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Retrospective Study of Low Dose Mifepristone and Misopristol for Induction of Early Induced Abortion

Mittal *Sujata*

Institution of Gynecological Cancer and Women's Diseases, Unit of Famicare Nursing Home, F-25/97, Sec-7, Rohini, NearAyodhya Chowk, Delhi.

OBJECTIVE – To investigate the clinical efficacy of combination of low dose of mifepristone and oral misopristol in induction of early abortion. **METHODS AND RESULTS** – A retrospective analysis of 102 cases of induction of early (upto 49 days of gestation) abortion by mifepristone and misopristol has been done from January ' 1999 to April 2002. Initially 150 mg of mifepristone and 600 µgm of misopristol were used in 40 cases. Thirty five (87.5%) women had complete abortion, two had missed abortion, two had incomplete abortion and one continued pregnancy for which surgical method of termination (suction evacuation) was used. This combination of 150 mg mifepristone and 600 µgm of misopristol was abandoned as reports started appearing that higher dose of mifepristone is more effective . For 62 women, 200 mg of mifepristone and 600 µgm of misopristol were used. Fiftyfive women (91.2%) had complete abortion, two had incomplete abortion, two had missed abortion and one had continuation of pregnancy which had to be terminated surgically. One woman had irregular bleeding for which she was put on oral contraceptive. **CONCLUSION** – Low dose mifepristone and oral misopristol can be a safe, effective and relatively acceptable method for induction of early abortion.

Key word : mifepristone, misopristol, induction of abortion

Introduction

Medical method of inducing abortion has always fascinated obstetricians. The introduction of antiprogestogen mifepristone orally followed two days later by antiprostaglandin analogue misopristol for the purpose is very promising. This combination is registered as a nonsurgical alternative to surgical termination of early intrauterine pregnancy in France and China (upto seven weeks of amenorrhea) and in Great Britain and Sweden (upto 9 weeks of amenorrhea)[1].

The recommended dose of mifepristone in Europe and USA is 600 mg but studies done under WHO Project have shown that a single dose of 200 mg of mifepristone or repeated second dose is equally effective[2-4].

This is a retrospective analysis done at a private setup to analyse the efficacy, failure rate and complications of mifepristone and misopristol combination for early induced abortions. We have compared 150 mg with 200 mg dose of mifepristone for early induced abortion when this method was in its infancy in India.

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Correspondence :
Dr. Mittal Sujata
Institution of Gynecological Cancer and Women's Diseases ,
F-25/97, Sec-7, Rohini, Near Ayodhya Chowk, Delhi.
Tel: 27040323/ 27045304 / 25052367

Material and Methods

A total of 500 women got registered between January 1999 and April 2002 for early induced abortion. All cases of incomplete abortion, missed abortion, spontaneous abortion were excluded from the study. Of the 500 women, 102 were of high socioeconomic status and adequate educational background. They were offered mifepristone and misopristol combination. Their ages ranged from 17 to 45 years and parity ranged from none to three. 98.02% (98) were married and 1.98% (2) were unmarried. Medicines were ordered and received from a Chennai based company named D.C. Import Company which imported them from China. Initially, from January 1999 to December 2000, 40 women were offered Regimen I which comprised of mifepristone 25 mg BD x 3 days followed by misopristol 600 µgm on day 4. Two women with previous one LSCS and one with previous 2 LSCS were included in Regimen I.

From January 2001 to April 2002, 62 women were offered Regimen II, which comprised of 200 mg of mifepristone (8 tablets of 25 mg each) on Day 1 followed by 600 µgm of misopristol orally on day 3. Two women with one previous LSCS were included in Regimen II.

Inclusion criteria were menstrual delay of upto 49 days from the last menstrual period, a positive pregnancy test and a uterine size on pelvic examination consistent with menstrual history. Each

woman signed an informed consent form and had medical and gynecological check up and estimation of Hb%, blood group, and urine albumin and sugar. Those suffering from asthma, glaucoma and heart disease were not included. No prior sonographic examination to assess gestational age was done. All were informed regarding 2-5% incidence of failure rate and possible need for blood transfusion and/or surgical method of termination.

When the drug was new in the market, initial 10 women were called on day 4 (Regimen I) and were kept under observation for 6 hours at our setup. As confidence was gained, telephonic calls were made by them on the day of expulsion of products of conception. All women were instructed to come immediately in case of excessive bleeding or bleeding beyond 5 days post-expulsion or persistence of pain beyond the day of expulsion.

When necessary they were prescribed antiemetic ondansetren 8 mg and pain killers like nimesulide 100 mg / tramadol HCl 100 mg. They were called back after 1 week for a review and a pelvic examination. If there was no pain and/or bleeding, they were asked to return after their next menstrual cycle. In case bleeding or pain persisted, an ultrasound evaluation was done.

Results

A total of 102 women included in the study were analysed. In both the groups, vast majority of the women were between 25 and 35 years of age and 85% in Regimen I and 90% in Regimen II were either para-1 or para-2 (Table II)

Table I : Age

	Total Number of cases	Range (years)	Mean age (years)	Standard Deviation
Regimen I	40	17-42	28.2	± 5.29
Regimen II	62	20-39	28.7	± 4.06

Table – II Parity Distribution

Parity	0	1	2	3	Total
Regimen I	2 (5%)	17 (42.5%)	17 (42.5%)	4 (10%)	40
Regimen II	2 (3.23%)	27 (43.54%)	29 (46%)	4 (6.45%)	62

Table III : Results

	Complete abortion	Incomplete abortion	Missed abortion	Continuation of pregnancy
Regimen I	35 (87.5%)	2 (5%)	2 (5%)	1 (2.5%)
Regimen II	57 (91.6%)	2 (3.3%)	2 (3.3%)	1 (1.3%)

Regimen–II had slightly better results in terms of achieving complete abortion without any need of further instrumental intervention. viz., 91.6% as against 87.5% in Regimen I.

Calculated Standard Error of Difference is 6.30 whereas the observed difference (91.6-87.5) was 4.1. In other words the observed difference between success rates i.e., 4.1 is less than the calculated Standard Error of Difference (for proportion) of 6.30. Hence there is no strong statistical evidence of superiority of Regimen – II over Regimen – I.

Discussion

Numerous protocols have been studied and are in use, but only one has been approved by the FDA (USA) on 28th September 2000. The FDA-approved regimen can be initiated upto 49 days after the first day of the LMP and consists of mifepristone 600 mg orally on day-1, misopristol 400 µgm orally provided at the doctor's office on day-3, and a follow-up appointment on days 12-20. With Regimen-I, the complete abortion rate in our study was 87.5% but the dose used was 150 mg which is considered to be less efficient as an abortificient. Only one study has mentioned the use of mifepristone in lower doses but in combination with gemeprost 0.5 mg-1 mg which is a strong prostaglandin analogue as compared to misopristol[4]. The lower dose of mifepristone would not only lower the cost of the treatment but will also be in accordance with the general pharmacological principle of using the lowest effective dose of any drug, only if it is found to be effective. We found a high complication rate of 12.5% and so this regimen was abandoned after 40 cases. Regimen-I was used initially because of limited availability of the drug, paucity of literature in 1999 and cost effectiveness.

With Regimen II the complete abortion rate was 91.6% which is comparable to that with FDA approved regimen and WHO Task Force study 1993[3]. Five percent incidence of missed abortion with Regimen II is quite high and unacceptable in a country like ours where women lack awareness and wait till emergency supervenes. But this study has been done on 62 women only. So a large trial using such protocols is required. Another evidence based regime which is catching attention is 200 mg mifepristone / 800 µgm vaginal misopristol with virtually 99.6% efficacy with 0.2% adverse effects, of which bleeding is the most frequent event[5].

Lowering the dose of mifepristone is an important consideration in India as it is a costly drug. Issue pertaining to these questions viz., which dose combination can achieve higher than 95% complete abortion rate, whether repeat dosage of mifepristone and misopristol can be given in case of continuing pregnancy, use in previous LSCS cases and whether misopristol alone in higher doses can result in evacuation in missed abortion cases, require further trials. Also, teratogenic effects of mifepristone and misopristol in cases of continuing pregnancy need more attention and studies.

Thus, mifepristone and misopristol combination is safe and effective for medically induced early abortion provided that its side effects and possibility of encountering emergency situations are accepted by women opting for it.

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