EFFICACY OF SINGLE DOSE VAGINAL MISOPROSTOL 800 μg IN I TRIMESTER ABORTION

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BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"EFFICACY OF SINGLE DOSE VAGINAL MISOPROSTOL 800 µg IN I TRIMESTER ABORTION"** is bonafide record work done by **Dr. K.R. CHELLAMMAL** under my direct supervision and guidance, submitted to the Tamil Nadu Dr. M.G.R. Medical University in partial fulfillment of University regulation for MD, Branch II –Obstetrics & Gynaecology.

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DECLARATION

I **Dr. K.R. CHELLAMMAL** solemnly declare that the dissertation titled **"EFFICACY OF SINGLE DOSE VAGINAL MISOPROSTOL 800 μg IN I TRIMESTER ABORTION"** has been prepared by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of MD. degree Branch – II (Obstetrics & Gynaecology) to be held in March 2008.

Place : Madurai **Dr. K.R. CHELLAMMAL**

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CONTENTS

INTRODUCTION

Medical abortion is a safe effective means of terminating a pregnancy and has been shown to be widely acceptable in both developed and developing countries in all world regions. This method uses pharmacological agents such as mifepristone and misoprostol to expel the contents of the uterus. Used in combination these medications stimulate uterine contractions and causes expulsion of the pregnancy.

Misoprostol alone may be useful where mifepristone is not available. The use of Misoprostol alone at the community and primary care levels has the potential to significantly increase, women's assess to safe abortion.

Considerable saving in resources can be made if routine curettage can be avoided and a medical rather than surgical abortion adopted.

AIM OF THE STUDY

1. To evaluate the efficacy of single dose 800 μg of vaginal misoprostol in I trimester pregnancy termination.
2. To critically evaluate the percentage of patients needing multiple doses
3. To study and evaluate the failure rate, complications and side effects with Misoprostol usage.

REVIEW OF LITERATURE

Our primary objective is to determine the efficacy of single dose of vaginal misoprostol 800 μg in complete expulsion of products of conception.

Following are the studies conducted by various authors about the efficacy of vaginal misoprostol 800 μg in first trimester pregnancy termination.

1. Salakos et al – Department of obstetrics and Gynaecology, University of Athens, aretoreion hospital, Greece, Dec 2005.

The objective of the study was to evaluate the efficacy and safety of 800 μg of misoprostol every 12 hrs for a period of 36 hrs for pharmacologic abortion. A group of 162 volunteer women with gestational age between 5.0 and 6.3 weeks received Misoprostol.

Outcome measures included :

Successful abortion (complete abortion without requiring surgery) side effects and a decrease in hemoglobin, mean time of vaginal bleeding, mean expulsion time and mean time of returning

menses. Complete abortion occurred in 148 of 162 ((91% , 95% confidence interval 87.95) patients.

The mean decrease in hemoglobin was statistically significant (p=0.001). Vaginal bleeding lasted 8.0 + 3.2 days, spotting 8.0 + 3.5 days and total bleeding 16 + 4.0 days. The mean expulsion time was 8.5 + 4.0 hrs.

According to the observed outcomes 800 μg of misoprostol vaginally could be a valid method to terminate pregnancies upto 9 weeks of gestation.

2. Kovavisaraels F. Jammansiri C. Sep 2005, Department of Obstetrics and Gynaecology. Rajavithi Hospital, Ministry of public health, Bangkok.

To compare the respective effectiveness and safety of 600 micrograms and 800 micrograms of intravaginal misoprostol for complete abortion in cases of early pregnancy failure (Occuring in the first 12 weeks)

A total of 114 women with diagnosis of early pregnancy failure was taken on to the study.

The rate of complete abortion with in 24hrs was significantly higher in the group that received 800μg of misoprostol (78.4%) than on the other group (45.5%). There was no significant difference in side effects.

3. Cartoneck JL et al, Hospital Docante Gineco –obstetrics Fusesio Hernandez (Materwidad obnera) Lindd de in Habana Cuba March 1999.

The objective of this study was to demonstrate the effectiveness and safety of self administration of misoprostol every 12 hrs without the need of post expulsion systematic curettage in late first trimester abortion (10-13 wks gestation) A group of 180 women with gestations from 64 to 91 days. Self administered 800 μg of vaginal misoprostol every 12 hrs for a maximum of three doses without performing post expulsion systematic preventive curettage. Successful abortion occurred in 153/180 (85%) subjects.

The high degree of acceptability, its efficacy and the fact that post abortion systematic curettage was not needed make misoprostol, a suitable alternative to the commonly available method for termination of pregnancy at 10-13 wks gestation.

4. Carbonell JL, et al, - the use of misoprostol for abortion at < or = 9 wks gestation. Eur. J. Corikacept Reprod. Health Care 1997.

5. Ngai Sh, Tang YS, Chan YM, HO PC Vaginal misoprostol alone for medical abortion up to 9 wks of gestation : Efficacy and acceptability : Hum Reprod. 2000.

6. In a study by creiwin et al (1997) Comparison was made between 400 μg oral misoprostol and 800 μg vaginal misoprostol for medical evacuation of early failed pregnancy with an embryo of 15 to 14 mm with no cardiac activity of an empty irregular gestational sac of atleast 16 mm diameter. The dose was repeated after 24 hrs in case of failure of expulsion.

The rate of complete expulsion with in 48 hrs was 25% in oral misoprstol and 88% percent in vaginal misoprostol group.

7. Zalanyi 1998 and Herabontya et al, 1997.

I Trimester Abortion

Abortion is the termination of pregnancy either spontaneously or intentionally before the foetus develop sufficiently to survive.

By convention, abortion is usually defined as pregnancy termination prior to 20 weeks gestation or less than 500gm birth weight.

More than 80 percent of abortion occur in the first 12 weeks of pregnancy and atleast half result from chromosomal anomalies. After the Ist trimester both the abortion rate and the incidence of chromosomal anomalies decrease.

Etiology :

The exact mechanism responsible for abortion are not always apparent but in the first 3 months of pregnancy, death of the embryo or fetus nearly always precedes spontaneous expulsion of the ovum. For this reason, finding the cause of early abortion involves ascertaining the cause of foetal death.

Foetal factors

Maternal factors

Paternal factors

Foetal factors :

Abnormal zygotic development

Aneuploid abortion

Euploid abortion

Maternal factors :

- Infection
- Chronic debilitating diseases
- Endocrine abnormalities

  Hypothyroidism

  Diabetes mellitus

  Progesterone deficiency
- Nutritional deficiency
- Drugs and environmental factors

  Tobacco

  Alcohol

  Caffeine

  Radiation

  Contraceptives

- Environmental toxins

  Arsenic

  Lead

  Formaldehyde

  Benzene

  Ethyl oxide

- Immunological factors

Paternal factors :

Chromosomal abnormalities in sperm have been associated with abortion.

Categories of abortion → **Spontaneous**

Induced

1. Threatened abortion
2. Inevitable abortion
3. Complete and incomplete abortion
4. Missed abortion
5. Recurrent abortion

SIGNS AND SYMPTOMS

The signs and symptoms of abortion are

1. Pain due to uterine contraction
2. Haemorrhage as the result of separation of the ovum
3. Dilatation of the cervix due to uterine contraction
4. Expulsion of a part of or the entire ovum

The patient generally gives a history of amenorrhoea followed by more or less severe pain in the lower abdomen and back accompanied by vaginal bleeding. The extent of the haemorrhage varies and may some times be so profuse as to cause severe collapse. Usually however the haemorrhage continues for some days, the quantity varying from day to day. The pain may be severe, but is never so great as in cases of ruptured ectopic gestation.

Where pain and haemorrhage are present dilatation of the cervical canal may be present and occasionally a portion or the whole of the uterine contents may be expelled.

Depending upon the signs and symptoms the following types of abortions may be recognized.

1. Threatened Abortion :

In this condition, after a period of amenorrhoea, the patient complains of slight colicky pains in the lower abdomen associated perhaps with back ache, frequency of micturition and slight bleeding per vaginum. If a careful bimanual examination is done the cervix will be found softened, the uterus enlarged and more or less globular the size depending on the period of pregnancy. The OS is generally closed or may in some cases be slightly patulous when there is no actual sign suggestive of death or expulsion of portion of the ovum, the condition is known as threatened abortion.

2. Inevitable or incomplete abortion :

This term denotes that the ovum has practically separated from the uterine wall and is therefore dead and bound to be expelled. In such cases, the pain is more severe, the bleeding more profuse, the cervix is dilated and occasionally a portion of the ovum may be felt protruding through the cervical canal. When only a part of

the products of conception has been expelled, it is termed incomplete abortion.

3. Complete Abortion :

This term is used when the entire ovum has been expelled. Once this has occurred the pain subsides and bleeding decreases and may have stopped by the time the patient is seen. The uterus is empty and is accordingly smaller in size than the period of amenorrhoea would suggest and the cervical canal may be closed, as it contracts very rapidly after the complete expulsion of the uterine contents.

4. Missed Abortion :

In this condition, symptoms of abortion occur but subside later without any part of the ovum being expelled. The ovum dies but is retained in the uterus. The patient gradually recover from the attack of pain and the vaginal haemorrhage subsides. The haemorrhage that has occurred in utero forms a clot round the dead ovum and changes takes place subsequently in and around the ovum. In the early stages, the clotted blood with the ovum in it presents a peculiar condition which is known as blood mole.

Later when the blood clot becomes organized the appearance changes. In the course of few weeks the whole of the uterine contents are changed into a dark red or brownish stagy mass known as carneous mole. Occasionally in these changes owing to the formation of hematoma of varying sizes between the amniotic and the chorionic membranes, a further change takes place resulting in the formation of what is known as tuberose mole. Where a mole has developed, the foetus may not be present or even if it does exist, it is of very small size. This is due to the fact that in the large majority of cases the malformation takes place in the early weeks of pregnancy. Consequent on the long lapse of time before the mole is expelled, the foetus may be absorbed or in some cases it may be found as a rudimentary vestigial structure. Where mole formation has taken place the amemorrhoea may persist but none of the progressive signs of pregnancy are present. Thus the uterus does not continue to enlarge in size. The breast changes cease the patients may not feel any of the subjective symptoms of pregnancy and generally presents herself for the persistent amenorrhoea. A bimanual examination will reveal that

the uterus though enlarged never corresponds to the period of amenorrhoea and is smaller.

The cervical softening does not persist and the uterus itself doesnot have the soft feel of a normal pregnancy. If a pregnancy test is done at the stage the result will be negative.

Febrile abortion :

In febrile abortion, signs and symptoms of abortion exist, with a rise of temperature.

This may be due to two distinct factors.

a) In one set of cases, the rise of temperature may precede the signs and symptom of abortion and may be the causative factor or atleast one of the causative factors. In such cases the temperature is the cause and not the result of abortion.

b) In other cases, the rise in temperature may be due to sepsis, and the patient besides presenting the usual symptoms of pain and haemorrhage, will have an offensive discharge per vaginum. This is called septic abortion.

Therapeutic Abortion :

Where abortion is induced as a therapeutic measure for the sake of the mother it is spoken of as therapeutic abortion.

In modern obstetrics, there are a few indications for therapeutic abortion.

Cardiac disease (Grade III and IV) and decompensation in a previous pregnancy and justifiable indication for termination of progress in the first trimester. It is necessary that optimum compensation be established prior to termination.

Epilepsy and other forms of psychosis in the mother who had a number of children may justify a therapeutic abortion.

Intractable hyperemesis gravidarum will necessitate termination of pregnancy.

If the mother contracts German measles in the early weeks of pregnancy, induction of abortion is advocated by some on the plea of a malformed foetus being born.

Chronic glomerulonephritis, malignant hypertension. Pregnancy following radical mastectomy for carcinoma of the breast are other indications.

In India, abortion is legalized by liberal act called Medical termination of pregnancy (MTP) act.

Chromosomal and enzyme abnormalities have now been identified as factors responsible for the transmission of certain inherited disorders. Some of these disorders may also be sex linked. It is possible to determine by examination of the liquor amni whether the intrauterine foetus will be affected or not.

If the investigations yield a positive result, it is now the practice to induce abortion. Sex linked diseases like hemophilia, progressive muscular atrophy and chromosomal abnormalities resulting in various genetically induced diseases as also iatrogenic disorders can now be diagnosed early and the therapeutic abortion performed.

Diagnosis :

Uterine abortion has to be differentiated from

1. Functional menstrual disturbances
2. Ectopic gestation
3. Hydatiform mole

In functional menstrual disturbances the woman has irregular menstruation there may be amenorrhoea for periods varying from six to twelve weeks but the history is generally suggestive. A profuse bleeding occurring at the end of that period may suggest the possibilities of an abortion, but a careful bimanual examination will reveal the absence of signs of pregnancy. In case of doubt pregnancy test and ultrasonography will helpful.

Difficulty is often encountered in differentiating uterine abortion with a retroverted gravid uterus from as un ruptured ectopic gestation or tubal abortion with a pelvic hematocele. In the two latter conditions, there may be history of a short period of amenorrhoea with occasional attacks of colicky pain in the lower abdomen and vaginal bleeding which is seldom profuse. Vaginal examination revealing a uterus smaller in size than the period of amenorrhoea would warrant an extremely tender mass in one or other of the fornices or the dounglas pouch separate from the uterus. Blood can most often be aspirated from the mass through the posterior fornix thus helping to clinch the diagnosis.

In vesicular mole, the uterus is often bigger than the corresponding period of amenorrhoea. The pregnancy test is positive in high dilutions and examination of any products passed per vaginum may reveal vesicles.

Methods of first Trimester pregnancy termination

Medical Method :

1. Prostaglandin
2. Anti-progesterone – RU 486 (Mifepristone and epostaine)
3. Methotrexate – intramuscular and oral

Surgical Methods :

Cervical dilatation followed by uterine evacuation

Curettage

Vaccum aspiration (suction curettage)

Dilatation and evacuation (D & E)

TECHINIQUES:

A. Vacuum aspiration or suction curettage or suction evacuation

The procedure of vacuum aspiration (VA) is described in two parts; dilatation and aspiration.

Dilatation:

1. The patient comes to the table after passing urine and is put in the lithotomy position. Shaving is not essential. Catheterization is not done. Bimanual examination is performed routinely to note the size and position of the uterus. If the uterus is retroverted, it is made anteverted wherever possible without producing much pain.
2. The vulva and vagina are cleaned with antiseptic solution. A posterior vaginal speculum is introduced. The cervix is painted with an antiseptic solution like 5-10% povidone –iodine. Drawing about 20 ml of 1% lignocaine with adrenaline in a syringe, 2 ml is injected into the cervix at the 12 o'clock position. The cervix is caught with a non-traumatic vulsellum (Jacob's tenaculum or strong Allis' forceps) 8 ml of lignocaine (Xylocaine) with 1:300,000 epinephrine or adrenaline is

injected at the 4 0’ clock and 8 o ‘ clock positions 2 mm underneath the mucosa at the cervicovaginal junction, producing blanching of the mucosa. Before pushing lignocaine, the piston is withdrawn to make sure that vessels have not been punctured. After waiting for 3-5 minutes, a uterine sound is passed gently to note the position and measure the size of the uterine cavity. It must not be pushed hard when resistance is met at the fundus, otherwise there will be perforation.

3. At this stage ergometrine 0.5 mg or methylergonovine (Methergine) 0.20 mg is given intravenously; instead of ergometrine, oxytocin 5 units may be injected intramuscularly. It reduces bleeding, particularly in late first trimester pregnancy cases, and hardens the uterus and lessens the chance of perforation. It does not produce any difficulty during dilatation.
4. The length of the uterine cavity, as measured by the sound, corresponds with the age of gestation from the first day of the last menstrual period, and on this measurement the cannula size

is chosen: e.g. 8weeks of pregnancy = 8 cm uterine depth = 8 mm cannula, 10 weeks =10 cm uterine depth =10mm cannula. If cervical resistance is too great, a cannula of 1 or 2 mm smaller size may be used, but the need for forceps and curette will be increased. To avoid cervical injury the cervix is held steadily with the forceps and dilators are introduced with steady force, keeping the index finger on the dilator in such a way that the top part is short of the uterine length, the dilator being held with the whole of the hand instead of in a pen-holding fashion. This technique also prevents uterine perforation in the case the dilator slips in suddenly, as happens sometimes. When there is much resistance, it is helpful to leave each dilator in place for 30-60 seconds. It should be remembered that it is the internal os which needs to be dilated and not the external os.

Aspiration

5. The cannula size is chosen according to the length of the uterine cavity and is fitted with the suction apparatus. The set should be tested for its air tightness before the procedure is

started. The cannula is gently introduced up to the fundus and the machine is started. When the vacuum is created, the cannula is moved against the uterine wall from above downwards to the level of the internal os repeatedly in a clockwise manner for 360 degrees, then in an anticlockwise manner up to the starting position os as to evacuate the contents and soft curette the uterus; the end point of curettage will be the uterine cry- this is a grating sensation covering the whole of the endometrial cavity.

6. Check curettage with a sharp curette is done routinely by most physicians so as to remove leftover fetal products, if any, but curettage should not be done too rigorously as it may produce synechiae and permanent oligomenorrhoea or amenorrhoea.
7. Ergometrine 0.5 mg or methylergonovine (Methergine) 0.20mg us given intramuscularly as a routine, irrespective of earlier administration of the ecbolics. Bleeding is checked. The tenaculum forceps and vaginal speculum are withdrawn. Bimanual examination is repeated so as to be sure that the

uterus is hard and smaller in size than prior to the procedure; this step ensures evacuation of the uterus.

8. The materials removed during the operation are placed in a glass container and carefully examined to see if the volume and nature of the matter is consistent with the gestational age. Some of these are materials placed in a glass container containing water, particularly when the tissues are small in amount, to ascertain fetal products. The fresh placental tissues always float water. In cases of doubt the tissues should be sent for histological examination. Routine pathological examination is unnecessary and is not done.

    If little or no tissue is obtained, the physician should think of the possibility of : (1) failure to interrupt the pregnancy, (2) non-pregnancy, (3) ectopic pregnancy, (4) incomplete abortion (5) very early intrauterine pregnancy, (6) false passage, or (7) uterine perforation. These cases should be watched and followed up carefully. In practice, however, this step is often not followed.

9. The patient is watched in a side room for ½ - 2 hrs depending upon the case and is then discharged with the necessary directions.

10. If laminaria tents have been introduced, after cleaning the vulva the tents are removed first by means of a sponge-holding clamp forceps. Dilatation is then performed.

B. Dilatation and evacuation(D&E)

This operation, also called dilatation and curettage (D&E), has two parts. The first part of dilatation is done in the same way as in vacuum aspiration following steps number 1 to 4. Ergometrine 0.5 mg is given intravenously as a routine. Ovum forceps of different sizes are available for the purpose; very small size for cavity length below 7 cm, medium size for cavity length 8-9 cm and large size for cavity length of above 9 cm are chosen after fixing the uterus with a tenaculum forceps. The ovum forceps is introduced in a closed position, opened inside the uterine cavity and rotated for 90 degrees in clockwise or anticlockwise manner, closed so as to hold fetal tissue tightly, and taken out as much as possible of the fetal

products. Curettage is then done by a sharp or blunt curette. The author prefers to use a sharp curette in early weeks of pregnancy and after the uterus is contracted towards the end of the operation in later weeks of first trimester pregnancy. Curettage must not be done too rigorously. Steps 7 to 10 as in vacuum aspiration are then followed.

Postoperative care and follow-up

Administration of routine antibiotic following VA or D&E is debatable. However, it should be given when local infection is present, where operations are not done with proper aseptic care under ideal circumstances, or where the procedures have involved more time or bleeding. Before discharge, the patient should be informed that she can fall pregnant even after 7-14 days. As such contraceptive measures should be undertaken from the very beginning.

Intrauterine device can be introduced at the time of D&E if infection is not present or likely, OC should be started within one week, barrier contraceptives should be used whenever

sexual intercourse is resumed and ligation of tubes can be performed at the time of abortion (PAI,1993).

The patient is advised to have normal activities except intercourse for the next 10-14 days, and to revisit the physician after 2 weeks for routine check-up, or earlier in case she develops any of the following features: (1) acute pain in lower abdomen, (2) rise of temperature, (3) persistent pain for more than 7 days, (4) heavy or persistent fresh bleeding, or (5) persistent pregnancy symptoms.

In cases with acute pain, ectopic or acute pelvic infection should be suspected and appropriate treatment must be immediately started after diagnosis. In cases with other features, vacuum aspiration and curettage are often repeated with or without antibiotics.

Complications and their remedies

Complications of VA and D&E depend a lot upon several factors of which the most important ones are operator's skill, available facilities and gestational age; others are type of

anaesthesia and instrumentation, patient's age, parity, socioeconomic status and pre-existing diseases.

Compared to other surgical operations legally induced first trimester pregnancy termination is remarkably safe, the major complications rate being less than 1 in 100 procedures (Grimes et al, 1977; Lewit, 1972) the risk of dying from these procedures is eleven times lower than the risk of dying from pregnancy and childbirth (Cates et al, 1979). Major complications following D&E are twice as frequent as with VA (PAI, 1993).

Uterine haemorrhage.

It occurs in 1-4% cases although blood transfusions are required in only 0.6 / 1000 –abortions. Haemorrhage happens more often with advanced gestational age, when D&E is performed instead of VA, and when general anaesthesia is used instead of local anaesthesia. It can be reduced to a great extent by the concomitant use of oxytocic drugs during the procedure and by prior use of laminaria tent.

Pelvic infection.

It ranges from 0.1 -1.5 %. It is due to incomplete evacuation and improper aseptic technique. The incidence can be reduced to a great extent by prophylactic use of antibiotic.

Cervical injury.

This complication occurs in 0.01-1% cases. It happens more often with D&E than with VA, in advanced gestational age and in nulliparous women. It can be minimized to a great extent by the use to Hawkins-Ambler or Pratt dilators instead of Hegar dilators, and by preoperative cervical priming and dilatation by the use of laminaria tents.

Uterine perforation.

This is the most dangerous complication, but fortunately it happens very rarely in0.1-0.28% cases. Nulliparous patients in whom laminaria tent had not been used had a 15 fold higher risk of cervical injury than multiparous women, according to a Baltimore study (King, 1977). The incidence of perforation can be minimized by using the proper technique as detailed earlier, by the use of Hawkins-Ambler or Pratt dilators and the use of

laminaria tent. When perforation occurs or is suspected, the patient should be kept under observation and antibiotics should be started. Usually she can be discharged in 24 hrs time. If there is strong suspicion or actual diagnosis of injury to the intestines or omentum, or if haemorrhage occurs, laparotomy should be performed followed by necessary steps.

Retained products.

Incomplete abortion happens in 24% of the cases. The incidence is reduced by performing check curettage following VA and by following proper techniques with the help of well-trained personnel. These cases need repeat D&E and antibiotics.

Continuation of pregnancy.

VA fails in about 1% cases; failure is more within two weeks of amenorrhoea.Routine follow-up, and reporting of patients if pregnancy symptoms continue or amenorrhorea continues for more than 4 weeks, will help diagnosis. Repeat VA and / or D&E is needed.

Maternal mortality and morbidity.

Cases et al (1979) and Lewit (1972) found that the morbidity rate is lowest between 7 and 8 weeks of pregnancy, after which the risk of complications rises by about 15-30% for each week of delay.

Mortality from VA and D&C is very rare, being 1.3 per 100,00 procedures in the large JPSA/CDC study in the USA from 1972-1977 (Cates et al, 1979); at 8 weeks' gestation or earlier, the death rate was 0.5/100,000 abortions; at 9-10 weeks 1.6, and at 11-12 weeks 3.3. Thus the risk of dying increased by 50% per week as the gestational age increased.

Menstrual regulation :

Menstrual regulation consists of aspiration of contents of uterine cavity by means of a plastic cannula (karman's cannula) and a plastic 50 ml syringe capable of creating a vaccum of over 60 cm Hg. It is carried out effectively with in 42 day of the beginning of the last menstrual period (LMP). A paracervical local anaesthetic block or preoperative sedative alone usually, suffices but some times in our apprehenside patient, general anaesthesia with intravenous thiopentone sodium may be necessary. The procedure can be performed in an office set up, out patient clinic or other day care centre. Since 1970, this method has been extensively evaluated and found to be efficient, safe and easy to use in terminating early pregnancy.

It is a good practice to examine the products of conception. The occasional complications encountered include failure to evaluate leading to continuation of pregnancy, incomplete evacuation, haemorrhage, cervical laceration, perforation, infection and anaesthetic complication.

Features of Medical and Surgical Abortion

	Medical Abortion	Surgical Abortion
1.	Usually avoids invasive procedure	Invasive procedure
2.	Usually avoids anaesthesia	Sedation used if desired
3.	Regular two or more visits	Usually requires one visit
4.	Days to week to complete	Complete in a predictable period
5.	Available during early pregnancy	Available during early pregnancy
6.	High success rate (95%)	High success rate (99%)
7.	Regular follow up to ensure completion of abortion	Doesn't require follow up in all cases
8.	Requires patient participation through out multi step progress	Requires participation in a single step process

From the American College of Obstetrics and Gynaecology 2001.

Contraindication of Medical abortion :

Allergy

Intra uterine disease

Severe anaemia

Coagulopathy

Active liver disease

Cardiovascular disease

Uncontrolled seizure disorder

Adrenal diseases

On glucorticoid therapy

From American College Obstetrics and Gynaecology 2001.

In this study, after counselling and making an informed decision to terminate a pregnancy with medications and a physical exam to ensure that the woman is medically eligible for medical abortion, the efficacy of single dose 800 μg misoprostol is evaluated.

MISOPROSTOL PHARMACOLOGY

Drug Pharmacology

Misoprostol:

PGE1 orally active analogue contain equal amounts of two diastereomers presented below with their enantiomers indicated by (±)

Molecular formula : $C_{22}\ H_{38}\ O_5$

Clinical Pharmacology:

Pharmacokinetics:

Misoprostol is extensively absorbed both orally, vaginally, undergoes rapid de esterification, to its free acid – misoprostolic acid which is responsible for its clinical activity, and unlike the parent compound, is detectable in plasma. The 'alpha' side chain undergoes beta oxidization and beta side chain undergoes Omega Oxidation followed by reduction of ketone to give Prostaglandin F analogs

Tmax: 12±3 min (1/2 life 20-40 min.) Sr. Protein binding is less than 90%.

Mechanism of Action:

Misoprostol is a myometrial stimulant which binds to E-2 and E-3 prostanoid receptors. Its active plasma metabolite is misoprostolic acid. It is rapidly absorbed after oral, vaginal and rectal administration. With oral administration the half life is less than 30 minutes, and peak level is at 15 minutes. After vaginal administration, there is a gradual rise to a maximum level at 60-120 minutes, but at 240 minutes (4 hours) the level is still at 60 percent of peak level.

Effects:

(a) GIT effects

PGE1, analogue, gastric anti secretory agent with protective effects on the gastroduodenal mucosa. The drug inhibits gastric acid secretion and protects mucosa from the NSAIDS.

(b) Genito Urinary &renal effects:

Misoprostol has been reported to increase the amplitude and frequency of uterine contractions and to produce stimulate

uterine bleeding and total or partial expulsion of uterine contents in pregnant women.

(c) Endocrine & Gonadal effects:

Misoprostol does not appear to have clinically important effects on serum levels of circulating prolactin, thyrotropin, somatotropin, thyroxine, FSH, LH, SHBG, Progesterone, testosterone, estradiol (or) gonadotropins. In some patients it increases serum cortisol concentration.

(d) Ocular:

Though no effect on ocular system is recorded, in some isolated cases reports of conjunctivitis is documented with misoprostol use.

(e) Hepatic effects:

Some studies suggest that there is elevated hepatic enzyme levels after their usage.

(f) Respiratory effects:

Though no major effects on respiratory system with Misoprostol usage were reported, rare incidence of upper

respiratory tract infection, bronchitis, bronchospasm, dyspnea, pneumonia, epistaxis are reported in few studies.

(g) Immunological effects:

Very rare development of anaphylaxis with misoprostol use is also recorded.

(h) Other effects:

Misoprostol have no effect on cell or humoral mediated immune response and does not affect platelet aggregation, or produce clinically important cardiovascular or respiratory changes.

Few studies show the occurrence of deafness, tinnitus, ear ache in patients using misoprostol.

Adverse effects

(a) GIT:

Diarrhoea (15-40%) and abdominal pain (13-20%) are common side effects with misoprostol usage. Diarrhoea is dose related and early to occur, hence should be avoided along with magnesium containing acids during misoprostol usage.

(b) Gynecological:

Women who received misoprostol during clinical trials reported the following gynecological disorders:

- ❖ Spotting (0.7%)
- ❖ Cramps (0.6%)
- ❖ Hypermenorrhoea (0.5%),
- ❖ Menstrual disorder (0.3%) and
- ❖ Dysmenorrhoea (0.1%).

(c) Skin:

There are also few adverse effects like rashes, dermatitis, alopecia, Pallor, and breast pain are also noted in few patients.

(d) Special senses:

Few cases also reported with abnormal taste, abnormal vision, conjunctivitis, deafness, tinnitus, ear ache as per some studies.

(e) Musculoskeletal:

Dermatitis, alopecia, pallor, musculoskeletal effects, arthralgia, myalgia, muscle changes, muscular and stiffness, back pain are also reported in some cases.

(f) CVS

Very few cases are reported infrequently with chest pain, edema, diaphoresis, hypertension, hypotension, arrhythmia increases in cardiac enzymes and syncope.

Others

In some clinical trials following adverse reactions were reported in more than 1% of the subjects.

They are,

- ❖ Nausea (3.2%)
- ❖ Flatulence (2.9%)
- ❖ Headache (2.4%)
- ❖ Dypepsia (2.0%)
- ❖ Vomiting (1.3%) and
- ❖ Constipation (1.1%)

Over dosage:

Cumulative total daily dose of 1600 mcg have been tolerated with minimal gastrointestinal discomfort.

Misoprostol is metabolized like a fatty acid.

Advantages of vaginal misoprostol over oral administration

1. Vaginal dose can be increased without much side effects. So, it makes the drug very useful for termination in later gestations also.
2. Vaginal Misoprostol increases the rate of complete abortion as shown by –E1 Relary et al and then Ashoketal and Schatt et al studies. Incidence of vomiting and diarrhea were significantly lower in vaginal users, which was supported by Zieman et al in his study.
3. Longer and sustained blood levels after vaginal administration are maintained.

Comparative Effectiveness of Vaginal and oral Administration of Misoprostol

Oral	Vaginal
❖ Side effects : more ❖ More dosage needed for the same gestations. ❖ Undergoes presystemic gastrointestinal and hepatic metabolism ❖ Bioavailability is less. ❖ 87% of success. ❖ 7% failure ❖ abortion with 4hrs -78%.	❖ Side effects: less ❖ Less dosage needed for the same gestations ❖ Bypasses presystemic gastrointestinal and hepatic metabolism ❖ Bioavailability is 3 times more than oral ❖ 95% of success ❖ 1% failure ❖ abortion within 4 hrs - 93%

Supported by EL Refaey et al 1995

Various dosage regimens used in abortion are

- ❖ 200 mcg every 4 hrs.
- ❖ 400 mcg every 6 hrs.
- ❖ 600 mcg every 12 hrs.
- ❖ 800 mcg every 24 hrs.
- ❖ 800 mcg every 12 hrs

MATERIALS AND METHODS

This study was carried out in the Department of Obstetrics and Gynaecology, Government Rajaji Hospital, Madurai during the period of February 2007 to July 2007.

The purpose of the study was to evaluate the efficacy of single dose 800 μg of vaginal misoprostol in I trimester pregnancy termination.

Patient's Selection Criteria :

50 patients with intra uterine pregnancy up to 12 weeks were randomly selected for the study.

The age group was between 20 to 34 years

Patient with scarred cervix, previous cervical surgery and previous scar in the uterus and with medical or surgical disease were excluded from the study.

Patient informed consent :

Written consent of the patients were taken and if the patient was a minor her parents consent was obtained. Patient was given prophylactic antibiotics.

Preparation of the patients :

After patient got admitted, complete history was taken

General examination and systemic examination was carried out.

A speculum and vaginal examination was done in all cases.

Patients were counselled regarding the method and side effects of the drug.

Investigations :

Urine Alb

Sugar

Dep

Haemoglobin

Haematocrit

Blood grouping and Rh typing

Bleeding time

Clotting time

Ultrasonogram

Preparation of patients :

The procedures and methodology was explained to the patients and they were asked to empty the bladder just before the procedure.

The patient was placed in lithotomy position

No anaesthesia was given.

Methodology :

Under aseptic precaution after putting in a speculum, posterior lip of the cervix was visualized and 800 μg of misoprostol soaked in normal saline was kept in the posterior fornix and the patient was instructed to stay in bed for 30 min.

Time of application of tablets was noted. Patient was carefully monitored for development of symptoms like

Nausea

Vomiting

Bleeding

Abdominal pain

Patient was monitored for complete expulsion of products of conception for 12 hours and if it does not occur 2nd dose of 800ug misoprostol was kept in posterior fornix.

Four hours later patient underwent USG examination to confirm the completeness of expulsion of product of conception.

Haemoglobin and hematocrit were checked after 48 hrs.

Coagulation profile also rechecked after expulsion.

Follow up :

Patient was advised to come for the follow up at the end of one month and at the end of 3 months to enquire about the cyclic regularity and the general status

ANALYSIS OF STUDY

50 CASES

Analysis was done in the following aspects

- Distribution of age
- Gestational age
- Parity
- Socio economic status
- Induction, abortion interval
- Requiring 2^{nd} dose and curettage
- Changes in Hb / PCV after expulsion
- Various side effects
- Success rate

RESULTS

Table 1

Age Distribution

Age in years	Cases	
	No	%
Less than 20	4	8
21 – 24	22	44
25 – 29	17	34
30 – 34	4	8
35 & above	3	6
Total	50	100
Mean S.D	24.86 4.9	

44% (22/50) of the patients were in the age group of 21-24 years

34% (17/50) were in the age group was 25-29 years

8% (4/50) were in the age group of 30-34 years

6% (3/50) were above 35 years of age.

Table - 2

Gestational age

Gestational Age in weeks	Cases	
	No	**%**
≤ 8	17	34
9 – 10	19	38
11 – 12	14	28
Total	50	100
Mean S.D	9.7 weeks 1.56	

In 34% (17/50) of patients the gestational age was < 8 weeks

In 38% (19/50) of patients the gestational age was 9 to 10 weeks

In 28% (14/50) of patients the gestational age was 11 to 12 weeks

Table - 3

Parity

Parity	Cases	
	No	%
Primi	25	50
Multi	25	50

50% (25/50) were primi para

50% (25/50) were multi para

Table - 4

Socio – economic status

Socio – economic status	Cases	
	No	%
Less than IV	-	-
IV	27	54
V	23	46
More than V	-	-
Total	50	100

All the cases belong to the lower economic strata of the society

Table - 5

Induction Abortion Interval

IAI in hours	Cases	
	No	%
Less than 5	-	-
6 – 10	24	58
11 – 15	10	20
16 – 20	9	18
More than 20	2	4
Total	50	100
Mean S.D	11.38 minutes 4.61	

In 58% (24/50) of patients the induction abortion interval was 6 to 10 hours.

In 20% (10/50) of patients the induction abortion interval was 11to15 hours.

In 18% (9/50) of patients the induction abortion interval was 16 to 20 hours.

Only in 4%(2/50) of patients the induction abortion interval exceeded 20 hours.

Table - 6

Efficacy

Cases requiring	Cases	
	No	%
Single dose only	37	74
Second dose	9	18
Curettage	4	8
Total	50	100

Success rate = 70%

74% (37/50)of the patients had a complete expulsion with single dose of 800 ug of vaginal misoprostol

18%(9/50) required a second dose after 12 hours.

8% (4/50) of the patients required a check curettage

Table - 7

Changes in haemoglobin

Hb	Mean	S.D
Before expulsion	9.73	0.84
After expulsion	9.59	0.86
Change	-0.14	0.11

The mean Hb of the patients before expulsion was 9.73 gm %

The mean Hb of the patients after expulsion was 9.59 gm%

There is no statistically significant difference in Hb after expulsion.

Table 8

Changes in Packed cell volume

PCV	Mean	S.D
At induction	28.48	3.63
After expulsion	28.14	3.47
Change	-0.34	0.21

The mean PCV of the patients at induction was 28.48

The mean PCV of the patients after expulsion was 28.14

There is no statistically significant difference in PCV after expulsion

Table - 9

Complication

Complications	Cases	
	No	%
a) Present		
Vomiting	3	6
Diarrhoea	6	12
Total	9	18
b) Absent	41	82

6% (3/50) of the patients had vomiting,

12% (6/50) of the patients had diarrhea

Hence, 18% (9/50) of the patients had minor side effects.

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

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

Using this software, frequencies, percentage, mean and standard deviations were calculated.

DISCUSSION

Cervical ripening and uterotonic effects of prostaglandin (PGE1 analogue – Misoprostol) is effectively utilized in this study for non invasive expulsion of products of conception.

Age :

In this study, 44%(22/50) of the patients were between age group of 21-24. 34%(17/50) of the patients were in the age group of 25-29 years. The youngest was 19 years and eldest was 39 years.

This study correlates with randomized control trial conducted by Salkos et al, Department of Obstetrics and Gynaecology, University of Athens, Aretacit Hospital, Greece, Dec. 2005 in which 80% of the patients were in the age group of 21-30 years.

Period of Gestation :

In our study 38%(19/50) of the patients were in the gestational age of 9-10 weeks.

34% (17/50) 1of the patients were on the gestational age < 8 weeks, hence majority of the patients gestational age was upto 10 weeks.

This study correlates with the prospective study conducted by Carbowell JL et al, Hospital Docante giveeco – Obstetric Evsebio hermandis (maternidad obrena) ginded de lathabama Cuba, March 1995 in which 90% of the patients gestational age was < 10 weeks.

Parity :

50% of the patients were primi gravida and 50% were multigravida.

The induction abortion interval was not affected by parity.

According to the study by Herabutya Y, O- Prasertsawat P, et al Thailand – 1997. Success of abortion was unaffected by parity.

Induction abortion interval :

In our study, the mean induction abortion interval was 11.38 hrs.

The study correlates with the prospective study conducted by Salakar et al. Department of Obstetrics and Gynaecology University of Athens, Aretaiein, Hospital Greece, 2005 involving a group of 162 volunteers. The mean expulsion time interval was 8.5+ 4.0 hrs.

Success rate :

Failure of procedure is defined as failure of expulsion in 12 hrs with single dose of 800 ug of vaginal misoprostol.

In our study, 74% of patients (37/50) had a complete expulsion of products of conception in single dose of 800 ug of vaginal misoprostol.

4 cases who had incomplete expulsion required a curettage after the first dose as they had profuse bleeding per vaginal.

9 cases needed a second dose of 800 ug of vaginal misoprostol

This study correlates with the prospective study conducted by Kovavisarach. F. Jamman sinic 2005, Department of Obstetrics and Gynaecology, Rajavithi Hospital, Ministry of public health, Bangkok. They showed 78.4% of patients had complete expulsion of products of conception.

Changes in Haemoglobin and PCV :

In our study, the hemoglobin decreased by a mean of 0.14 and PCV decreased by a mean of 0.34.

None of the patients required any blood transfusion for reduction in Hb%. This indicates that blood loss is minimum with this method.

This study correlates with the study done by Thomas betry, Habeebnillah et al JOG Ind. Vol 54 with their mean fall of Hb being 0.4 gm %

Complications :

Out of the 50 patients, 9 patients had minor side effects for misoprostol, 3 patients had vomiting and 6 patients had diarrhea.

No major effects was noted in our study which was very much comparable with the study done by Feldman DA et al and herabutya H et al. They showed no additional side effects with 800 ug of misoprostol.

Post expulsion USG :

All 50 patients underwent ultrasound examination after 4 hours of expulsion and in 92%(46/50) of the patients their uterine cavity was found empty.

8% (4/50) patients revealed bits of conceptus and they underwent curettage.

Follow up :

All cases were followed up for cycle regularity and other side effects like continuous spotting, any profuse white discharge suggestive of infection and general status of the patient. None of the patients had the above said symptoms.

SUMMARY

This study was conducted in the Department of Obstetrics and Gynaecology, Government Rajaji Hospital, Madurai between the period of Feb 2007 to July 2007.

50 patients underwent this study.

In this study, 78%(39/50) of the patients were between age group of 21-29 years.

50%(25/50) were primi gravida and 50%(25/50) were multigravida. Success rate were unaffected by parity.

Majority of the patients were in the gestational age of < 10 weeks

74% of the patients had complete expulsion of products of conception with single dose of 800 ug of vaginal misoprostol

8% of the patients required curettage of the uterine cavity.

18% of the patients required a second dose of 800 ug of vaginal misoprostol.

The mean induction abortion interval was 11.38 hrs.

Out of 50 cases 9 had minor side effects like vomiting and diarrhea.

Hence single dose of vaginal misoprostol (800ug) is found to be effective in I trimester pregnancy termination with minimal side effects.

CONCLUSION

Vaginal prostaglandin E1 analogue (misoprostol) is a very safe and effective method of termination of I trimester pregnancy

Single high dose of vaginal misoprostol (800ug) is found to be effective in I trimester pregnancy termination with minimal side effects and shorter duration abortion interval and hospital stay.

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PROFORMA

Name : Age :

IP.No. : Unit :

Address :

Socio economic class : I II III IV V

Parity : Primi Multi

Period of Pregnancy :

Whether any medical disease

Associated with pregnancy :DM / HT / Heart Disease / hepatic /Renal

Ultra sonogram findings :

Coagulation Profile :

Hb & HCT before induction with misoprostol :

Hb & HCT 48 hours after expulsion

Date of application of misoprostol

Time of first vaginal application of misoprostol

Initial Dosage

No.of doses applied

Date of expulsion

Time of expulsion

Induction expulsion interval :

USG after expulsion : Complete Incomplete

Whether patient

Underwent curettage later :

Side effects : Vomiting Diarrhoea

Follow up after 1 month :

ABBREVIATIONS

SCC - SOCIO ECONOMIC CLASS

I A I - INDUCTION ABORTION INTERVAL

Y - YES

D - DIARRHOEA

V - VOMITING