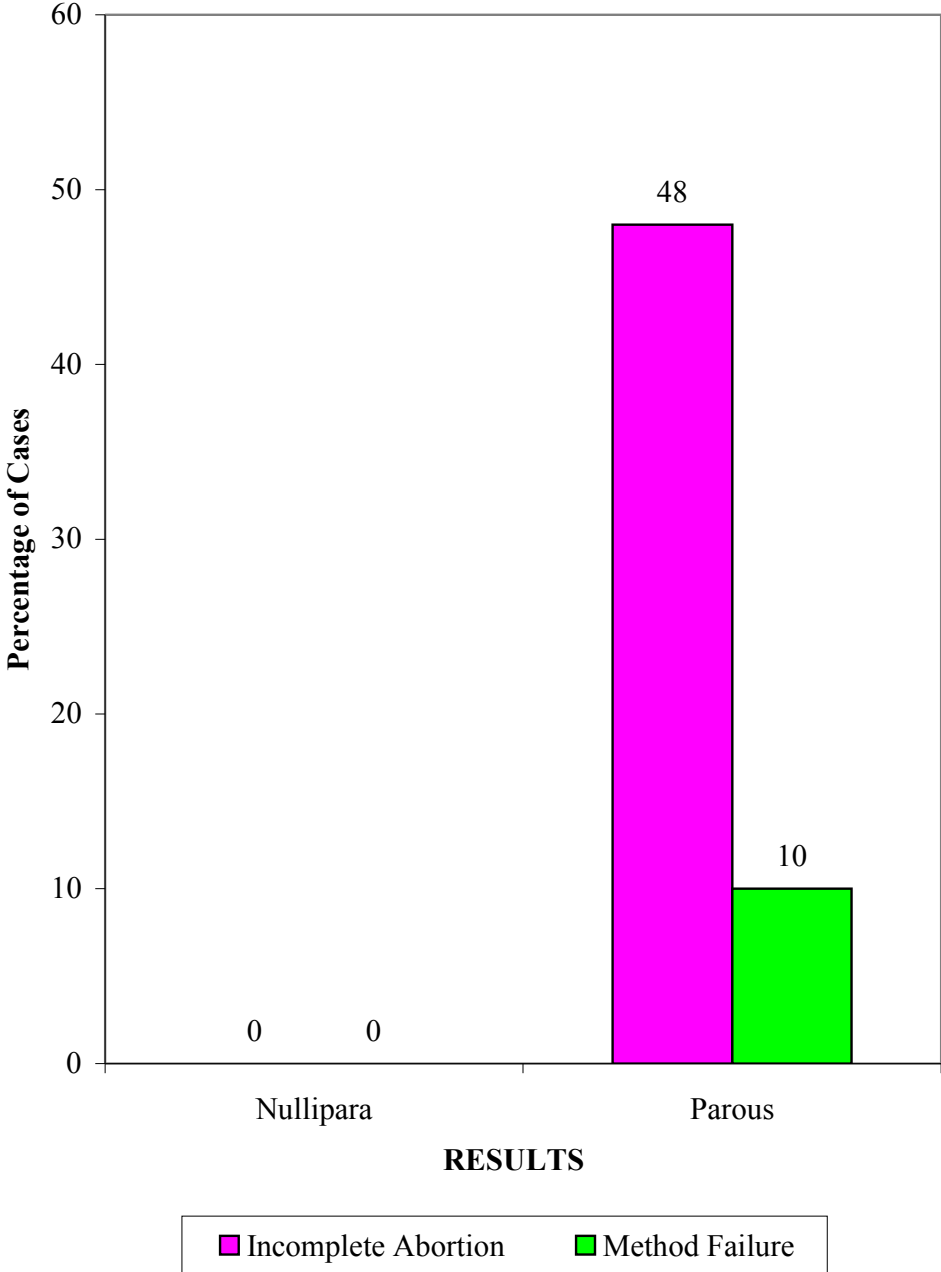


TABLE 7 : ANALYSIS OF SYMPTOMS

Sl. No.	Symptoms	Mifepristone + 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 significant incidence of side effects. However a larger study will be required to confirm the results ($p = 0.001$).

ANALYSIS OF SYMPTOMS

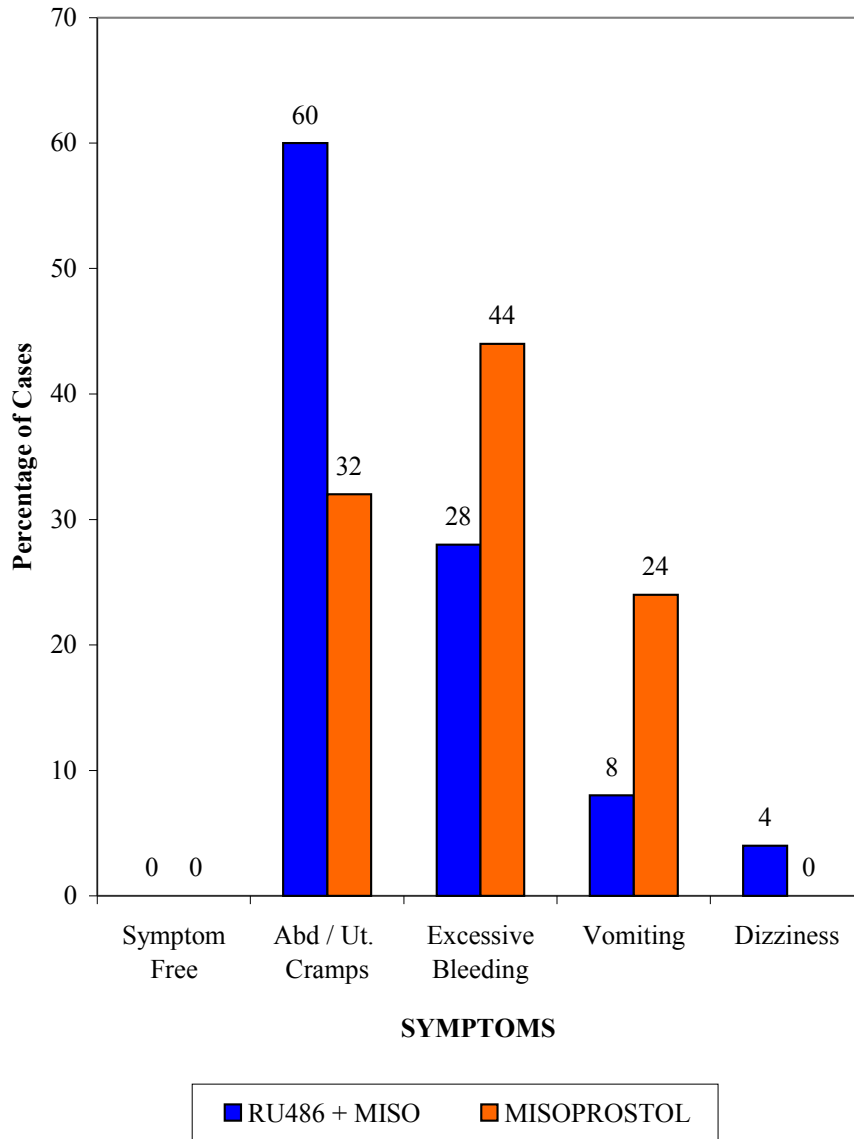
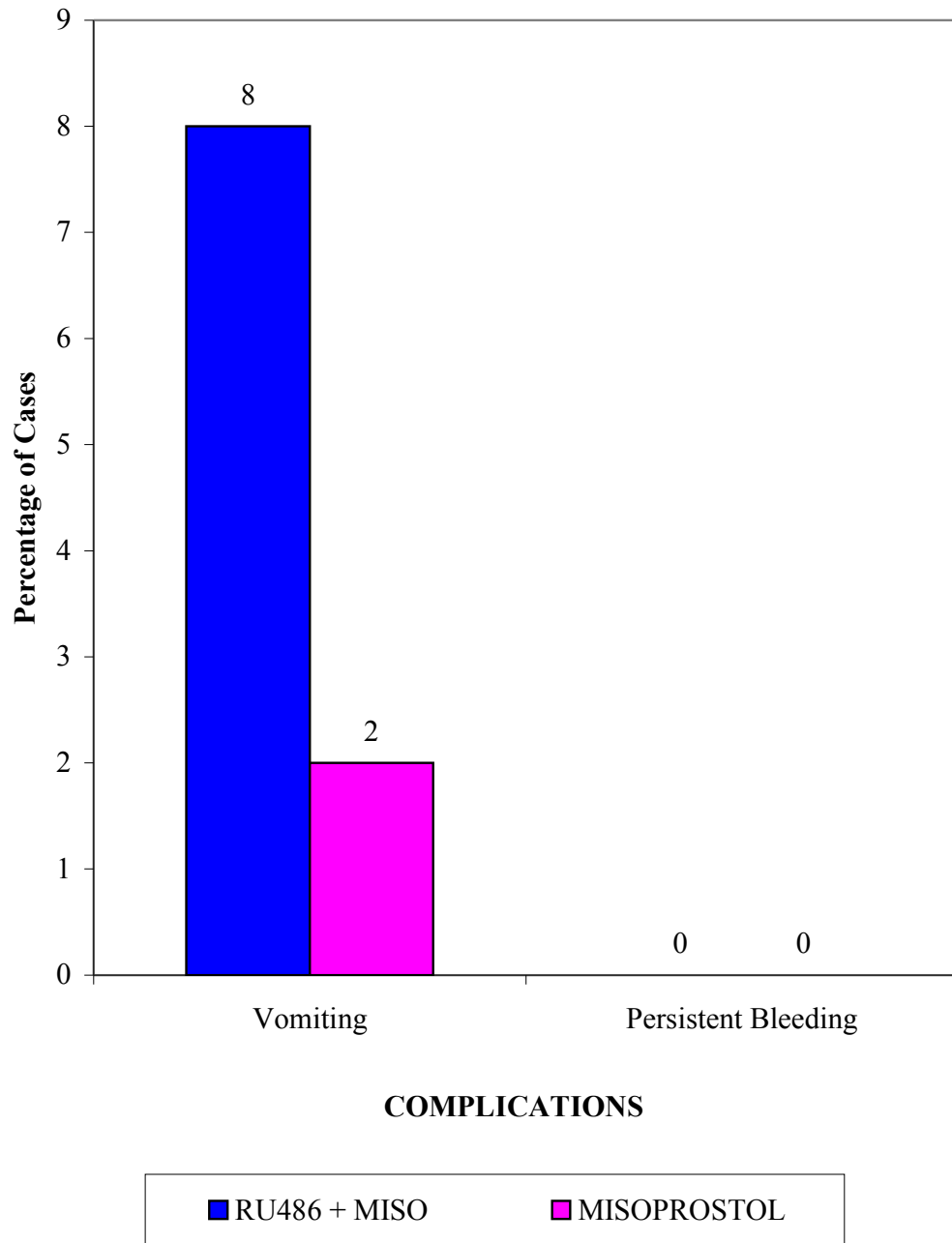


TABLE 8 : ANALYSIS OF POST ABORTIVE COMPLICATIONS

Sl. 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 mifepristone + misoprostol had vomiting whereas 2% of women in misoprostol had vomiting, No women had persistent bleeding in both the groups.

ANALYSIS OF POST ABORTIVE COMPLICATIONS



DISCUSSION

This study was conducted at Institute of Obstetrics and Gynaecology, Egmore, Chennai -600 008, during the period of 2007 - 2008. 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.

Table - 1 : Age

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-1994²⁹

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 ($p=0.001$).

Table - 2 : Parity

Looking at the parity of women seeking MTP in the first trimester it was found that more than 80% of patient were second gravida, 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 complete abortion in nulliparous women when age of gestation was > 7 weeks.

	Gestational Age In Days	Complete Abortion
Nulliparous	< 49	98.6%
	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
Parous	<49	96.2%
	50-56	93.1%
	57-63	91.8%
	>63	10%

This is a retrospective analysis of 3161 cases by Bartley et al⁴⁴.

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.

Table - 3 : Analysis of Socio Economic Status

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.

Table - 4 : Gestational Age

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 amenorrhoea 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 mcg of misoprostol was introduced vaginally.

-GolkeEULacolin⁴⁵

Spitz⁶ also concur with other studies where it has been established that lesser the gestational age more is the success rate.

Our study also compares well with these studies; complete abortion rate being 94% when the period of amenorrhoea is <49 days.

INDUCTION ABORTION INTERVAL

In EL.Rafecy et al²⁴, 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. Rafecy et al²⁴.

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 Blanchard¹⁰, Velazco⁴⁶, and Carboneil 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

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 El Refacy 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 that complete abortion is more with vaginal administration than oral route. Peyron et al²⁴ 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 al⁴ 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 metalanalysis 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

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 Cabeza et al⁴⁷ in 1998 where it was 15%. Though Spitz⁶ 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 arose in our study. However blood loss was not a common side effect in the WHO, 2000³⁰ study also.

60% of women from our study experienced pain that was similar to the rate of pain reported by Cabaze et al.⁴⁷ Though pain was noted in many patients it was not very severe. Pain and bleeding increases with increasing gestational age in Henshaw et al.³³

ANALYSIS OF POST ABORTIVE COMPLICATIONS

In our study 8% of women from Mifepristone + Misoprostol group had vomiting whereas only one percent (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 Institute of obstetrics and Gynaecology, Egmore, Chennai - 600 008.

Total no. of patients - 100

No. of women who were given mifepristone & misoprostol combination - 50

No. of 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 symptoms in both groups
4. Expulsion was complete in the mifepristone / misoprostol group with only 2 women needing check curettage for confirmation of complete abortion. However in one woman, 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 25 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 within 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 an early abortion is required.

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