RANDOMIZED COMPARATIVE STUDY OF SAFETY AND EFFICACY OF ORAL AND VAGINAL MISOPROSTOL IN THE TERMINATION OF SECOND TRIMESTER PREGNANCY OVER A PERIOD OF ONE YEAR AT TERTIARY CARE INSTITUTION

Dissertation submitted to

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

In partial fulfillment of the requirements
for the award of the degree of

M.S. OBSTETRICS & GYNAECOLOGY

KILPAUK MEDICAL COLLEGE
KILPAUK, CHENNAI.

APRIL 2014

BONAFIDE CERTIFICATE

This is to certify that the dissertation titled **"RANDOMIZED COMPARATIVE STUDY OF SAFETY AND EFFICACY OF ORAL AND VAGINAL MISOPROSTOL IN THE TERMINATION OF SECOND TRIMESTER PREGNANCY OVER A PERIOD OF ONE YEAR AT TERTIARY CARE INSTITUTION"** is a bonafide work done by **Dr.S.LUIJIMMALA,** Department of Obstetrics & Gynecology, Govt. Kilpauk Medical College, Chennai, in partial fulfillment of **THE TAMILNADU DR.MGR MEDICAL UNIVERSITY** rules and regulations for the award of **M.S.DEGREE** in **OBSTETRICS & GYNECOLOGY**, under our guidance and supervision, during the academic period from May 2011 to April 2014.

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DECLARATION

I **Dr. S.LUIJIMMALA** solemnly declare that this dissertation titled "**RANDOMIZED COMPARATIVE STUDY OF SAFETY AND EFFICACY OF ORAL AND VAGINAL MISOPROSTOL IN THE TERMINATION OF SECOND TRIMESTER PREGNANCY OVER A PERIOD OF ONE YEAR AT TERTIARY CARE INSTITUTION"** was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Prof. Dr.K.L.MALARVIZHI, M.D., D.G.O.**, **DNB.,** Professor, Department of Obstetrics and Gynecology, Govt. Kilpauk Medical College and Hospital, Chennai. This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the University regulations for the award of the degree of M.S.(Obstetrics and Gynecology).

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ACKNOWLEDGEMENTS

I wish to express my sincere thanks to my guide **Prof. Dr. K.L. MALARVIZHI, M.D., D.G.O.**, **DNB.,** Professor, Department of Obstetrics and Gynecology, Govt. Kilpauk Medical College and Hospital, Chennai. Her vast experience and in depth knowledge in the field of Obstetrics and Gynecology have helped me in completing my research work in Obstetrics and Gynecology. No work of this magnitude could have been accomplished without her unmatched guidance, valuable suggestions, constant encouragement and critical evaluation. I would like to record my deep sense of gratitude and indebtedness to her.

I am grateful to my Dean, **Prof. Dr.P.Ramakrishnan M.D,** Dean, Govt. Kilpauk Medical College and Hospital, Chennai, for his keen interest, valuable suggestions, support and constant encouragement during the course of my research work.

I express my sincere thanks to my professor **Dr. A. Kala M.D., D.G.O.,** Professor and Head of the Department of Obstetrics and Gynaecology, Govt. Kilpauk Medical College, Kilpauk, Chennai for her painstaking supervision, valuable help and encouragement.

I sincerely thank **Dr. Shobhakumar, M.D, DGO, Dr.G.Geetha M.D, DGO**, **Dr.V.Sumathi M.D,DGO**, **Dr.T.K.Shaanthy Gunasingh M.D,DGO., Dr.P.S.Jikkikalaiselvi M.D,DGO,** Professors and all my Assistant Professors, Govt. Kilpauk Medical College and Hospital, Chennai for their encouragement and valuable suggestions.

I would like to express my deep sense of gratitude to my parents, **Mr. R. Selvamohan & S.Ezhilarasi,** my husband **Dr. C. Munish,** my sons **Mr.M.Takshan & M.Ezhilselvan** and to **my friends** for their encouragement, patience and prayers.

I am thankful to **Dr. K.R. Mani,** Former Director, Central Research Institute, Kasuali, HP for his help in the analysis of statistical data and valuable suggestions.

I am grateful to Dr. T. Sekar, Sr. Research Assistant, Pasteur Institute of India, Coonoor for his help in the preparation of Chart and Tables and **Mr. Padmanaban,** Statistician, Govt. Kilpauk Medical College and Hospital, Chennai for his help in the analysis of statistical data.

I would like to extend my thanks to **all my patients** for their cooperation during the course of my research work.

ABSTRACT

OBJECTIVES: A prospective randomized study was conducted in 72 pregnant women, with the gestational period (between 12 and 20 weeks), to compare the efficacy and safety of oral versus vaginal administration of misoprostol for second trimester pregnancy termination. **PLACE & DURATION OF STUDY:** The Department of Obstetrics and Gynaecology, Govt. Kilpauk Medical College and Hospital (KMCH), Chennai from November 2012 and November 2013. **METHODOLOGY:** Women aged 18-38 years requesting MTP for maternal reason, fetal congenital anomalies and intrauterine fetal demise were randomly assigned into two groups. Group A (n=36) had misoprostol orally while the Group B (n=36) received misoprostol by vaginally route. Dosage regimen was similar in both the groups that was 200 µg every 4 hrs until the abortion occurred or maximum up to 6 doses. **MAIN OUTCOME MEASURES:** Efficacy included induction to delivery interval and safety included maternal complications and side-effects like nausea, vomiting, diarrhoea, fever and abdominal pain and results were compared. **RESULTS:** The percentage of women who delivered was significantly higher in the vaginal group than the oral group (94.44% vs. 66.67%, $P<0.03018$) within 24 hrs. The induction to delivery interval and incidence of side-effects were noted. **CONCLUSION:** Vaginal administration of misoprostol resulted in a higher success rate and misoprostol is safe and effective drug for second trimester pregnancy termination.

Key words: Misoprostol, oral and vaginal route, second trimester pregnancy termination

CONTENTS

ABBREVIATIONS

MTP	Medical Termination of Pregnancy
AN	Antenatal
GA	Gestational age
LMP	Last Menstrual Period
MVA	Manual Vacuum Aspiration
EVA	Electric Vacuum Aspiration
PGE1	Prostaglandin

1. INTRODUCTION

1.1. ABORTION

Abortion is theoretically defined as termination of pregnancy before the foetus becomes viable (capable of living independently). This has been fixed administratively at 28 weeks, when the foetus weighs approximately 1000g. Medical abortion is becoming extremely popular today. The accepted method of medical abortion worldwide is a combination of Mifepristone with the prostaglandin. Unsafe abortion results in complications are main public health problems in developing countries. Abortion is legal for a wide range of medical and social reasons even in our country.

Khan et al. 1999[1] in his study observed that problems such as abortion services by trained medical personnel in registered facilities, the stigma connected with induced abortion, the threat of forced contraceptive acceptance, and low levels of awareness regarding the legality of the procedure compel them to undergo illegal abortion under untrained practitioners using unsafe conditions resulting in chronic reproductive tract morbidity such as chronic disability, infertility and infections.

1.2. INCIDENCE IN INDIA

According to the Consortium on National Consensus for Medical Abortion in India, every year an average of about 11 million pregnancies are terminated by medical ground and 20,000 women died every year due to abortion-related complications. [2] Most abortion-related maternal deaths are attributable to illegal abortions. [3] . The number of abortions reported includes legal and induced abortions are shown in the following table.[4]

Year	1972	1975	1980	1985	1990
No. of abortion	24300	214197	388405	583704	581215

Year	1995	2000	2003	2007	2010
No. of abortion	570914	725149	763126	641786	620472

Worldwide 42 million legal abortions and 10 to 12 million clandestine abortion take place every year, of which 10 to 15% is

performed in second trimester. In India alone, 6.7 million induced abortions occur annually, of which late abortion constitute 10-7 to 15%[5]

1.3. TYPES OF ABORTION

1.3.1. Induced

Induced abortion is medically referred to as a therapeutic abortion when it is performed to save the life of the pregnant woman and hence the physical or mental health of women is not disturbed. It is carried out in cases where the child will have a significantly increased chance of premature morbidity or mortality or disabled and to avoid the risk of multiple pregnancies.

1.3.2. Spontaneous

A spontaneous abortion consists of expulsion of the products of conception before the fetus is viable i.e upto 28 weeks of gestation. In developed countries advanced management in neonatal care can salvage some babies at and after 20 weeks of gestation, with the fetus weighing > 5 gram. Hence, their definition of abortion is limited to 20 weeks of pregnancy. 75% abortions occurred in the first trimester and only 25% occur in the second trimester.

The causes of a spontaneous abortion cannot be elucidated in many cases, but some well known causes are (i) **Fetal causes:** Abnormal embryo and blighted ova, accounting for 50% of early abortion, are caused by chromosomal anomalies, such as trisomy, triploidy, Turner's syndrome and autosomal chromosomal abnormalities, which are lethal to the growth of the fetus. (ii). **Gametes:** aging ova and abnormal sperms cause poor fertilization, which leads to a blighted ovum. (iii). **Placenta:** Praevia, multiple pregnancy, H. mole and acutehydramnious are well known obstetric cause of spontaneous abortion. (iv). **Hormonal cause:** Progesterone deficiency is well known cause of an early abortion. Thyrotoxicosis and uncontrolled diabetes may rarely cause a pregnancy loss. (v) **Nutritional factors, smoking, excessive alcohol consumption:** These factors contribute to spontaneous abortion. Other causes include (vi) Trauma, (vii) Maternal diseases, (viii) Drugs, (ix) Abnormalities in the genital tract and (x) Immunological factors.

1.4. THE MEDICAL TERMINATION OF PREGNANCY ACT 1971

1.4.1. MTP Act 1971

Liberalization of the medical termination of pregnancy Act was approved by Parliament in the year 1971 and was implemented in 1972 and revised in 1975. It was last amended in 2006. It lays down the

conditions under which MTP can be performed in India. According to the act, Medical Termination of Pregnancy in India is allowed up to 20 weeks. However there is no definitive method for MTP between 13 and 20 weeks resulting more unsafe abortion during this period. The following conditions which warrant termination of pregnancy are stipulated under MTP Act 1971:

a. Medical – where continuation of the pregnancy would endanger the life of the pregnant women or cause grave injury to her physical or mental health.

   Examples are grade 3 or 4 hypertension, cervical or breast malignancy and severe epilepsy.

b. Eugenic- where substantial risk exist to the child being born with some serious physical or mental abnormality.

c. Social Indications – include pregnancy caused by rape or incest or unplanned pregnancy or pregnancy due to contraceptive failure

1.4.2. Conditions

The written consent of the patient on a special form is necessary prior to the procedure. If the women are less than 18 years of age or she

is mentally abnormal, the written consent of the legal guardian must be obtained.

1.4.3. Who can perform MTP?

Only a registered medical practitioner having post graduate training in Obstetrics and Gynecology or who has had special training in MTP can perform the procedure. For termination of pregnancies up to 12 weeks of gestation the opinion of one registered medical practitioner is enough. However, in the case of second trimester MTP, the opinion of two registered medical practitioners is essential.

1.4.4. Where can MTP be performed?

According to the act, MTP can be performed only in a hospital established and maintained by the government or in a place recognized and approved by the government for this purpose. Abortion services should be provided in strict confidentiality.

1.4.5. Benefits of the MTP Act

The incidence of septic abortion has definitely come down the following the liberalization of abortion. Though MTP does indirectly promote family planning, repeated abortions are detrimental to a women's health and hence MTP should not be considered as a family planning

method. It is imperative that women undergoing MTP be counseled about the available contraceptive methods. [5]

1.5. METHODS OF MTP

Methods of MTP can be broadly classified as follows:

1.5.1. Methods of first trimester MTP

- Menstrual regulation
- Dilatation and suction evacuation
- Cervical softening prior to dilatation and suction evacuation

1.5.2. Methods of second trimester MTP

- Surgical evacuation
- Extraovular instillation of drugs
- Extrauterine methods

The above methods are used singly or in combination. The second trimester abortion is associated with more risks than a first trimester procedure and hence should not be under taken lightly. The opinion of two registered medical practitioners is essential before performing a second trimester abortion. An ultrasound is a good prerequisite especially to confirm and document the gestational age. The upper limit is 20 weeks.

The oxytocic drugs stimulate myometrial activity and shorten the induction-abortion interval in the second trimester. Similarly, the use of prostaglandins (gel, suppository) a few hours prior to the procedure helps to attain a gradual softening and atraumatic dilatation of the cervix, facilitating further dilatation and evacuation procedures. The incidence of second trimester MTP has drastically come down and is mainly employed today for fetal malformations.

1.5.2.1. Medical methods

Prostaglandins

Prostaglandins have been used by various routes: orally, vaginally, intramuscularly, intra-amniotically, and extra-amniotically. Natural prostaglandins and prostaglandins analogues have been used. Recently very good success rates are being obtained with the use of PG E1 analogue, misoprostol. 400 µg vaginally, 3 doses and 3 hrs apart have been shown to give good results and is usually the first choice. Various other doses and regimens are also being tried.

Mifepristone and misoprostol

This combination is also being studied and showing promise. 200 mg mifepristone followed 48 hrs later by 600 µg of misoprostol vaginally

and then by 400 µg misoprostol vaginally every 3 hrs is one regime. There are various other regimens are being tried.

Ethacridine lactate or Emcridil

Ethacridine lactate has been used extra- amniotically for a very long time and is shown to be safe and effective. The side effects are also minimal. It works by the release of prostaglandins from the decidua. 10 ml of 0.1 % ethacridine is used for each gestational week up to a maximum of 150 ml. It is introduced extra-amniotically by means of a Foley catheter. Oxytocin can be used for augmentation and to reduce the induction delivery interval. In case of failure, reinstallation can be tried.

Hypertonic saline and urea

These were being used intra-amniotically previously. Hypertonic saline was associated with maternal deaths and thereby has been largely abandoned in most countries. The main complication of saline are haemorrhage, infection and hyper natremia. Disseminated intra vascular coagulation is another rare albeit serious complication.

1.5.2.2. Surgical method

Dilatation and evacuation

This can be used up to 16 weeks but requires cervical dilatation with the help of laminaria tents or vaginal misoprostol. Evacuation is done using ovum forceps. Once the evacuation is complete, suction evacuation and if necessary a curettage can be done to ensure completeness of the procedure. The complications are similar to those following first trimester evacuation.

Hysterotomy

This involves the removal of the fetus through an incision in the lower segment as in caesarean section. After opening the abdomen, the uterovesical fold of peritoneum is divided and the bladder pushed down. If possible, a transverse incision is made, but sometimes a vertical incision may be necessary. The fetus is removed and the incision closed in two layers. If needed, sterilization can be done at the same time. Hysterotomy is almost never performed as a primary procedure, but only when all other methods have failed.

Hysterectomy

This is also never done as a primary procedure except if there is a co existing problem like cancer cervix.

The currently used first line methods for second trimester abortions are misoprostol alone or with mifepristone [6,7].

1.5.2.3. Other Methods

There are number of methods using herbs in folk medicines such as black cohosh, pennyroyal and the new extinct silphium. The side-effects cannot be ruled out in the practice and thus it is not legally recommended.

1.6. MISOPROSTOL

1.6.1. Pharmacology

Misoprostol is a synthetic analog of prostaglandin E_1. It is used in prevention of gastric ulcers induced by non-steroidal anti-inflammatory agent. In addition, it has been used in the treatment of duodenal or gastric ulcer. It is an important drug in Obstetrics and Gynecology practices because of its priming action on uterus and cervix. The clinical application of misoprostol as follows:

- Medical Abortion

- Induction of labor
- Cervical priming before surgical procedure
- Medical evacuation for miscarriages and
- Management of postpartum hemorrhage

1.6.2. Structure of misoprostol

Misoprostol was registered in 1986 for the prevention and treatment of peptic ulcers resulted from Non-Steroidal Anti-Inflammatory Drugs (NSAID). It is safe and well tolerated within the recommended dose of 800 µg per day. The Prostaglandin E series (naturally occurring) was discovered by Robert *et al* in the year 1967. [8] The E series have three drawbacks that stalled their clinical application:

- Several side-effects
- Chemical volatility leading to a short shelf life and
- Rapid metabolism resulting in a lack of oral activity and it had short duration action when given parenterally.

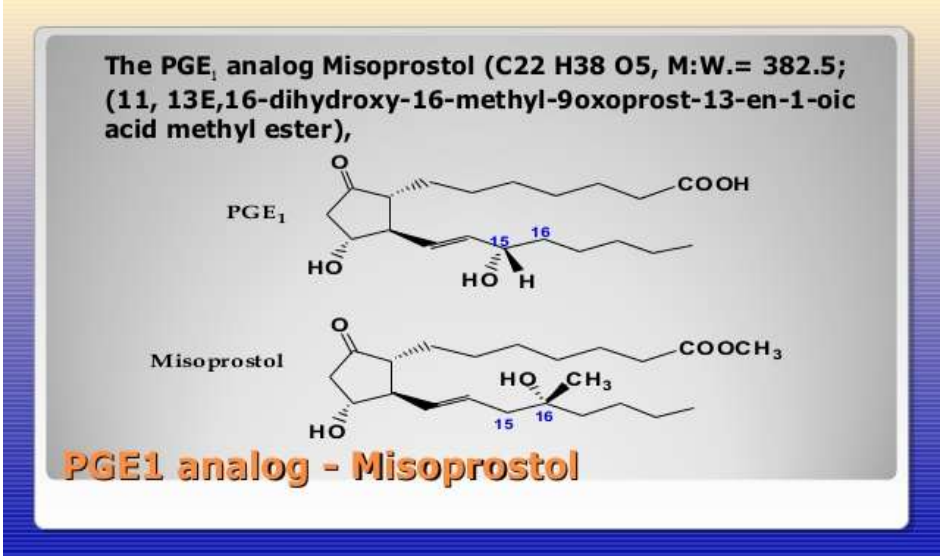

Figure 1. PGE1 Analog – Misoprostol.

Misoprostol is available in many countries worldwide and has advantages over the rest of the prostaglandins as it is inexpensive, thermo and light stable and has shelf life of several years even in tropical conditions and is easy to use. Its action upon the contractility of myometrium is extensive and is very efficient in dilating the cervix. It can be used alone or with combination of Mifepristone

1.6.3. Route of Administration

The routes of administration of Misoprostol are

- ❖ Oral
- ❖ Buccal
- ❖ Sublingual
- ❖ Vaginal

- Rectal.

1.7. ADVERSE REACTION OF MISOPROSTOL

The most common side-effects after administration of misoprostol are

- Vomiting
- Abdominal pain
- Headache
- Chills
- Fever
- Shivering
- Diarrhea

1.8. AIM AND OBJECTIVES OF THE STUDY

Considering the merits of misoprostol and its beneficial effect on uterus and cervix to expel the fetus under MTP, the present study was under taken in the Department of Obstetrics & Gynecology, Govt. Kilpauk Medical College Hospital, Chennai, with the following objectives:

1. To compare the efficacy and safety of both oral and vaginal misoprostol in second trimester pregnancy termination
2. To study the Induction-abortion interval with misoprostol by oral and vaginal route

2. REVIEW OF LITRATURE

Dickinson JE *et al*.[9] (1998) conducted a study on 100 women found that intravaginal misoprostol was as effective as gemeprost in achieving delivery within 24 hours (alpha = 0.1, 80% power) in second-trimester pregnancy. Women with fetal death in utero, severe fetal anomaly, or psychosocial pregnancy termination between 14 and 28 weeks gestation were recruited and randomized to receive either 1 mg gemeprost 3 hourly for 5 doses, or 200 mcg misoprostol 6 hourly for 4 doses, intravaginally . Delivery within 24 hours occurred in 75.1% of women receiving gemeprost and 74.9% receiving misoprostol (P = 1.0).There was no significant difference in the incidence of maternal fever > 37.5 degrees C, nausea, diarrhea, or placental retention. A 200-fold pharmaceutical cost advantage was observed with the use of misoprostol compared with gemeprost. Intravaginal misoprostol performs as effectively as gemeprost in achieving delivery in the second trimester without increase in adverse effects and displaying a significant cost advantage.

Carbonell JL *et al*.[10] (1998) demonstrated in their study the effectiveness and safety of misoprostol without the need of post-expulsion

systematic curettage in early second-trimester abortions, i.e. at 13-15 weeks' gestation. A group of 151 women, with gestations from 85 to 105 days, received 800 micrograms of vaginal misoprostol every 25 h for a maximum of three doses, without having post-expulsion systematic preventive curettage performed. A complete abortion occurred in 121/151 subjects (80%; 95% confidence interval, 78-87%). The decrease in hemoglobin was statistically significant (p = 0.0001), but without clinical relevance (11.8 mg/dl (SD, 0.9) before treatment and 11.4 mg/dl (SD, 1.0) afterwards. No statistically significant differences were found between the success rate and any of the women's characteristics. Vaginal bleeding lasted 6 +/- 3 days, spotting 6 +/- 3 days, and total bleeding 12 +/- 5 days (median, 11 days; range, 1-29). The acceptable expulsion time in 80% of the cases, the fact that post abortion systematic curettage was not needed, the clinically insignificant hemoglobin loss and the abortion rate obtained, show that misoprostol by vaginal administration may be an alternative for interrupting gestation in the early second trimester of pregnancy.

Suk Wai *et al*.[11] (2000) included a total population of 142 healthy patients and randomly assigned into two groups, group 1 received 200 mg mifepristone plus 400 μg misoprostol orally every 3 hrs upto the maximum dose of 5 doses. Group 2 received 200 mg mifepristone plus

200 μg misoprostol vaginally every 3 hrs upto the maximum dose of 5 doses. In their study, it found that the rate of complete abortion was 81.40% in the oral group and 75.40% in the vaginal group. The complete abortion rate in the vaginal group was insignificant than oral group. The median induction to abortion interval was similar in both the groups i.e. 10.40 versus 10.0 hrs. Both the occurance of diarrhoea [40.0 (oral) versus 23.20% (vaginal), p value =0.03] and the amount of drug used in this study (1734 compared with 812, P<0.0001) were significantly higher in the Group 1 (oral) than in the vaginal group. The percentage of women who aborted in 24 h was found to be 81.4% in the oral group and 87.0% in the vaginal group.

Wong KS *et al*.[12] (2000) in their study 148 randomly selected women aged 16-40 years were given vaginal misoprostol 400 microg every 3 h for a maximum of five doses in 24 h for group 1. Women in group 2, were given vaginal misoprostol 400 microg every 6 h for a maximum of three doses in 24 h. The same regimen was repeated if women did not abort in 24 h. The median induction-abortion interval was found to be 15.2 h and 19.0 h in group 1 and group 2 respectively and it was observed in their study that the median induction to abortion interval was significantly very shorter, $p < 0.01$, than that in the group 2 (vaginal).

The pregnant women in the study who achieved the successful abortion was 90.50% and 75.70% within 48 hrs for group 1 and group 2, respectively. It is found that the rate of successful abortion in group 1 was also significantly higher (<0.02) than that in the group 2.

Gilbert A *et al*.[13] (2001) conducted a trail study to evaluate the safety and efficacy of misoprostol in termination of mid trimester pregnancy by selecting a population of 55healthy pregnant women. Of the 55 cases, 26 women received all dose of misoprostol orally and 29 received vaginal route. The regimen of misoprostol dose was 400 µg a the first dose followed by a second dose of 200 µg 2 h later and then 40 h 200 µg doses until delivery or 32 h from commencement of the treatment. The average induction-delivery interval in the vaginal group was 17.5 hrs compared to 33 hrs in the oral group (p=0.0003). The percentage of women who delivered at 24 h was 93% and 19% for the vaginal administration group and oral administration group, respectively. At 48 hrs, the percentage of women who delivered was 100% and 70% for the vaginal administration group and oral administration group (p <0.05), respectively.

Pongsatha S and Tongsong T [14] (2001) in their study administered 800 microgram misoprostol tablet intravaginally every 12 hours. The mean induction delivery time was 21.38 + 13.68 hours, mean abortion time was 21.56 +/- 13.68 hours. Diarrhea was the most common side effect occurring in 40 per cent of patients.

Dickinson JE *et al*. [15] (2003) conducted an MTP study to compare the clinical efficacy and side effects of oral misoprostol with vaginal misoprostol for second-trimester pregnancy termination on a sample size of 225 women. Three misoprostol regimens were compared: 400 microg vaginally at 6-hour intervals (group 1), 400 microg orally at 3-hour intervals (group 2), and a loading dose of 600 microg vaginally followed by 200 microg orally at 3-hour intervals (group 3). There was a significant difference in the median time to achieve delivery among the three groups: group 1, 14.5 hours (95% confidence interval 12.0, 16.9), versus group 2, 25.5 hours (13.5, 23.8), versus group 3, 16.4 hours (interquartile range 14.2-37.3) (P =.042). Within 24 hours of commencement 85.7% of women in group 1, 44.8% in group 2, and 74.1% in group 3 delivered (P =.003). At 48 hours 0% in group 1, 20.7% in group 2, and 3.7% in group 3 were undelivered (P =.011).

Suneeta Mittal *et al*. [16] (2005) in their trial study, 150 healthy pregnant women of < 63 days of amenorrhoea received mifepristone (200 mg) orally on day one and followed by misoprostol 0.80 mg orally and vaginally on day three. In their study, it was seen that the rate of completion abortion rate in each groups was 96 to 100% and further noticed that there was no further increasing successful outcome and shortening of duration or amount of bleeding when extra dose of 0.40 mg misoprostol twice a day from day four to ten was adminstered.

Pongsatha S and Tongsong T [17] (2004) observed in their study that the success rates of termination in pregnancy within 12, 24, 36, 48 hrs were 50.80%, 84.10%, 88.90% and 92.10% respectively when the regimen of 400 μg of misoprostol was given intravaginally at every 6 hrs. In their study, the mean induction to delivery time in cases of delivery within 48 hrs was 13.2 ± 8.4 hrs, the range was 2.25-22.9 hrs. The most frequent maternal side-effect was chill (33.3%). No serious maternal complication was detected. 400 μg misoprostol given orally at every 4 h is more effective for pregnancy termination in cases of intra-uterine fetal death and may be an alternative regimen because of its easiness and convenience. Time interval to fetal expulsion for misoprostol administration was 25.9 +/- 34. 1 hour, the range 4.0-142.7 hours. This

result reconfirms the efficacy of misoprostol and suggests that misoprostol may comparatively be safer even in cases with previous cesarean section. The high incidences of adverse reactions were chill (23.50%), fever (47.10%) and nausea (17.60%). In this series, no uterine rupture occurred at all.

Subir Kumar Bhattacharyya *et al* [19] (2006) observed in their study that there was no significant difference in the success rates at 24 and 48 h (Regime A: 97.18 and 98.59%; Regime B: 95.45 and 95.45%), and in mean induction-abortion interval (12.97 versus 12.13 h). However, mean misoprostol requirement was significantly higher for Regime A (1701.4 versus 1269.7 µg). The incidence of fever was significantly less in Regime B (32.4 versus 14.9%). Use of vaginal misoprostol for second trimester abortion had comparable efficacy with less drug requirement for the 600 µg loading dose followed by 200 µg 3-hourly regimes compared to the 400 µg 3-hourly regime.

Behrashi M *et al* [20] 2008 observed in their study that the percentage of women who delivered was significantly higher in vaginal group than the oral group (86.70 versus 43.30 p=0.0006) when the initial doses 400 µg was followed by 400 µg up to the

maximum of 3 doses (1200 μg) was administered both orally (Group-1, n=30) and vaginally (Group-2, n=30). In induction to expulsion interval and complications rates no significant differences were observed.

Mahjabeen *et al* [21] 2009 in their study of sixty healthy pregnant women at second trimester of gestation found that after oral misoprostol Group-1 (n=30) and vaginal misoprostol Group- 2 (n-30) of 200 μg 4 h apart. They found the mean induction abortion interval was found to be 11.80±8.30 and 12.80±8.50 h, respectively for the group 1 and group 2 patients. The result obtained in his study was insignificant statistically. No reports on the common side effects in both the groups (dizziness, nausea, diarrhea, pyrexia and hyper stimulation).

Helena von Hertzen *et al* [22] (2009) in their study selected randomly selected 681 healthy pregnant women and administered each 400 mg of misoprostol vaginally and sublingually every 3 hrs up to the maximum of 5 doses. They further administered a quantity of 400 mg misoprostol every 3 hrs up to 5 doses, if abortion did not take place at 24 hrs. In their study, it was noted that at 24 hrs, the success (complete or incomplete abortion) rate was 85.90% in the vaginal administration group

and 79.80% in the sublingual group, respectively. The study concluded that higher effectiveness was seen in vaginal administration than sublingual administration of misoprostol in termination of second trimester pregnancies, but the results in their study were mainly determined by nulliparous women.

Sumant R. Shah *et al* [23]. (2010) conducted a study in order to find out the safety and effectiveness of vaginal misoprostol for second trimester termination of pregnancy. It was a prospective study involving 30 women with 12-20 weeks gestation requesting termination. Four hundred microgram misoprostol was inserted in the vagina followed by 200µg every four hourly. The mean age of the women was 25.96 years. The mean gestational age was 15.66 weeks. Chi-square test was used for statistical analysis. 93.3% of women aborted within 16 hours without any significant side effects. Vaginal misoprostol is a very effective and safe method for second trimester pregnancy termination. It reduces the time and the cost of second trimester pregnancy termination.

Deshpande Sonali *et al*. [24]. (2010) in their study demonstrated that 200 healthy women within 63 days of amenorrhea were selected for medical abortion and administered 200 mg of mifepristone. After 48 h,

they were administered misoprostol 400 µg vaginally. At the end of 4 h, reinstallation of misoprostol 400 mg was given vaginally whenever required. The complete abortion rate in pregnant women with amenorrhea ≤49 days versus 50-63 days was 99.16% and 98.75%, respectively. The average duration of bleeding in women with amenorrhea ≤49 days versus 50-63 days was 6.26 (S.D. 2.43 days) and 6.98 days (S.D. 2.26 days), respectively and the difference of both the groups was statistically significant ($p < 0.05$). The study has confirmed that the use of the above combination was safe and effect for inducing medical abortion in pregnant women with amenorrhea up to 9 weeks gestation (63 days). 741 pregnancy terminations were carried out using misoprostol with dosage varied from 50 µg to 800 µg, mostly 400 µg intravaginal route every 3 h. The most common incidence of side effects for termination of pregnancy was severe thalassemia (35.80%). The majority of cases in the study were pregnancies with live fetus and 18.20% were linked with dead fetus in utero. The success rate of pregnancy termination within 48 h was 85.90%. The pregnant women with previous cesarean section accounted for 8.6% of cases. The mean abortion

time and gestational age was 25.35 h (ranging from 1.25 to 247.888h) and 20.94 weeks, respectively. Two most common adverse effects in the study were fever and chill (34.30% & 43.70%). There was no adverse complications (uterine rupture) were found. The study finally concluded that misoprostol had high efficacy for the termination of pregnancy with acceptable minor side effects and it was relatively safe.

Pongsatha and Tongsong (2011) [25] found the most common complications to be chill (43.7%), analgesic-requiring pain (39.3%) and fever (34.3%) in their patients who received 400 μg misoprostol through the intravaginal route every 12 h. High doses (800 μg in 24 h) may have affected the higher complication rates.

Anupama Goel *et al* [26] (2011) in their study found that eighty eligible healthy women were selected with single intrauterine pregnancy of more than ≤ 7 weeks of gestation. They administered 200 mg of mifepristone orally and 400 μg of misoprostol vaginally simultaneously in Group 1 and Group 2, respectively at 24 hr interval. The rate of complete abortion was 95% and 97.50% for 38 women in (Group 1) and 39 women (Group 2), respectively. The induction abortion interval of Group 1 and

group 2 was 6.50 ± 1.48 and 5.95 ± 1.81 h, respectively. The p value for the rate of complete abortion and the induction abortion interval was p=0.56 and p=0.13, respectively. The combined administration of mifepristone and misoprostol (400 μg) vaginally is very effective alternative to standard regimens for medical abortion was up to 7 weeks of gestation period.

Nagaria Tripti *et al* [27] (2011) conducted a study on the safety and efficacy of misoprostol alone and mifepristone with misoprostol in second trimester pregnancy termination by selecting a population of 200 healthy pregnant women. They divided the 200 cases in two groups of 100 each. In the study group, 200 mg of mifepristone was given at every 12 h hrs before intravaginal insertion of misoprostol 600 μg followed by 400 μg misoprostol every 3 hrs up to the maximum interval of 5 doses or till the abortion occurs. In their study, it is found that in both groups, the side effects were similar noted in both the groups were similar for the most part of vomiting, fever, nausea, abdominal cramps. The mean induction abortion interval from the insertion of the first misoprostol was significantly shorter in the pretreated group (mifepristone) 6.72 plus or minus 2.26 h as compared to misoprostol alone group (12.93 ± 3.4 h), the p value of the study was P\0.001.

Sumera Tahir *et al* [28]. (2011) carried out a study to compare the efficacy & safety of Misoprostol for termination of pregnancy in second trimester in scarred versus unscarred uterus. During 6 months period from 22nd March 2007 to 22nd September 2007. 60 patients (30 with scarred and 30 with unscarred uterus) were admitted for second trimester termination of pregnancy for maternal reason, fetal congenital anomalies and intrauterine fetal demise and induced with vaginal misoprostol. The loading dose of 400 mcg followed by maintenance dose of 200 mcg at 4 hourly interval to a maximum of 4 doses. Efficacy included induction to delivery interval & safety included maternal complications and side effects like uterine rupture, hysterectomy, severe haemorrhage, pyrexia, nausea & vomiting. Success rate of T.O.P. was 96.7% in group A (scarred uterus) VS 93.3% in group B (unscarred uterus) Maternal complications were nausea & vomiting 3.3% in group A VS 0% in group B, Pyrexia 3.3% in each group, no case of uterine rupture was recorded. Misoprostol is safe and effective drug for Midtrimester T.O.P. in scarred as well as unscarred uterus.

Krishna Dahiya *et al* [29]. (2012) conducted a study on a population of 100 pregnant women having gestational age >56 days and divided the groups randomly into Group A and Group to study the safety and efficacy

of mifepristone and buccal misoprostol versus buccal misoprostol alone. In Group A , on day 1, women received 200 mg mifepristone followed by buccal misoprostol 800 µg on day 2. . In Group B, on day 1, women received 800 µg buccal misoprostol only on day 2. In their study, the rate successful abortion in group A and Group B was 92% (n=46) and 74% (n=37), respectively. The percentage of incomplete abortion with retained products of conception in Group A patients and Group B was 8% (n=4) and 16% (n=16), respectively. The 6% (n=3) of pregent women had missed abortion and 4% (n=2) had continued pregnancy in Group B whereas in Group A none of the women had missed abortion and continued pregnancy. The acceptance of overall method and overall route was 100% and 83% respectively. The regimen of misoprostol alone was a very low cost and compared to that of mifepristone / misoprostol. Though the safety and efficacy of mifepristone followed by buccal misoprostol is better, buccal misoprostol alone can be used for termination of pregnancy in patients where mifepristone is either unavailable or contraindicated.

A study conducted by Murat Bozkurt *et al* [30]. (2012) involved an investigation of the effectiveness and complications of oral and vaginal misoprostol use on the termination of second trimester pregnancies. A total of 103 cases were recruited from the medical records of the

Gynecology and Obstetrics Clinic of Taksim Research and Training Hospital and Şırnak İdil State Hospital. Women underwent therapeutic termination of pregnancy between the 14 to 28th week of gestation using the defined combined misoprostol regimen. After the women were admitted, 200 μg vaginal (100 μg intracervical, 100 μg into the posterior fornix), 200 μg oral doses and 200 μg of sequential doses were administered in the 2nd and 4th hour. Subjects were excluded from the study if they were out of the defined gestational weeks using additional drugs with misoprostol; their data has not been recorded in detail. Of the 103 cases, 86 had an abortion within 24 h and the mean expulsion time was calculated as 15.42 ± 7.14 h (min 6.39 to max 20.03) in this group. The success rate for the 24 h was found to be 83.4%. Six more cases had an abortion when the second dose was given. The mean expulsion time was found to be 9.31 ± 3.26 h (min 6.45 to max 13.21) for the second 24 h. The success rate over 48 h rose to 89.3%. The total expulsion time was 18.30 ± 8.74 h. There was a history of previous caesarean sections in 2 out of 11 cases that did not have an abortion and one of these cases underwent a hysterotomy. The pregnancy was terminated by evacuation and curettage, as abortion did not occur despite 3 different high dose misoprostol regimens as in the other cases. Pregnancies of the remaining 9

cases were terminated with different misoprostol doses, oxytocin infusion and the evacuation and curettage method. of the 103 cases, 86 had an abortion within 24 h and the mean expulsion time was calculated as 15.42 ± 7.14 h (min 6.39 to max 20.03) in this group. The success rate for the 24 h was found to be 83.4%. Six more cases had an abortion when the second dose was given. The mean expulsion time was found to be 9.31 ± 3.26 h (min 6.45 to max 13.21) for the second 24 h. The success rate over 48 h rose to 89.3%. The total expulsion time was 18.30 ± 8.74 h. There was a history of previous caesarean sections in 2 out of 11 cases that did not have an abortion and one of these cases underwent a hysterotomy. The pregnancy was terminated by evacuation and curettage, as abortion did not occur despite 3 different high dose misoprostol regimens as in the other cases. Pregnancies of the remaining 9 cases were terminated with different misoprostol doses, oxytocin infusion and the evacuation and curettage method. When complication rates were evaluated, analgesic requiring pain (18.4%) was the leading complication, followed by nausea (11.6%), fever (7.7%), headaches and dizziness (5.8%), transfusion-requiring haemorrhage (3.8%) and diarrhea (1.9%). Uterine rupture or death did not occur. A combined misoprostol regimen is relatively safe

with acceptable side effects when used carefully for the termination of second trimester pregnancies.

Sonal Kumar *et al* [31]. (2013) undertook a study to determine the efficacy and the side effect profile of a regime of 200 mg of mifepristone administered orally followed by 800 mcg of vaginal misoprostol after 48 h. 50 cases of medical abortion meeting the inclusion criteria were included. On day 1, 200 mg of oral mifepristone was given. On day 3, the patient was called back, and 800 mcg of Misoprostol administered per vaginum and was observed for 6 h. The patients were then called back for review after two weeks to make sure that the abortion was complete. Although, in most cases, this was clinically evident, an ultrasonography was repeated to confirm the completion. Out of the 50 patients, four were lost to follow up, and of the remaining 46 patients, abortions were complete in 44 (95.65 %), while two (4.35 %) patients required surgical intervention. Medical abortion with 200 mg oral mifepristone and 800 mcg vaginal misoprostol is an effective, safe, reliable, and noninvasive method with a success rate of 95.65 %. The availability of this low-cost medical treatment using agents which do not require special cold storage and transport facilities and negligible operating theater time makes this

provision of safe abortion feasible in settings especially of developing countries, like India, where medical facilities are limited.

Kranti K. Kulkarni *et al* [32]. (2013) studied the efficacy and safety of combining mifepristone before misoprostol use in second trimester to considerably reduce the induction–abortion interval with the lowest possible dose and adverse reaction. A prospective study was conducted which included 60 patients visiting the antenatal OPD for elective abortions between 13 and 20 weeks of gestation as per the MTP act. They were randomly divided into two groups of 30 each—the study group received mifepristone 200 mg orally before misoprostol, whereas the control group was induced with misoprostol alone. The results were analyzed. Statistical analysis of the study was done using χ^2 test. The induction–abortion interval was significantly shorter in the study group, thereby decreasing the side-effects of the drug as well as duration of hospital stay.

3. MATERIALS AND METHODS

3.1. STUDY DESIGN

Randomized prospective study of seventy two healthy women, between age 18 and 38 years, with 12-20 weeks of pregnancy, requesting second trimester termination of pregnancy, were admitted in Department of Obstetrics and Gynaecology, Government Kilpauk Medical College, Chennai

3.2. STUDY AREA

The study was conducted in the Department of Obstetrics and Gynecology, Govt. Kilpauk Medical College (KMC), Chennai.

3.3. STUDY PERIOD

The study was conducted between November 2012 and November 2013.

3.4. SAMPLE SIZE

- Population size (for finite population correction factor or fpc)(N) 500

- Hypothesized % frequency of outcome factor in the population (*p*):5%+/-5

- Confidence limits as % of 100(absolute +/- %)(*d*): 5%

- Design Effect (for cluster surveys-*DEFF*): 1

- Equation for Sample Size *n* = [DEFF*N p(1-p)]/ [(d2/Z21-α/2*(N-1)+p*(1-p)]

- For a confidence limit of 95% the sample size is 64, hence the sample size was selected as 72.

3.5. SELECTION OF CASES

Seventy two healthy women, between age 18 and 38 years, with 12-20 weeks of pregnancy, requesting second trimester termination of pregnancy, were included in this study. The indications for termination were in consonance with the MTP Act. Written informed consent was taken from all the women. Sonography was done in women whenever necessary for deciding maturity of the fetus. Ethical clearance was obtained from the hospital ethical committee in July 2013. The schematic diagram for participants is shown in Fig. 2.

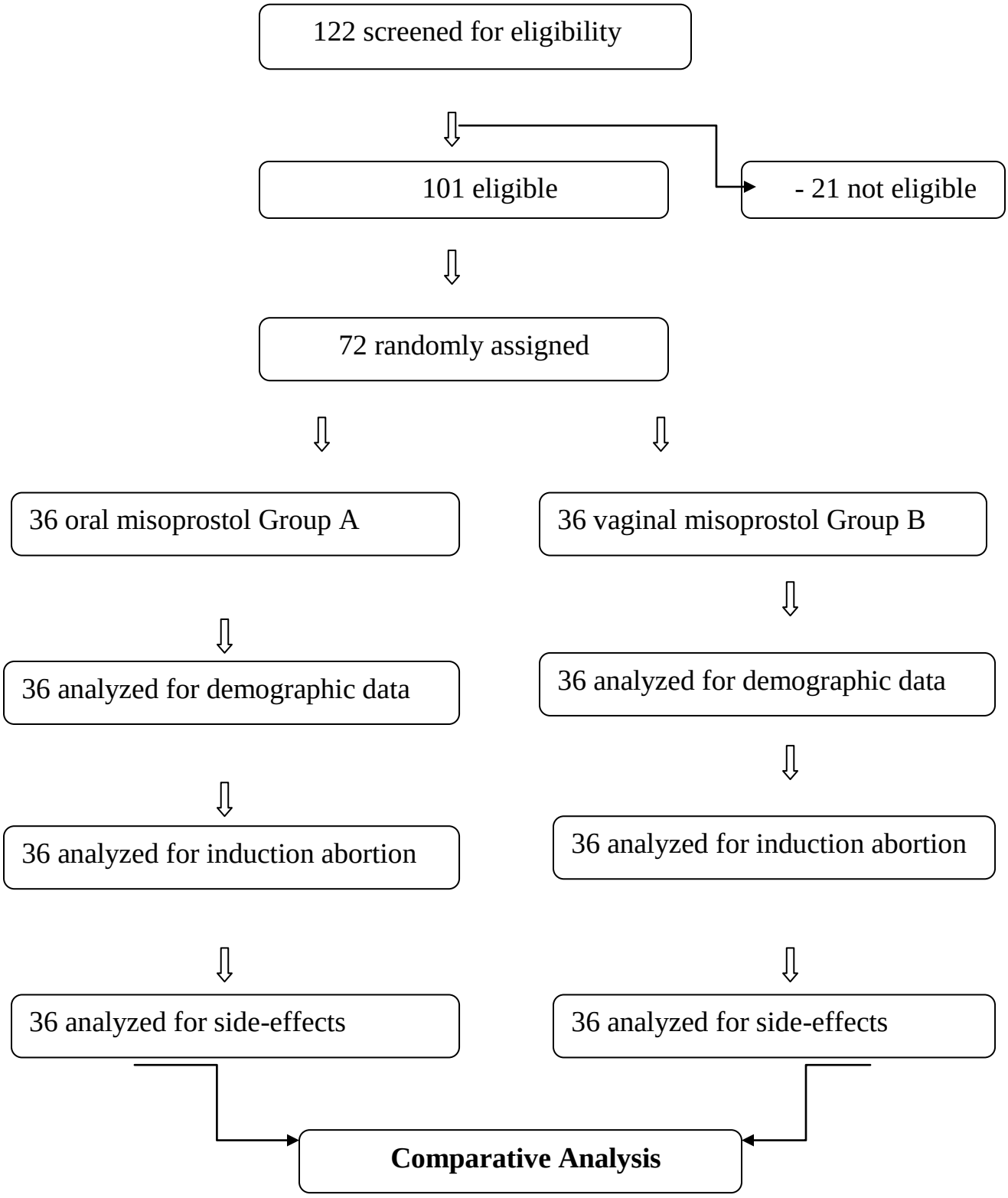

Figure 2. The schematic diagram of the trial profile

3.5.1. EXCLUSION CRITERIA

a. Women with baseline hemoglobin <8gm/dl.

b. Maternal local or systemic infection.

c. Maternal respiratory disease, liver or kidney disease

d. CVS disease.

e. Severe Bronchial Asthma

f. Chronic adrenal failure or steroid therapy

g. Uncontrolled seizure disorder

3.5.2. INVESTIGATION

The following investigations were done prior to misoprostol administration.

1. CBC
2. RFT
3. Urine routine
4. Blood group
5. USG
6. BT and
7. CT
8. VDRL

9. HIV

10. HBS Ag

3.6. STUDY GROUP

The patients were randomly allocated to Group A (n=36) who received oral tablet misoprostol and Group B (n=36) who received vaginal tablet misoprostol.

3.7. PROCEDURE OF MISOPROSTOL USE

A total of 72 cases between 12 and 20 gestational weeks who had undergone for medical abortion by using the defined misoprostol regime were included in the study. The misoprostol regimes were given in the hospital. The patients allocated to Group A, misoprostol 200 µg (Zytotec) was given orally every 4 hrs until the abortion occurred or maximum up to 6 doses. Doses administered through the oral route were observed. The expulsion rate of this regimen at different time intervals [<24 hrs (4-6 h, 6-8 h, 8-10 h, 10-12 h, 12-16 h and 16-24 h) and <48 h)] and complications were investigated. The incidence of side-effects, vital signs, amount of bleeding and uterine contractions were investigated every 3 hrs. The pelvic examination was done every 3 hrs. The gestational weeks

of the patient were calculated based on the first day of the last menstrual period. The calculated gestational weeks were confirmed with ultrasonography. A second course of misoprostol was administered if abortion did not happen after 24 hrs. After the abortion process was complete, pervaginal examination and ultrasonography was done to rule out any retained products and confirm the completion.

For patients in Group- B, misoprostol 200 µg (Zytotec) were vaginally administered every 4 hrs till the expulsion of fetus or up to a maximum of 6 doses. Doses administered through the vaginal route were noted. Vaginal misoprostol was soaked in saline solution and administered to the posterior fornix and intracervical region. The management and observation of the subjects were followed as in case of the procedure followed for Group-A.

Information about side effects was taken from each woman including nausea, vomiting, diarrhoea, fever and abdominal pain. The expulsion rates were evaluated at the <24 h and <48 h. After the passage of abortus, check curettage was carried out in all women in a routine manner under sedation. Procedure related complications like uterine perforation, cervical tear or laceration were noted in few women. Perforation was due to uterine curettage. There was no case of rupture

uterus. All the women were kept in hospital for 24 hours under observation. Those who were willing for permanent sterilization were considered for laparoscopic tubal ligation. On discharge they were asked to come for follow- up after a week or earlier if need arises. On follow up, a pelvic examination was performed on all the women. Any abnormal bleeding or delayed side effects were also enquired.

3.8. EFFICACY OF MISOPROSTOL

The induction- expulsion (abortion) interval was defined as "the interval between the time of administration of the first dose of misoprostol to the time when the fetus aborted".

The complete abortion was defined if fetus and placenta was expelled completely without resorting to further surgical or medical means.

The rates of successful abortion after initial misoprostol administration, induction – expulsion interval, the incidence of side effects and complete abortion in both the groups, oral and vaginal were tabulated, compared. The results were statistically analyzed and evaluated using Fisher' exact test (Open Epi programme, Version 2.3, 2009).

4. RESULTS

A total of 72 women with gestation between 12 and 20 week who needed second trimester termination of pregnancy, were included in the present study. The two groups of 36 women each were compared for various characteristics such as age, parity, previous MTP and LSCS and duration of amenorrhea.

4.1. AGE DISTRIBUTION OF PREGNANT WOMEN

Table 1 shows age distribution of pregnant women in the age group ranged from 18 to 38 years. The maximum number of women was found in the age group 26-30 (41.6%) and 21-25 (44.4%) for oral (Group A) and vaginal (Group B) route of administration, respectively. The minimum number of women was seen in the age group >35 years (2.7%) both for oral and vaginal route of administration. The mean age of women was 26.13 years for Group A and 25.15 years for Group B.

Table 1. Age distribution of pregnant women

Age in years	Number (%)	
	Group A (n=36)	Group B (n=36)
<20	03 (8.3%)	04 (11.1%)
21-25	13 (33.3%)	16 (44.4%)
26-30	15 (41.6%)	13 (33.3%)
31-35	04 (11.1%)	02 (5.5%)
>35	01 (2.7%)	01 (2.7%)
Mean Age (years)	**26.13**	**25.15**

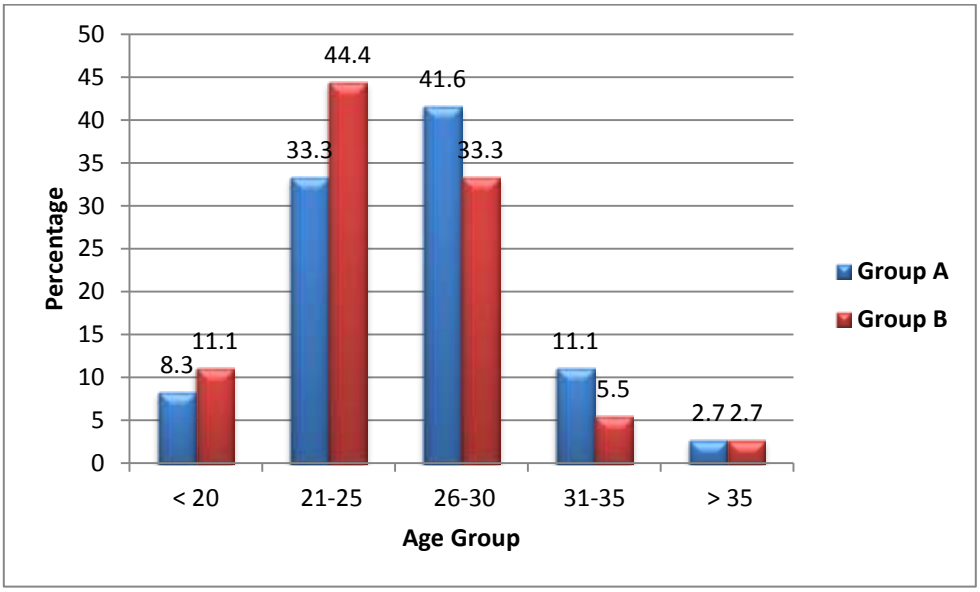

Figure 3. Age distribution of pregnant women

4.2. DEMOGRAPHIC DATA OF PREGNANT WOMEN

Table 2 shows that the maximum number of women was multiparous 77.7% for Group A and 66.6% for Group B. The number of women who had previous MTP for Group A and Group B was found to be 28 11.11% and 8.3%, respectively. In Group A only one woman (2.7%) was found to have undergone LSCS.

Table 2. Demographic profile of pregnant women

Parameter	Group A (n=36)	Group B (n=36)
Parity No. (%)		
Primi	08 (22.2%)	12 (33.3%)
Multi	28 (77.7%)	24 (66.6%)
Previous MTP	04 (11.11%)	03 (8.3%)
Previous LSCS	01(2.7%)	0 (0%)

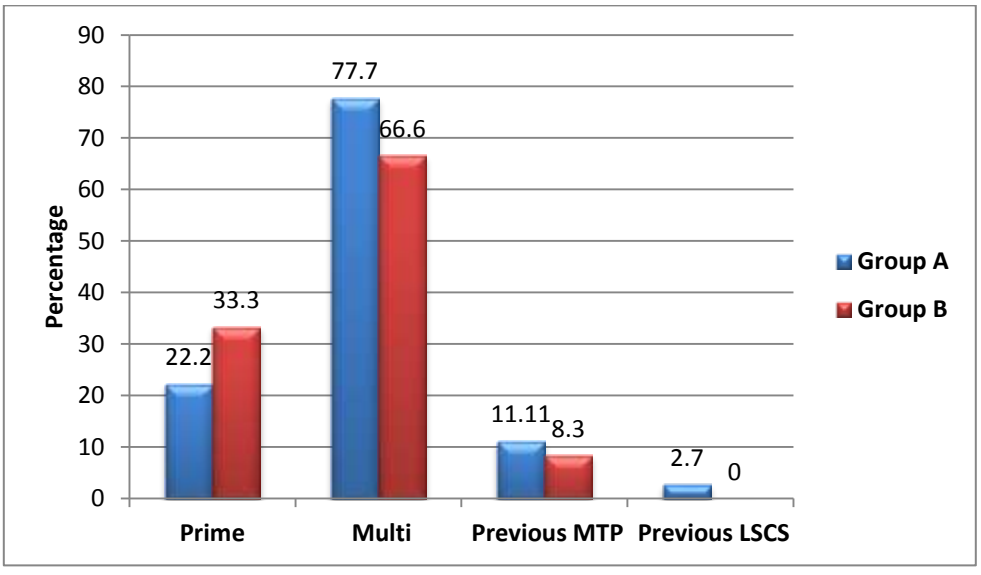

Figure 4. Demographic profile of pregnant women

Table 3 shows that the maximum number of women was found to be 11 (30.5%) in the gestation period 12-14 and 11 (30.5%) in the period of gestation 14-16 for Group A and Group B, respectively. The minimum number of women was found to be in the gestation period 18-20 for both Group A (19.4%) and Group B (16.6%). The mean gestation age was 15.66 weeks for Group A and 15.61weeks for Group B.

Table 3. Period of gestation of pregnant women

Weeks	Number (%)	
	Group A (n=36)	Group B (n=36)
12-14	11 (30.5%)	10 (27.7%)
14-16	09 (25.0%)	11 (30.5%)
16-18	09 (25.0%)	09 (25.0%)
18-20	07 (19.4%)	06 (16.6%)
Mean gestation age (weeks)	**15.66**	**15.61**

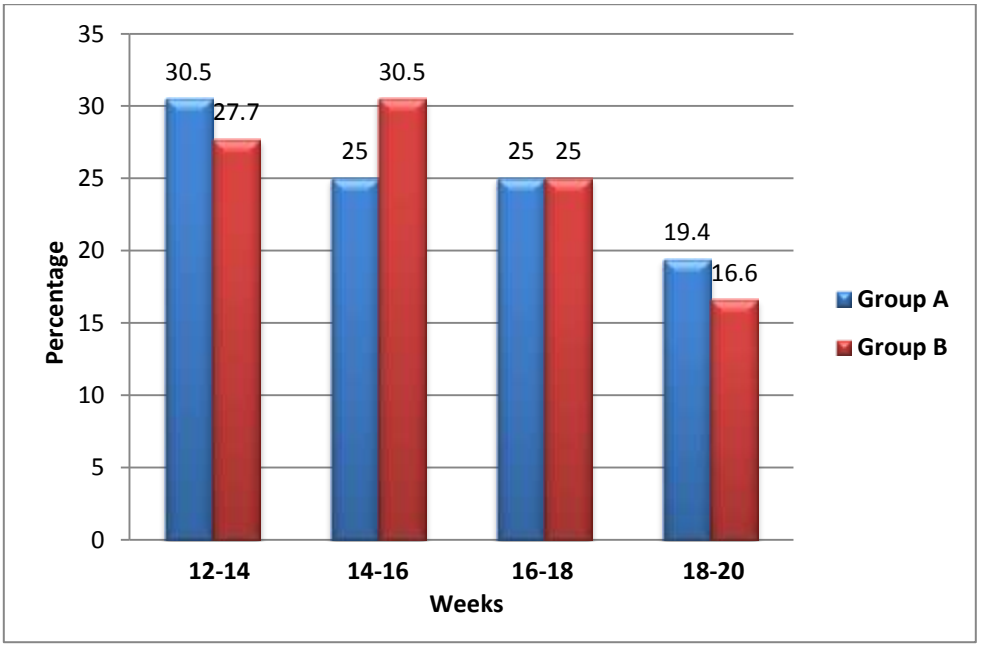

Figure 5. Period of gestation of pregnant women

Table 4 & 5 show the relationship of induction-abortion interval to the gestational age. Most of the women aborted between 6 and 8 hours (36.0%) for oral misoprostol Group-A and 25% for vaginal misoprostol Group-B for 12-16 gestational age. For the gestational age of 16-20, the maximum number of induced abortion was found to be 13.8% and 16.6% for oral misoprostol (Group A) and vaginal misoprostol (Group-B), respectively. The mean induction abortion interval (for 12-16 weeks) for Group A and Group B was 10.05 and 9.05 h respectively. The mean induction abortion interval (for 16-20 weeks) for Group A and Group B was 12.43 and 12.52 h respectively.

Table 4. Induction-abortion interval of oral misoprostol (Group-A)

Weeks	<24 hr						<48 hr	Total
	4-6 h	6-8 h	8-10 h	10-12 h	12-16 h	16-24 h		
12-16 Group A	1	6	4	0	2	1	4	18+(2*)
16-20 Group A	0	5	3	1	2	1	4	14+(2*)

*Two women each in 12-16 and 16-20 gestation period under Group A did not abort. Extra vaginal misoprostol dose was given to make the termination complete.

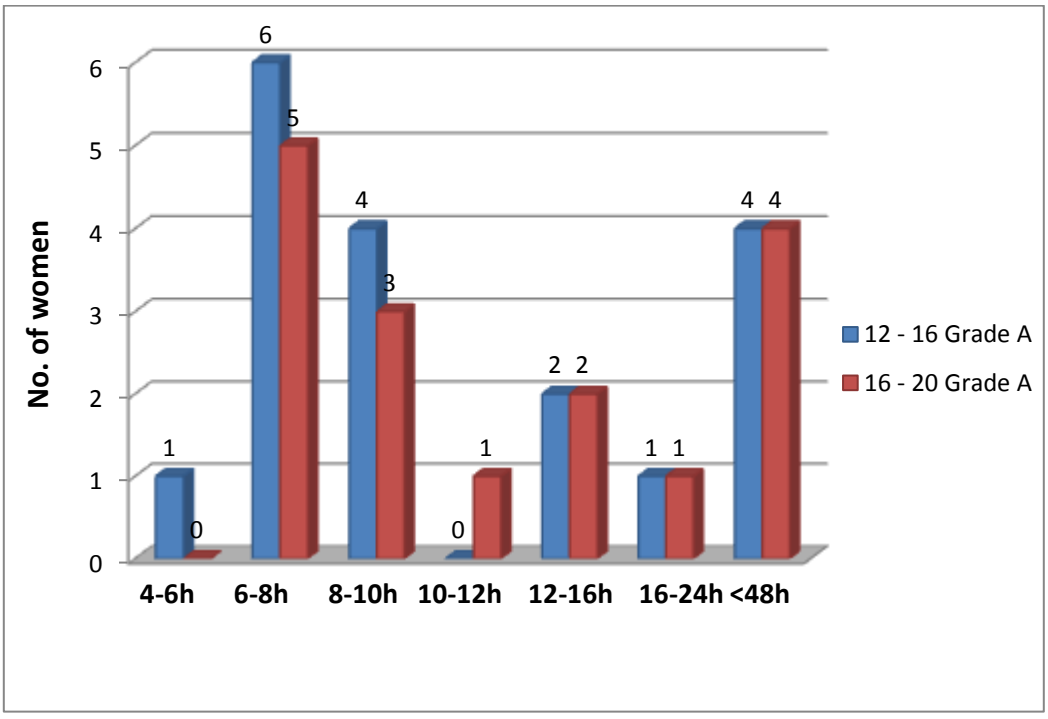

Figure 6. Induction-abortion interval of oral misoprostol (Group-A)

Table 5. Induction-abortion interval of vaginal misoprostol (Group B)

Weeks	<24 hr						<48 hr	Total
	4-6 h	6-8 h	8-10 h	10-12 h	12-16 h	16-24 h		
12-16 Group B	1	9	5	1	2	0	1	19
16-20 Group B	0	7	3	2	3	1	1	17

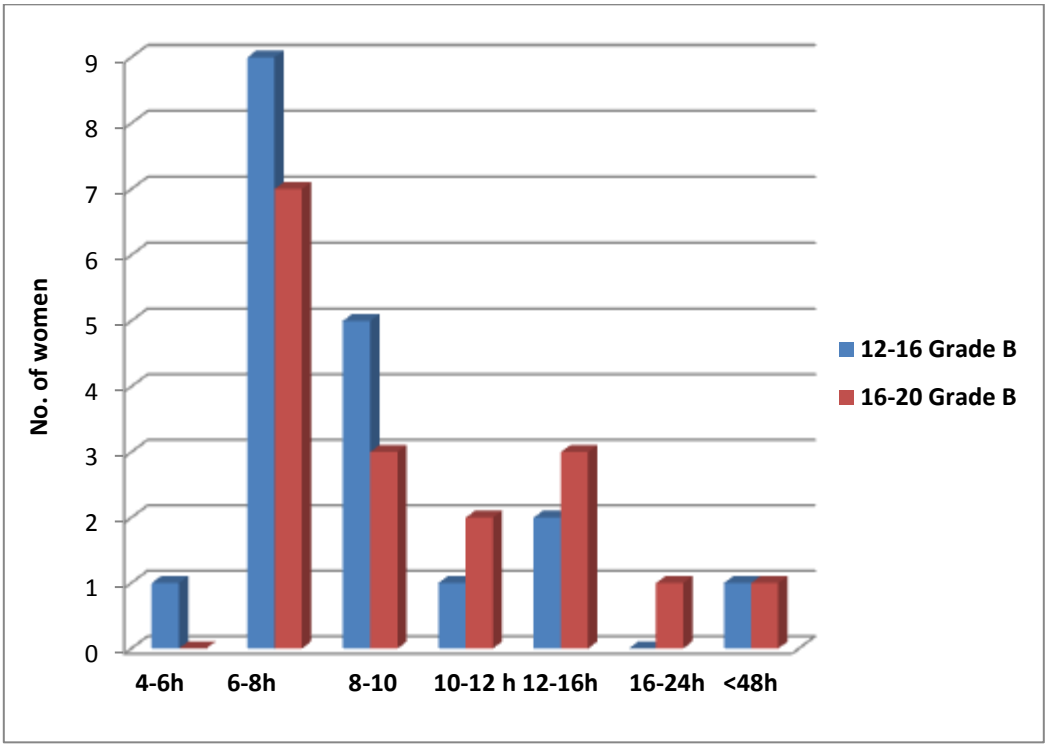

Figure 7. Induction-abortion interval of vaginal misoprostol (Group B)

4.3. STATISTICAL ANALYSIS

The induction-abortion rate was calculated for Group A and B for gestation of 12-16 and 16-20 (weeks) within 24 hrs and <48 hrs by Statistical Analysis. The values are given in the Table 6 & 7.

Table 6. Induction to expulsion interval for 12-16 gestation weeks

Time (hrs)	Frequency of (Group A)	Frequency of (Group B)
<24 h	14 (70%)	18 (94.73%)
<48 h	4 (20%)	1(5.26%)
Total	20	19

(P<0.05) Fisher exact 2-tailed test, P value = 0.3061

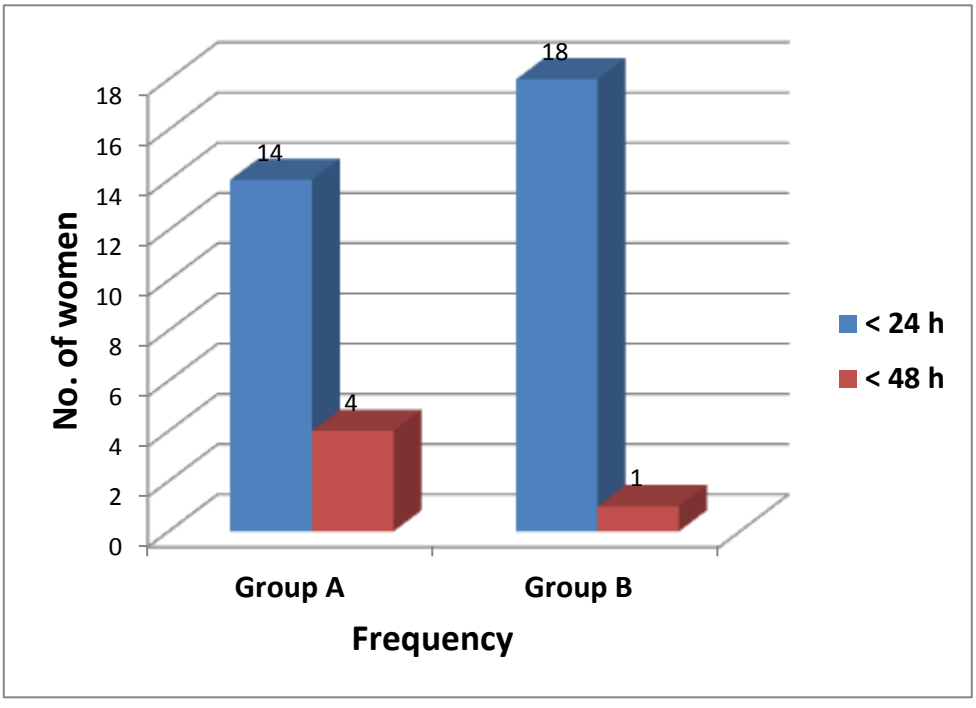

Figure 8. Induction to expulsion interval for 12-16 gestation weeks

Table 7. Induction to expulsion interval for 16-20 gestation weeks

Time (hrs)	Frequency of (Group A)	Frequency of (Group B)
<24 h	10 (62.5%)	16 (94.12%)
<48 h	4 (25.0%)	1(5.88%)
Total	16	17

(P<0.05) Fisher exact 2-tailed test, P value = 0.2239

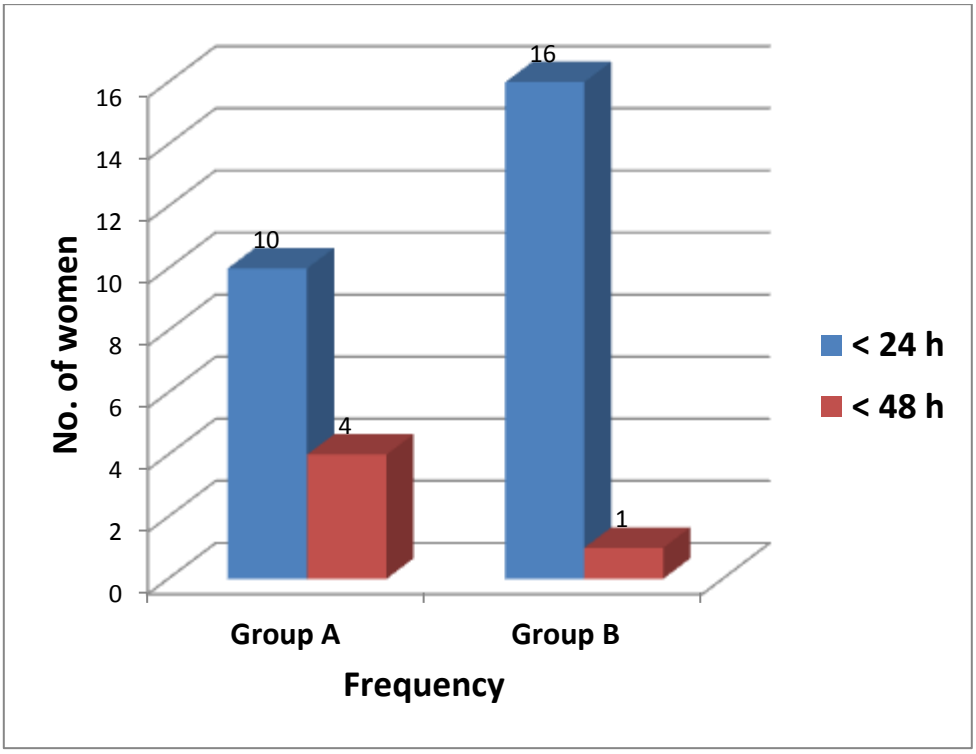

Figure 9. Induction to expulsion interval for 16-20 gestation weeks

Since the cell values obtained for Group A and B for gestation of 12-16 and 16-20 (weeks) within 24 hrs and within 48 hrs were less than 5 and the values in Table No. 6&7 were grouped into a single value. The values are given in the Table 8. The number of women (in percentage) who aborted in the vaginal group was significantly higher than the oral group. It is to be noted that the success rate of group A was 66.67% and that of group B was 94.44% within 24 hrs. The induction to expulsion rate in the vaginal group was significantly higher than that in the oral misoprostol group ($P<0.03018$).

Table 8. Induction to expulsion interval for oral and vaginal groups

Time (hrs)	Oral misoprostol Group A (n=36)	Vaginal misoprostol Group B (n=36)
<24 h	24 (66.67%)	34 (94.44%)
<48 h	8 (22.21%)	2(5.56%)
Total	32 (4*)	36

(P<0.05) Fisher exact 2-tailed, P value = 0.03018

Statistically significant between the groups

*Four women in 12-16 and 16-20 gestation period under Group A did not abort. Extra vaginal misoprostol dose was given to make the termination complete.

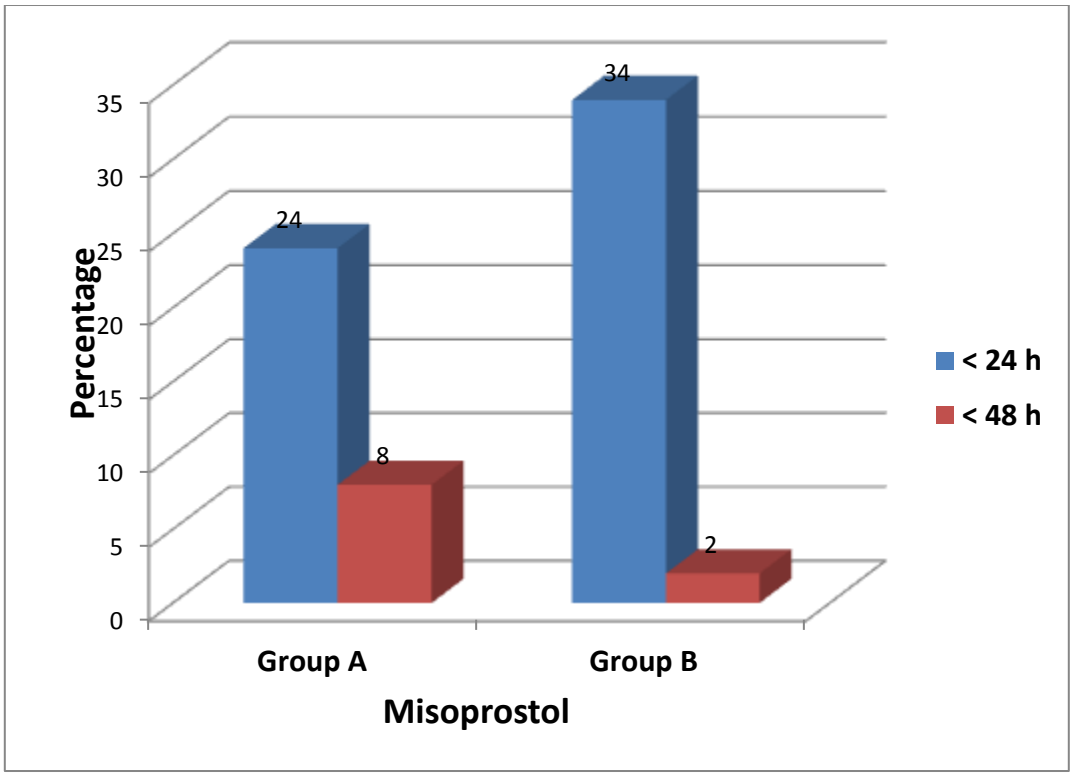

Figure 10. Induction- expulsion interval for oral and vaginal groups

Table 9 shows the rate of side effects after administration of misoprostol. After misoprostol administration, the women were observed hourly for side effects, onset of bleeding and vitals. Maximum number of women had nausea (22.2% and 36.1%) for oral misoprostol group (group A) and vaginal misoprostol groups (group B), respectively. The percentage of women who had abdominal pain was found to be 30.5 and 33.3 for oral misoprostol group (group A) and vaginal misoprostol groups (group B), respectively. Maximum number of women (33.3%) had temperature $>38^0$C in oral misoprostol group (group A), whereas in vaginal misoprostol group (group B), it was only 11.1%. Side-effects such as vomiting, diarrhoea, dizziness, headache, breast tenderness and rash were not significant in both the groups.

Table 9. Side effects after misoprostol administration

Parameter	Oral misoprostol Group A (n=36)	Vaginal misoprostol Group B (n=36)
Nausea	8 (22.2%)	13 (36.1%)
Vomiting	1(2.7%)	0 (0%)
Diarrhoea	0 (0%)	0 (0%)
Dizziness	1 (2.7%)	0 (0%)
Headache	1 (2.7%)	0 (0%)
Breast tenderness	3 (8.3%)	2 (5.5%)
Lower abdominal pain	11 (30.5%)	12 (33.3%)
Temperature>38^{0}C	12 (33.3%)	4 (11.1%)
Rash	1 (2.7%)	0 (0%)

Values are expressed as number (%)

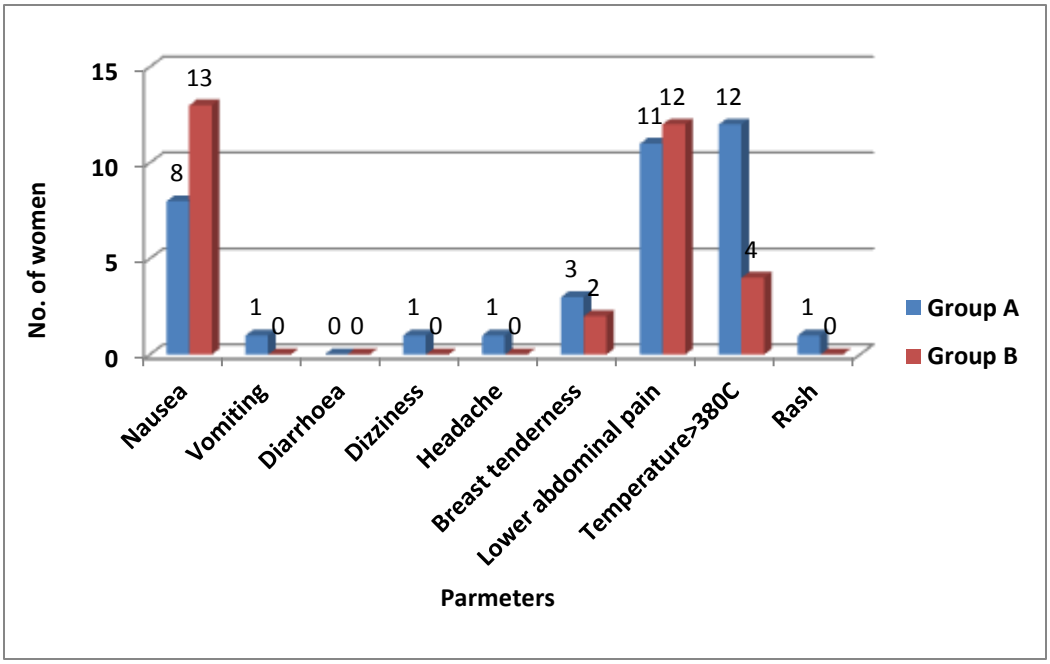

Figure 11. Side effects after misoprostol administration

4.4. OUT COME OF TREATMENT

32 women in oral misoprostol (Group A) and all women in vaginal misoprostol (Group B) were successfully induced complete abortion (MTP). However, the remaining 4 women in oral misoprostol group (Group A) were also given vaginal misoprostol and pregnancy termination was completed.

4.5. COMPARATIVE ANALYSIS OF TWO GROUPS OF STUDY

From the Table No.10, it is understood that the vaginal misoprostol was found to be 100 effective in complete expulsion of fetus, whereas in oral the termination of pregnancy was complete only in 88.8% of women. The remaining (11.2%) women were given additional dose of vaginal misoprostol to complete termination. The side-effects due to oral misoprostol (11.6%) were more than using vaginal misoprostol (9.5%). In case of oral misoprostol (8.3%) the placenta had to be extracted manually. However, in case of vaginal route, no such complication was noticed. No significant differences in the Pharmacological management of side-effects were noted between oral (Group A) and vaginal (Group B).

Table 10. Labour Induction results in two groups

Parameters	Oral misoprostol Group A (n=36)	Vaginal misoprostol Group B (n=36)
Complete expulsion (%)	88.8 (n=32)	100 (n=36)
Side-effects (average %)	11.6	9.5
Pharmacological management of side-effects (%)	14.0 (n=5)	14.0 (n=5)
Manual extraction of placenta (%)	8.3 (n=3)	0

Values are expressed as number (%)

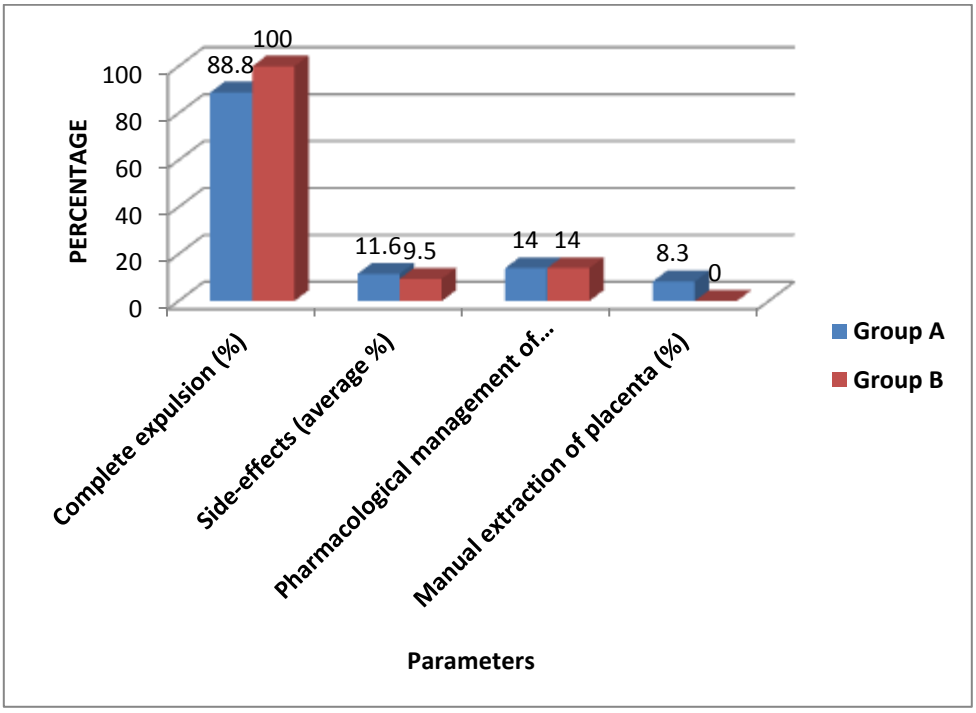

Figure 12. Labour Induction results in Group A and Group B

In the present study, no women had to undergo medical termination of pregnancy by surgical treatment. No severe complications such as heavy bleeding or uterine rupture even in women with previous cesarean delivery history were noticed.

5. DISCUSSION

Abortion is defined as termination of pregnancy by any means before the fetus is viable. In my study, a total of 72 pregnant women of >12 and <20 weeks were taken and divided into two groups. Group A (n=36) received oral misoprostol whereas Group B (n=36) received vaginal misoprostol.

Misoprostol, while as being accepted as a labour inducing agent, is also found to be safe and very effective for the termination of pregnancy because of cervical ripening and uterotonic properties. Before misoprostol's widespread use, PGE2, vaginal suppositories and PGF2α were dominant in the early stage of labour and act mainly on the cervix. Even though effective and efficacious, these are associated with side effects such as nausea, vomiting, diarrhea and fever in high percentage of patients.

The importance of misoprostol as a cervical ripening agent, in its own, is clear. Misoprostol is cheap, less expensive and more convenient to administer. It does not require refrigeration for its storage, as it is stable at room temperature.

5.1. INDUCTION-ABORTION INTERVAL

In the present study, most of the women aborted between 6 and 8 hours (36.0%) for oral misoprostol (Group-A) and 25% for vaginal misoprostol (Group-B) for 12-16 gestational age. For the gestational age of 16-20, the maximum number of induced abortion was found to be 13.8% and 16.6% for oral misoprostol (Group A) and vaginal misoprostol (Group-B), respectively.

In this study, four cases of gestation age 16-20, in addition to oral misoprostol administration; vaginal misoprostol was administered to complete MTP. El-Refaey & Templeton [33] (1995) and Ashok & Templeton [34] (1999) in their study noticed nearly upto 97% abortion within 15 hrs of administration when combination of vaginal and oral misoprostol administration was carried out.

About 80 % of pregnant women aborted within 24 h of misoprostol administration. (Suk Wai Ngai *et al* 2000) [11] When the dose of oral misoprostol was increased from 200 to 400 µg every 3 h.

Misoprostol has proven its efficacy as an effective abortifacient for the second trimester termination of pregnancy. It is being successfully used through all the routes i.e. sublingual, oral and vaginal and in

different regimens with the induction abortion interval varying from 12 h to as high as 33 h.(Wong KS *et al*. 2000 [12] and Pongsatha S *et al*., 2001) [14].

Gilbert and Reid 2001 [13] reported higher success rate for vaginal administration of misoprostol than oral route (93 vs 19) in mid trimster of pregnancy termination. This rate increased within 48 h for vaginal and oral groups (100 vs 70% respectively. The dosing regimen in their study was 400 µg as the initial dose followed by a second dose of 200 µg 2h later and then 4h 200 µg doses until delivery or 32h from commencement of treatment. Overall, the average induction to delivery interval in vaginal and oral route was more.

Bebbington *et al* (2002) [36] used misoprostol orally and vaginally for mid trimster of pregnancy. They randomly assigned 140 women. 65 and 39 women had received misoprostol orally in dose of 200µg every hr for 3h and vaginally in dose 400 µg every 4hr, respectievely. The protocol was followed for 24 hr. According to their results, significantly more patients were delivered in vaginal group within 24hr (85.50 versus 39.50%).

Behrashi M *et al*. (2008) [20] observed in their study that a population of sixty healthy women requesting termination of pregnancy

were randomly divided into two groups. One group received vaginal misoprostol and other one received oral misoprostol. In their study, it was found that the delivery percentage of vaginal group was significantly higher than oral group (86.7 versus 43.30, p value is 0.0006). The induction to delivery interval and complication rate in both the groups showed no significant and the success rate in vaginal administration was higher than the oral group.

The findings reported by (Mahjabeen *et al*. 2009) [21] that sixty healthy pregnant women at second trimester of gestation found that after oral misoprostol Group-1 (n=30) and vaginal misoprostol Group- 2 (n-30) of 200 μg 4 h apart. They found the mean induction abortion interval was found to be 11.80±8.30 and 12.80±8.50 h, respectively for the group 1 and group 2 patients. The result obtained in his study was insignificant statistically. There was no reported cause of diarrhea, dizziness, nausea, shivering, pyrexia and hyper stimulation in both the groups.

Suman R. Shah *et al*. (2010) [23] observed in their study in order to find out the safety and effectiveness of vaginal misoprostol for second trimester termination of pregnancy, a prospective study involving 30 women with 12-20 weeks gestation requesting termination was

conducted. Four hundred microgram misoprostol was inserted in the vagina followed by 200μg every four hourly. The mean age of the women was 25.96 years. The mean gestational age was 15.66 weeks. Chi-square test was used for statistical analysis. 93.3% of women aborted within 16 hours without any significant side effects. Vaginal misoprostol is a very effective and safe method for second trimester pregnancy termination. It reduces the time and the cost of second trimester pregnancy termination.

5.2. ABORTION RATE

In this study, the vaginal misoprostol was found to be 100 effective in complete expulsion of fetus, whereas in oral the termination of pregnancy was complete only in 88.8% of women. The remaining (11.2%) women were given additional dose of vaginal misoprostol to complete termination. The success rate of group A was 66.67% and that of group B was 94.44% within 24 hrs. The induction to expulsion rate in the vaginal group was significantly higher than that in the oral misoprostol group ($P<0.03018$). The results obtained in my study are similar or comparable to the following findings:

The success rate was found to be 89% within 24 hrs when a regime of 200 µg misoprostol was given vaginally at every 12 hr. (Jain and Mishell, 1994) [37].

Nuutila *et al*., 1997) [38]. In their study noticed that 200 µg of vaginal administration of misoprostol resulted in abortion rates of 40% and 92%, in 24 and 48 h respectively.

Herabutya and O-Prasertsawat (1998) [39] administered a 200, 400 and 600 µg misoprostol regimen every 12 h. Abortion success rates over 48 h were found to be 70.6, 82 and 96%.

Schaff *et al*., (1999) [40] in their comprising of 933 pregnant women that a regimen of misoprostol, 0.80 mg self administered vaginally at home after pre-treatment with a regimen of 200 mg of mifepristone resulted in 97% complete abortion. There was no significant difference in the side effects.

Kazandi *et al* . (1999) [41] administered misoprostol through the intravaginal and intracervical routes and an oral combined form. Combined use resulted in a 64% abortion rate over 12 h, 80% over 24 h and 100% over 48 h. The mean expulsion time was found to be 12.6 ±

10.4 h. Time to complete the procedure was found to be 9.2 in dead fetuses and 19.6 h in live fetuses ($p < 0.05$).

Wong KS *et al*.[12] (2000) reported short induction-abortion interval in trimester pregnancy, when vaginal administration of misoprostol 400 ug every 4 h with the maximum of 5 doses in 24 h was given and it resulted in expulsion of live fetus. The complete abortion rate was 80% within 24 hrs.

Feldman *et al*. (2003) [42] compared oral and vaginal misoprostol for the termination of second trimester pregnancy with different protocol. In a randomized clinical trial, all patients received 800 µg of vaginal misoprostol and were assigned randomly to receive 400 µg of vaginal misoprostol or 400 µg oral misoprostol every 8 h. According to their findings, induction time and hospital stay were slightly shorter for oral group, however, the difference were not significant.

In a study conducted by Suneeta Mittal *et al*. (2005)[16], revealed that there was no significant difference statistically amongst three groups who had vaginal administration of misoprostol.. Long lasting and continuously increasing uterine contractility can be attributed to vaginal

administration unlike in oral administration of mesoprostol.Gemzell-Dannielsson K, 1999) [43

In another study conducted by Prachasilpchai *et al*. (2006) [44], 400 μg intravaginal misoprostol was administered every 12 h. The success rate over 48 h was found to be 89.4% and the mean expulsion time was found to be 17.07 ± 9.96 h. Both the success rate over 48 h and the mean expulsion time were similar to those of ours.

Sixty healthy women who were candidates for therapeutic termination of pregnancy at second trimester of gestation were recruited for the course of study. The grandmultipara, women who had the history of hypersensitivity of prostaglandins and scarred uterus were excluded. The subjects were assigned into 2 groups. Group-1 (n=30) had misoprostol orally, whereas the group-2 (n=30) received the drug by the vaginal route. The dosage regimen was similar in both groups that was 200 μg 4 h apart till the expulsion of fetus or the maximum of up to 5 doses. The main outcome measures of the study were induction expulsion interval, need for maternal complications and surgical evacuation. The mean induction expulsion interval in Group-1 and 2 was 11.8 ± 8.3 and 12.8 ± 8.5 hours, respectively, which was not different statistically. The

development of expulsion was complete in 53.30% of subject in both groups by misoprostol only, whereas 36.60% required surgical evacuation in oral group versus 33.30% in vaginal group. The rate of failed induction in group-1 and 2 was 10% and 13.30%, respectievely. (Mahjabeen *et al*. 2009) [21].

Shah Sumant R *et al*. (2010) [23] in their study to find out the safety and effectiveness of vaginal misoprostol for second trimester termination of pregnancy.This is a prospective study involving 30 women with 12-20 weeks gestation requesting termination. Four hundred microgram misoprostol was inserted in the vagina followed by 200µg every four hourly.Mean age of the women was 25.96 years. Mean gestational age was 15.66 weeks. Chi-square test was used for statistical analysis. About 93.3% of women aborted within 16 hours without any significant side effects. It was concluded that vaginal misoprostol is a very effective and safe method for second trimester pregnancy termination. It reduces the time and the cost of second trimester pregnancy termination.

This study conducted by Murat Bozkurt (2012) [30] involved an investigation of the effectiveness and complications of vaginal and oral misoprostol use on the termination of second trimester pregnancies. A

total of 103 cases were recruited from the medical records of the Gynecology and Obstetrics Clinic of Taksim Research and Training Hospital and Şırnak İdil State Hospital. Women underwent therapeutic termination of pregnancy between the 14 to 28th week of gestation using the defined combined misoprostol regimen. After the women were admitted, 200 μg vaginal (100 μg intracervical, 100 μg into the posterior fornix), 200 μg oral doses and 200 μg of sequential doses were administered in the 2nd and 4th hour. Subjects were excluded from the study if they were out of the defined gestational weeks using additional drugs with misoprostol; their data has not been recorded in detail. Of the 103 cases, 86 had an abortion within 24 h and the mean expulsion time was calculated as 15.42 ± 7.14 h (min 6.39 to max 20.03) in this group. The success rate for the 24 h was found to be 83.4%. Six more cases had an abortion when the second dose was given. The mean expulsion time was found to be 9.31 ± 3.26 h (min 6.45 to max 13.21) for the second 24 h. The success rate over 48 h rose to 89.3%. The total expulsion time was 18.30 ± 8.74 h. There was a history of previous caesarean sections in 2 out of 11 cases that did not have an abortion and one of these cases underwent a hysterotomy. The pregnancy was terminated by evacuation and curettage, as abortion did not occur despite 3 different high dose

misoprostol regimens as in the other cases. Pregnancies of the remaining 9 cases were terminated with different misoprostol doses, oxytocin infusion and the evacuation and curettage method.

5.3. INCIDENCE OF SIDE-EFFECTS

In this study, the most common side effects were observed. After misoprostol administration, the women were monitored hourly for vitals, side effects and onset of bleeding. Maximum number of women had nausea (22.2% and 36.1%) for oral misoprostol group (group A) and vaginal misoprostol groups (group B), respectively. The percentage of women who had abdominal pain was found to be 30.5 and 33.3 for oral misoprostol group (group A) and vaginal misoprostol groups (group B), respectively. Maximum number of women (33.3%) had temperature $>38^0$C in oral misoprostol group (group A), whereas in vaginal misoprostol group (group B), it was only 11.1%. Side-effects such as vomiting, diarrhoea, dizziness, headache, breast tenderness and rash were not significant in both the groups.

A median dose of about 1000 µg produced vomiting (57%) and diarrhoea (29%) in their study of El-Refaey and Templeton (1995). The incidence of side effects was not truly associated to total amount of

misoprostol used. They also observed that side effect of fever was found to be 32.4% and 12.2% in the group 1 and group 2, respectively.

Wong *et al*. 2000 [12] observed in their study that the dosage of misoprostol upto 4000 µg over 48hr were tolerated. The side effects were solely gastrointestinal and fever but these were soft.

Javed *et al*. (2004) [45] reported nausea and vomiting in 4% of the vaginal protocol of the study subjects. Nausea and vomiting was much higher in the study of Iqbal, in addition to headache, fever and chills, reason of which could be comparatively higher dose (Iqbal *et al*. 2007) [46]. Gilbert and Reid (2001) [13] also reported no significant difference in side effects between both groups of oral and vaginal misoprostol. However, Bebbington *et al.* (2002) [36] reported increased febrile morbidity in patients who received misoprostol by vaginal route. This may be due to high dose of the drug (400 µg) in their study. Dickinson *et al.* (2003) [47] also noticed more side effects with higher dosage of vaginal misoprostol, while Kamal et al. (2005) [48] reported no significant difference between side effects of misoprostol while comparing vaginal with oral route.

The side-effects such as fever (24.5%), abdominal pain (16%), nausea and vomiting (5.3%) were noticed (Prachasilpchai *et al*. 2006)[44].

Behrashi M and Mahdian M (2008) [20] noticed in their study that in vaginal misoprostol group, fever was the most complication (20%) and in oral group shivering (33%) and fever (20%) were the most complained. Neither of the women in both groups had abdominal pain, vomiting or diarrhoea as a side-effect of therapy. Severe complications such as uterine perforation and heavy bleeding have not been seen in both groups of study.

Helena von Hertzen *et al*. (2009) [22] in their study noticed that side effects such as chills, shivering and fever were more common in misoprostol vaginal administration (28.2%) than in sublingual administration (18.5%) and these findings are controversial to some of the studies. The more side effects are attributed to the higher concentration of serum misoprostol in case of sublingual administration (Tang et al., 2007). No pharmacokinetics studies have as yet been in print on the repeated dose of misoprostol administration when the doses are repeated.

No significant maternal side effects were noted in both groups. Vomiting was reported in one case (3.3%) of vaginal group. However,

vomiting commenced after starting the oxytocin infusion, therefore, it may be due to the side effect of oxytocin (Mahjabeen *et al*. 2009) [21]

In the literature, apart from pain, the side effects of misoprostol are usually mild and self-limited (Wildschut *et al*., 2011) [49]. In his study, except for pain, complication rates were low and other complications except nausea were self-limited. Half of the cases were given antiemetic medications for nausea.

Pongsatha and Tongsong (2011) [25] found the most common complications to be chill (43.7%), analgesic-requiring pain (39.3%) and fever (34.3%) in their patients who received 400 μg misoprostol through the intravaginal route every 12 h. High doses (800 μg in 24 h) may have affected the higher complication rates.

Herabutya and O-Prasertsawat (1998) [50] administered a 200, 400 and 600 μg misoprostol regimen every 12 h. Abortion success rates over 48 h were found to be 70.6, 82 and 96%. Nausea-vomiting was found to be 3.9, 12 and 20%, respectively. Diarrhea rates were 0, 6 and 22%; fever rates were 0, 2 and 28% and incomplete abortion rates were 35.3, 28 and 22%, respectively. In the study conducted by Murat Bozkurt (2012), the rate of nausea (11.6%) was found to be similar, fever rate (7.7%) was

found to be higher however diarrhea rate (1.9%) was found to be lower based on the 24 h results. As seen in this study, the success rate increased as the dosage increased, however complication rates also increased. Severe complications like uterine rupture and mortality were also not seen in our study. Of the cases in our study group, 9.7% had a history of caesarean sections. Abortion was achieved with this protocol in 80% of these cases. The remaining two cases underwent surgical interventions like hysterotomy and dilatation and evacuation. Uterine rupture complication did not develop in the subjects who had the history of caesarean section.

Minor side effects of pyrexia (3.3%) in each group & nausea & vomiting in group A were noticed by Sumera Tahir (2011) [28] in their study, which is comparable to 4% by Lubna Javed and associates (2004) and 0% noted by Jan. E. Dickinson (2003) [51] .

Murat Bozkurt (2012) [30] in his study noted that complication rates were fever 7.7%, nausea 11.6% and the combined oral and vaginal use was seen to reduce fever incidence however, it increased nausea incidence. It is obvious that misoprostol use will lead to abdominal pain by causing uterine contractions. Pain is the leading complication

described in many studies in the literature. However, what was different in his study was that analgesic requiring pain was taken as a complication, except for abdominal pain, which may be seen in almost every case.

6. SUMMARY AND CONCLUSION

This research study entitled “Randomized comparative study of safety and efficacy of oral and vaginal misoprostol in the termination of second trimester pregnancy over a period of one year at tertiary care institution” was carried out in the Department of Obstetrics & Gynecology, Govt. Kilpauk Medical College Hospital, Chennai. Out of 122 second trimester pregnant women, 101 were eligible as per the inclusion and exclusion criteria. Out of 101 eligible, 72 women were randomly selected for two groups (Group A and B) of study. Group A comprising of 36 women were given tablet misoprostol 200 µg (Zytotec) orally every 4 hrs until the abortion occurred or maximum up to 6 doses. Women in Group B were given vaginal misoprostol 200 µg (Zytotec) every 4 hrs till the expulsion of fetus or up to a maximum of 6 doses.

The age distribution and demographic profile of women in Group A and B were analyzed. The maximum number of women was found in the age group 26-30 (41.6%) and 21-25 (44.4%) for oral (Group A) and vaginal (Group B) route of administration, respectively. The maximum number of women was found to be multiparous, 77.7% for oral (Group A) and 66.6% for vaginal (Group B).

The maximum number of women was found to be 11 (30.5%) in the gestation period 12-14 and 11 (30.5%) in the period of gestation 14-16 for Group A and Group B, respectively.

The induction -abortion interval was analyzed. Most of the women aborted between 6 and 8 hours (36.0%) for oral misoprostol (Group-A) and 25% for vaginal misoprostol (Group-B) for 12-16 gestational age. For the gestational age of 16-20, the maximum number of induced abortion was found to be 13.8% and 16.6% for oral misoprostol (Group A) and vaginal misoprostol (Group-B), respectively.

The incidence of side effects after administration of Misoprostol was briefly studied. After Misoprostol administration, the women were observed hourly for side effects, vitals and onset of bleeding. The Maximum number of women had nausea (22.2% and 36.1%) for oral misoprostol group (group A) and vaginal misoprostol groups (group B), respectively. The percentage of women who had abdominal pain was found to be 30.5 and 33.3 for oral misoprostol group (group A) and vaginal misoprostol groups (group B), respectively. Maximum number of women (33.3%) had temperature $>38^0$C in oral misoprostol group (group A), whereas in vaginal misoprostol group (group B), it was only 11.1%.

Side-effects such as diarrhea, vomiting, headache, dizziness, rash and breast tenderness were not significant in both the groups.

32 women in oral misoprostol (group A) and all women in vaginal misoprostol (group B) were successfully induced complete abortion (MTP). However, the remaining 4 women in oral misoprostol group (group A) were also given vaginal misoprostol and pregnancy termination was completed.

The comparative analysis for the Group A and B was made to evaluate the efficacy of misoprostol by oral and vaginal route of administration. The vaginal misoprostol was found to be 100 effective in complete expulsion of fetus, whereas in oral, the termination of pregnancy was complete only in 88.8% of women. The remaining (11.2%) women were given additional dose of vaginal misoprostol to complete termination. The success rate of group A was 66.67% and that of group B was 94.44% within 24 hrs. The induction to expulsion rate (success rate) in the vaginal group was significantly higher than that in the oral misoprostol group ($P<0.03018$). The side-effects due to oral misoprostol (11.6%) were more than using vaginal misoprostol (9.5%). In case of oral

misoprostol (8.3%) the placenta had to be extracted manually. However, in case of vaginal route, no such complication was noticed.

In conclusion, the present research study reveals that vaginal misoprostol administration was found to be superior, more effective and efficacious in second trimester pregnancy termination than the oral administration due to the achievement of complete termination within 48 h. Shorter hospital stay and less expenditure are the advantages of vaginal misoprostol administration. This effect is due to improved pharmacokinetics associated with vaginal administration. Moreover, the side-effects noticed after vaginal misoprostol administration were minimal compared to oral misoprostol administration. In case of oral misoprostol administration for some women additional dose of vaginal misoprostol administration was warranted.

It is, therefore, recommended that for the second trimester termination pregnancy, it is preferable to use vaginal misoprostol administration.

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ANNEXURE I

MASTER CHART

GROUP – A

CASE No	AGE	PARITY	MARITAL STATUS M-MARRIED UM-UNMARRIED	PREVIOUS MTP	PREVIOUS LSCS	GESTATIONAL PERIOD				INDUCTION - ABORTION INTERVAL		SIDE-EFFECTS								
						12-14	14-16	16-18	18-20	<24	<48	NAUSEA	VOMITTING	DIARRHOEA	DIZZINESS	HEADACHE	BREAST TENDERNESS	ABDOMINAL PAIN	TEMP. >38^{0}C	RASH
1.	25	MULTI	UM			1					1	1								
2.	26	MULTI	M				1			1										
3.	28	PRIMI	M					1		1		1								

4.	31	PRIMI	M	1		1					1	1							1	
5.	24	MULTI	M							1							1			
6.	27	MULTI	M			1				1										
7.	25	MULTI	M					1			1								1	
8.	27	PRIMI	M				1			1										
9.	32	MULTI	M			1				1									1	
10.	22	MULTI	UM					1		1										
11.	20	MULTI	UM						1		1		1							
12.	26	MULTI	M				1			1					1				1	
13.	24	MULTI	M			1				1										
14.	29	PRIMI	M					1		1		1								
15.	21	MULTI	UM			1				1									1	
16.	19	PRIMI	UM					1			1									
17.	30	MULTI	M				1			1						1	1			
18.	23	MULTI	UM			1					1								1	
19.	28	MULTI	M	1				1		1										
20.	33	MULTI	M	1					1			1							1	

21.	22	MULTI	UM			1				1										
22.	27	PRIMI	M					1			1									
23.	30	MULTI	M				1			1										
24.	22	PRIMI	M					1		1									1	
25.	26	MULTI	M			1				1									1	
26.	38	MULTI	M	1	1				1	1		1					1			1
27.	22	MULTI	M						1			1								
28.	30	MULTI	M				1			1									1	
29.	23	MULTI	M					1		1										
30.	29	MULTI	M				1			1										
31.	20	MULTI	UM			1				1									1	
32.	26	MULTI	M				1				1									
33.	34	MULTI	M						1	1		1								
34.	21	PRIMI	UM						1										1	
35.	27	MULTI	M				1			1										
36.	25	MULTI	M			1			1											

GROUP – B

CASE No	AGE	PARITY	MARITAL STATUS M-MARRIED UM-UNMARRIED	PREVIOUS MTP	PREVIOUS LSCS	GESTATIONAL PERIOD				INDUCTION - ABORTION INTERVAL		SIDE-EFFECTS								
						12-14	14-16	16-18	18-20	<24	<48	NAUSEA	VOMITTING	DIARRHOEA	DIZZINESS	HEADACHE	BREAST TENDERNESS	ABDOMINAL PAIN	TEMP. >38^{0}C	RASH
1.	23	MULTI	UM				1			1		1								
2.	26	PRIMI	M			1				1							1			
3.	25	MULTI	M					1			1							1		
4.	27	PRIMI	M			1				1		1							1	
5.	19	PRIMI	UM			1				1										
6.	27	MULTI	M				1			1								1		

7.	24	MULTI	M			1				1									1	
8.	30	MULTI	M	1				1		1								1		
9.	29	MULTI	M				1			1		1								
10.	28	MULTI	M					1		1								1		
11.	22	PRIMI	UM			1				1									1	
12.	25	MULTI	M				1			1										
13.	27	MULTI	M						1	1								1		
14.	24	MULTI	M				1			1										
15.	27	PRIMI	M					1		1		1								
16.	24	MULTI	M				1			1								1		
17.	22	MULTI	M						1	1		1								
18.	23	MULTI	UM				1			1									1	
19.	20	PRIMI	UM			1				1								1		
20.	30	PRIMI	M						1	1										
21.	25	MULTI	M				1			1		1						1		
22.	29	PRIMI	M	1					1		1									
23.	24	MULTI	M			1				1		1								

24.	19	MULTI	UM					1		1										
25.	28	PRIMI	M					1		1									1	
26.	24	MULTI	M			1				1		1								
27.	27	MULTI	M					1		1		1							1	
28.	26	PRIMI	M						1	1										
29.	23	MULTI	UM				1			1		1								
30.	21	PRIMI	M					1		1									1	
31.	35	MULTI	M						1	1		1								
32.	20	MULTI	UM			1				1										
33.	33	PRIMI	M				1			1		1							1	
34.	22	MULTI	M				1			1										
35.	38	MULTI	M	1				1		1										
36.	21	MULTI	UM			1				1		1								

ANNEXURE-II

PROFORMA

NAME:

AGE:

ADDRESS:

EDUCATION QUALIFICATION:

OP/IP NO:

LMP:

EDD:

PREGNANCY CONFIRMED BY 1.UPT

2. USG

WILLING TO PAICIPATE IN THE STUDY:

BOOKED & IMMUNISED:

REFFERED FROM:

MENSTURAL HISTORY:

MARITAL HISTORY:

OBSTETRIC HISTORY:

PAST HISTORY:

GENERAL EXAMINATION:

HEIGHT

WEIGHT

BMI

VITALS

CVS

RS

PER ABDOMINAL EXAMINATION:

INVESTIGATIONS:

CBC

RFT

Urine routine

Blood group

VDRL

HIV

HBS Ag

USG

BT

CT

OTHERS

ANNEXURE-III

INFORMATION SHEET

I am conducting a study on **"Randomized comparative study of safety and efficacy of oral and vaginal misoprostol in the termination of second trimester pregnancy over a period of one year at tertiary care Institution"** among patients attending Govt. Kilpauk Medical College Hospital, Chennai and for that your specimen may be valuable to us.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled. The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator Signature of Participant

Date :
Place :

ANNEXURE-IV

PATIENT CONSENT FORM

Study Detail :"**RANDOMIZED COMPARATIVE STUDY OF SAFETY AND EFFICACY OF ORAL AND VAGINAL MISOPROSTOL IN THE TERMINATION OF SECOND TRIMESTER PREGNANCY OVER A PERIOD OF ONE YEAR AT TERTIARY CARE INSTITUTION"**

Study Centre : Govt. Kilpauk Medical College Hospital, Chennai.
Patient's Name :
Patient's Age :
Identification NO :

Patient may check (√) these boxes

a. I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.

b. I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

c. I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

d. I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.

e. I hereby consent to participate in this study.

f. I hereby give permission to undergo complete clinical examination and hematological tests.

Signature/thumb impression
Patient's Name and Address:
Name:

Signature of Investigator
Study Investigator's

DR.S.LUIJIM MALA

ANNEXURE-V

ETHICAL COMMITTEE APPROVAL

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Ref.No.2318/ME-1/Ethics/2012 Dt:04.04.2013
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "A Study of randomized comparison of safety and efficacy of oral and vaginal misoprostal in termination of second trimester pregnancy" - For Dissertation Purpose.submitted by Dr.S.Luijm Mala, MS (O&G), PG Student, KMC, Chennai-10.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

6/6/13
CHAIRMAN
Ethical Committee
Govt.Kilpauk Medical College, Chennai

GOVT. KILPAUK MEDICAL COLLEGE
06 JUN 2013
Kilpauk, Chennai-10

5/6/13

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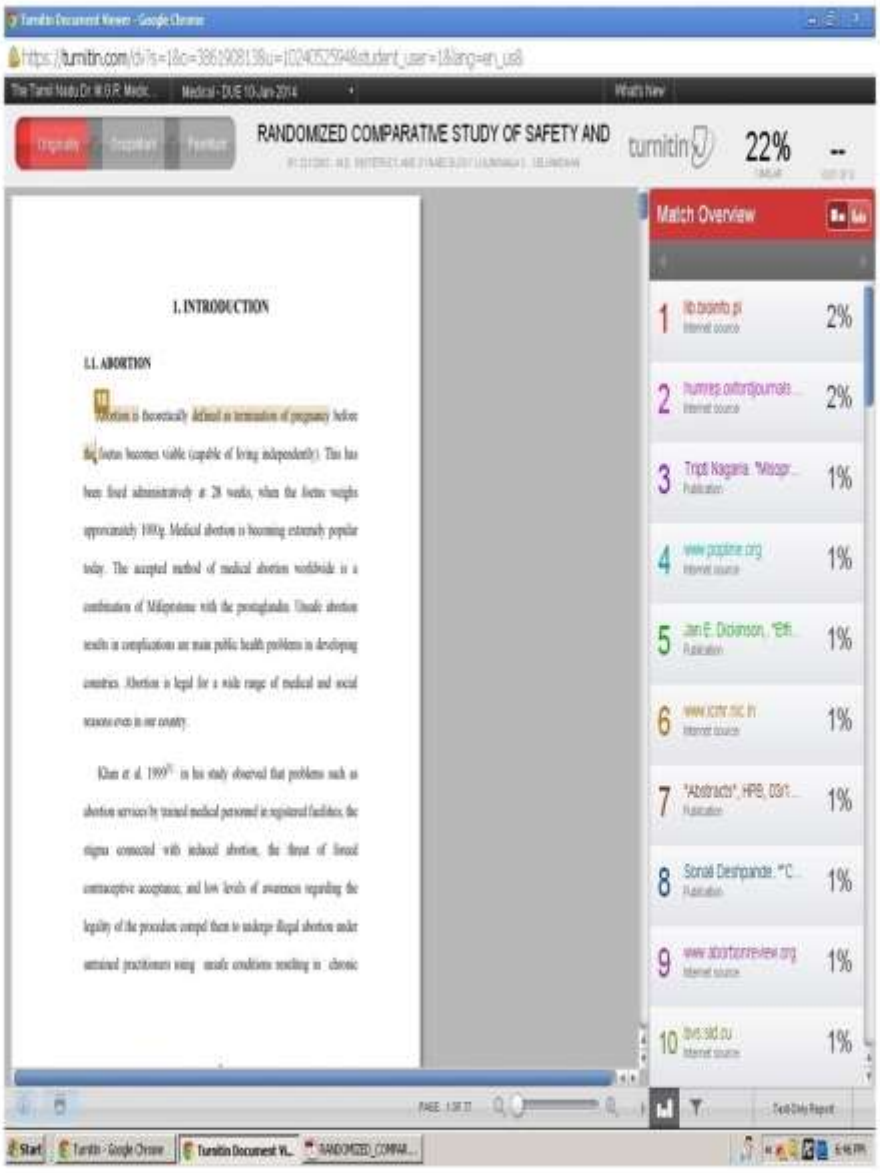
Assignment title	Medical
Author	22112683 . M.d. Obstetrics And Gynaecology LUIJIM MALA S . SELVAMOHAN
E-mail	drcmunish@yahoo.co.in
Submission time	04-Jan-2014 08:12PM
Total words	11880

First 100 words of your submission

1. INTRODUCTION 1.1. ABORTION Abortion is theoretically defined as termination of pregnancy before the foetus becomes viable (capable of living independently). This has been fixed administratively at 28 weeks, when the foetus weighs approximately 1000g. Medical abortion is becoming extremely popular today. The accepted method of medical abortion worldwide is a combination of Mifepristone with the prostaglandin. Unsafe abortion results in complications are main public health problems in developing countries. Abortion is legal for a wide range of medical and social reasons even in our country. Khan et al. 1999[1] in his study observed that problems such as abortion services by trained medical...



1. INTRODUCTION

1.1. ABORTION

Abortion is theoretically defined as termination of pregnancy before the foetus becomes viable (capable of living independently). This has been fixed administratively at 28 weeks, when the foetus weighs approximately 1000g. Medical abortion is becoming extremely popular today. The accepted method of medical abortion worldwide is a combination of Mifepristone with the prostaglandin. Unsafe abortion results in complications are main public health problems in developing countries. Abortion is legal for a wide range of medical and social reasons even in our country.

Khan et al. 1999[1] in his study observed that problems such as abortion services by trained medical personnel in registered facilities, the stigma connected with induced abortion, the threat of forced contraceptive acceptance, and low levels of awareness regarding the legality of the procedure compel them to undergo illegal abortion under untrained practitioners using unsafe conditions resulting in chronic