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Research Article

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Mifepristone-Misoprostol for Second Trimester Termination of Pregnancy: Experience at a Teaching Hospital

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Abstract

Objectives: To assess the effectiveness of mifepristone and Misoprostol in second trimester termination of pregnancy among women admitted to a teaching hospital in Ethiopia.

Methods: A cross-sectional study was conducted was conducted using a structured questionnaire to collect data clinical profile of patients, the total dose of misoprostol used, the timing of expulsion and complications. The protocol used was: Mifepristone 200 mg oral and 400 mcg misoprostol for gestational age of 13 to 24 weeks and 100 mcg for 24 to 27 + 6 weeks of gestation given intra-vaginally every 3 hours until a maximum of 10 doses in 48 h. Data was entered and analyzed using SPSS.

Results: In this study 102 patients with 2nd trimester pregnancy between gestational age of 14 to 27 wks + 6 days were given a combined Mifepristone and Misoprostol. About 98 (81.7%) cases have expelled the fetus within 24 hrs. whereas 111 (92.5%) of the cases expelled within 48 hrs of the initiation of medical termination. In 79 cases (77.5%), fetal expulsion has occurred with the first course of misoprostol and about 91 cases (89.2%) have completed the expulsion with the second course of the treatment. There were no cases of uterine rupture and bleeding necessitating blood transfusion.

Conclusion: Mifepristone and misoprostol combination use for second trimester termination of pregnancy is safe, effective and is not associated with significant complications.

Keywords

Mifepristone, Misoprostol, Second trimester pregnancy, Termination

Abbreviations

ACOG: American College of Obstetricians and Gynecologists; FIGO: Federation International Obstetrics and Gynecology; WHO: World Health Organization

Background

Abortion can be spontaneous or induced and there are various methods of effecting evacuation of products of conception [1-3]. Modern methods use medication or surgery for abortions [4]. Medical abortions are those induced by abortifacient pharmaceuticals. Medical abortion became an alternative method of abortion with the availability of prostaglandin analogs in the 1970s and the anti-progestogen mifepristone (also known as RU-486) in the 1980s [4,5]. Both medication abortion and surgical abortion are safe and effective in the second trimester, the choice of which may depend on patient and clinical characteristics or expertise of the [1,2]. But the drug mifepristone in combination with prostaglandin appears to be as safe and effective as surgery during the first and second trimester of pregnancy [4,5]. Misoprostol, a prostaglandin E1 analogue has gained a wide popularity in obstetrics; it can be used for cervical ripening and labor induction at term, for treatment of postpartum hemorrhage, and also for first and second trimester abortions [3,4]. Misoprostol has

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advantages over other prostaglandins and other drugs in the set of pregnancy termination, it is inexpensive, and widely available in many countries, it is stable at room temperature and it has multiple routes of administration (oral, vaginal, rectal or sublingual) [4-7].

Medical abortion regimens using mifepristone in combination with a prostaglandin analog are the most common methods used for second-trimester abortions in Canada, most of Europe, China and India, [8] in contrast to the United States where 96% of second-trimester abortions are performed surgically by dilation and evacuation [9].

Termination of pregnancy in the second trimester using misoprostol has been shown to be safe and effective, with a success rate up to 90% in some of the published series [6,8-11]; however, the ideal regimen of misoprostol still remains to be determined, with more than thirty different dosage regimens described in the literature for its use in obstetrics [2,8].

Although the effectiveness of Mifepristone and Misoprostol is well studied in developed countries, very little is known about the use and effectiveness of medical termination of second trimester pregnancy in developing countries. To the best of our knowledge, this is the first study conducted in Ethiopia to assess the use and effectiveness of mifepristone and misoprostol for second trimester termination of pregnancy.

Methods

This was a cross-sectional study done at Saint Paul's Hospital in Addis Ababa, Ethiopia. The hospital is one of the tertiary referral hospitals under the federal ministry of health. The Obstetric and Gynecologic department of the hospital is one of the largest service provision areas. Nearly 4,634 attended antenatal care and around 8,677 deliveries were attended in 2007 Ethiopian fiscal year. Around 1,200 women receive abortion care in the hospital annually. There is a family planning fellowship program and Comprehensive abortion care is provided at the hospital until Ga of 24 wks.

The protocol of second trimester pregnancy termination at the hospital is as follows: Pregnant women whose gestational age between 13-24 weeks of gestation were given 400 mcg every 3 hourly for about 5 doses. Whereas pregnant women whose gestational age 24 weeks up to 27 + 6 weeks were given 100 mcg every three hourly for about 5 doses and repeat dose was given for those who did not expel with first course of misoprostol (after 12 hrs of rest).

The study subjects were all women with second trimester

Table 1: Sociodemographic characteristics of patients with second trimester pregnancy who were included in the study at Saint Paul hospital, Addis Ababa, Ethiopia.

Category		Frequency	Percentage (%)
Age (years)	< 20	17	16.7
	Between 20 and 35	83	81.4
	> 35	2	2
Marital status	Married	60	58.8
	Separated	2	2
	Single	35	34.3
	Divorced	5	4.9
Place of residency	Out of Addis	42	41.2
	Addis	60	58.8
Reproductive Performance	Multi gravida	52	51
	Primigravida	50	49
Religion	Orthodox	65	63.7
	Muslim	23	22.5
	Protestant	14	13.7
Occupation	House wife	38	37.3
	Private employed	14	14.7
	Gov. Employed	17	14.2
	Student	16	15.7
	Daily laborer	12	11.8
	NGO employed	5	4.9
Educational status	Primary school	44	43.1
	University degree	25	24.5
	Secondary school	18	17.6
	Unable to read and write	14	13.7

pregnancy who came for medical termination of pregnancy. Purposive sampling was done and all women who presented for 2nd trimester termination of pregnancy who fulfilled the inclusion criteria were sequentially recruited.

The Inclusion criteria was: All pregnant women who were between 13 to 27 completed weeks of gestation. The gestational age was calculated from reliable LMP. In the absence of LMP GA was calculated from early ultrasound. Women with spontaneous abortions, those with any contraindications for medical termination of pregnancy those with multiple pregnancies and those who were not given Oral mifepristone were excluded from the study.

Data was collected employing a structured, pretested interviewer administered questionnaire and chart review of patients. The questionnaire included information about reproductive performance (gravidity, parity) and gestational age of patients; reasons for termination; number of misoprostol doses, time interval from start of misoprostol and expulsion of the fetus and placenta, side effect profile of the drugs and maternal complications of the termination process. Card number and phone number of mothers was registered up on admission for later tracing of maternal outcome. Data collectors were trained nurses and general practitioners.

Failure of medical termination of pregnancy was defined as absence of expulsion of the fetus within 48 hrs of the start of mifepristone. Complications of the treatment considered were: Need for blood transfusion, uterine rupture, hysterectomy and retained placenta.

The collected data was checked, coded and entered using SPSS version 21. Descriptive statistics was done and results were displayed as frequencies, percentages and tables.

Ethical clearance for the conduct of the study was obtained from the college's ethical review board. Permission to conduct the study was taken from the hospital administration. Participants were given explanation about the study and verbal consent to participate was taken.

Results

In the study period, 121 women with second trimester of pregnancy visited the hospital for medical termination of pregnancy. But one patient who underwent hysterotomy for an impression of scar dehiscence and about 18 patients who were not given mifepristone before misoprostol were excluded from the study. Hence analysis was made for 109 women with singleton pregnancies between 13 weeks and 27 + 6 weeks of gestation. Most of the subjects were from Addis Ababa (58.8%), multigravidas. (51%), House wives (37.3%), and 44 (43.1%) competed primary school (Table 1). Twenty-one cases (20.6%) had history of abortion; about 55% of the pregnancies were unplanned and 60.8% of them were not using any form of contraception. The primary reason for termination was unwanted pregnancy (49%), followed by congenital anomaly and missed abortions accounting for 31.4% and 10.8% respectively (Figure 1).

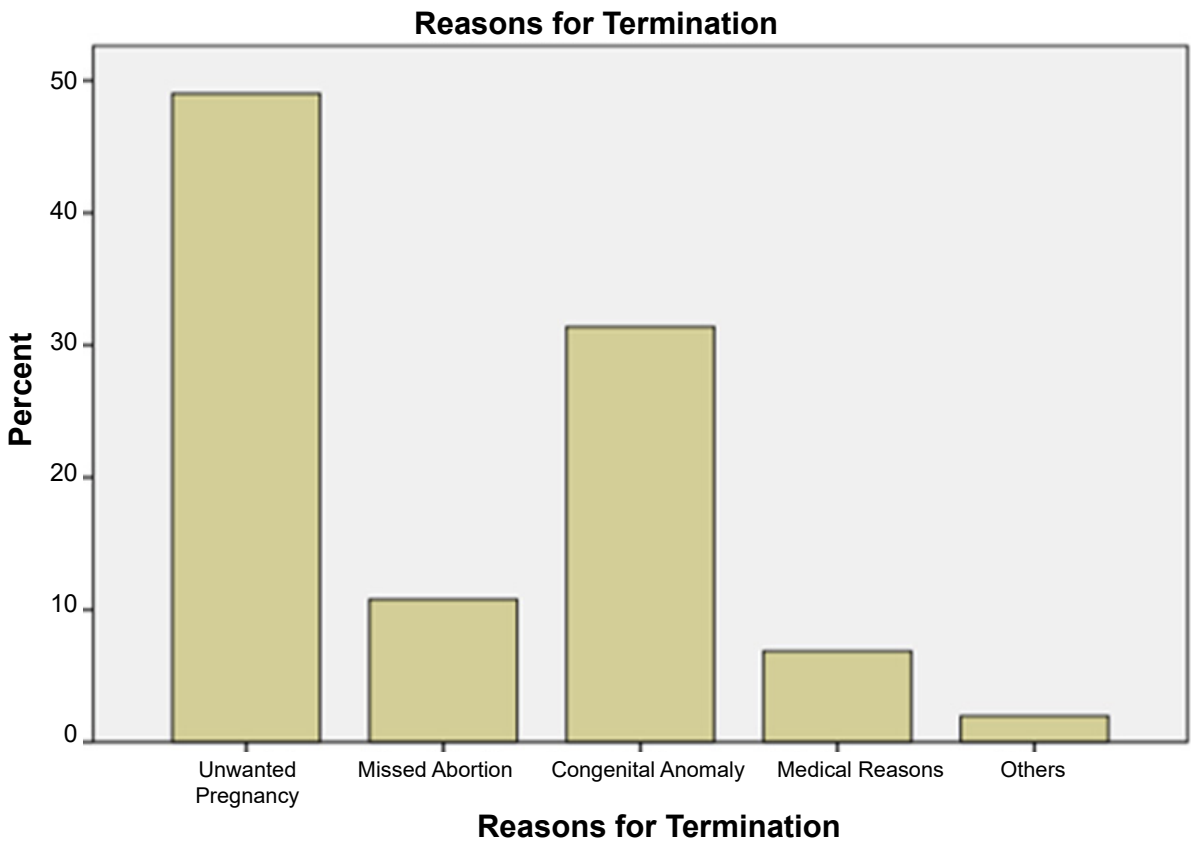

Figure 1: Reasons for pregnancy termination.

Table 2: Time Interval between administration of mifepristone/misoprostol verses expulsion time of the abort us.

Elapsed time between mifeprostone and misoprostole	Expulsion time of products of conception				Total
	Less than 12 hrs	12 to 24 hrs	24 to 48 hrs	Greater than 48 hrs	
less than 24 hrs	9	4	1	0	14
24 to 36 hrs	14	6	1	2	23
36 to 48 hrs	33	16	10	6	65
Not given	14	2	1	1	18
Total	70	28	13	9	120

Table 3: Number of Doses of misoprostol.

	Frequency	Percent	Cummulative Percent
First Dose	95	79.2	79.2
Second Dose	13	10.8	90.0
Third Dose	11	9.2	99.2
Other Management	1	0.8	100.0
Total	120	100.0	

Most of the women (92%) expelled within 48 hrs after the start of medical termination. There were about 8 cases of treatment failure in this study population giving the failure rate of 7.8%. Regarding the interval from initiation of medical abortion to expulsion, 56 (54.9%) expelled within the first 12 hrs of initiation of the protocol, about 82 (80.4%) within 24 hrs and 94 (92.2%) at the end of 48 hrs (Table 2).

In 79 cases (77.5%), fetal expulsion has occurred with the first course of misoprostol and about 91 cases (89.2%) have completed the expulsion with the second course of the treatment (Table 3). There was one patient who was given oxytocin after one course of misoprostol and expelled after wards. Out of patients who had expelled within 48 hrs of the start of misoprostol 14.9% of them had the elapsed time between mifepristone and misoprostol less than 24 hrs, and 32.8% had elapsed time of 24 to 36 hrs, 62.76% had elapsed time of 36 to 48 hrs.

There were about 15 cases of women with a late second trimester pregnancy (24 weeks to 27 + 6 weeks) which accounts for 14.7% of the study population. Out of these 13 (86.66%) have expelled in less than 24 hrs and about 14 (93.3%) has expelled in less than 48 hrs. There were no complications such as excessive vaginal bleeding, need for blood transfusion, uterine rupture and hysterectomy.

Discussion

Ethiopia expanded its abortion law in 2005, which had previously allowed the procedure only to save the life of a woman or protect her physical health [12]. Abortion is now legal in cases of rape, incest or fetal impairment. In addition, a woman can legally terminate a pregnancy if her life or physical health is in danger, if she has physical or mental disabilities, or if she is a minor who is physically or mentally unprepared for childbirth [12]. Since then the number of safe abortions has dramatically increased. But from clinical observations, the method of choice for termination of second trimester pregnancy has been variable among health care providers in Ethiopia. The national protocol on termination of second trimester pregnancy is based on recommendations from the WHO and professional societies. We believe this study has come up with important contextual information and evidence on the use of mifepristone and misoprostol for second trimester termination of pregnancy in Ethiopia.

The combination of mifepristone and misoprostol is used worldwide efficiently and with minimal side effects such as fever, nausea, vomiting and diarrhea which occasionally required treatments. WHO recommends misoprostol 400 mcg for gestational age 13-24 weeks every 3 hrly for 5 doses followed by 12 hrs of rest and then another 5 doses of misoprostol with the same dose and individualized for gestational age above 24 weeks of pregnancy, if it does not work, and then failure rate can be declared [13].

In this study the WHO's protocol was followed and the overall success rate of expulsion of product of conception was 92%. This success rate is consistent with findings from studies in Portugal which reported 88.9% [14]. But slightly lower than the 96% rate reported in a European review involving 386 women, [15], an Armenia study of 99.5% [16] and the 98.8% in an Indian comparative study [17]. There is limited experience in medical termination of second trimester pregnancy in developing countries. But in a Cohort study done in South Africa comparing clinical outcomes of second trimester abortions before and after introduction of the combined use of mifepristone and misoprostol showed that 97% have successfully expelled [18].

One of the areas of controversy or rare information is the use of misoprostol between gestational age of 24 weeks to 27 + 6 weeks. The WHO recommends either increasing the interval of use of misoprostol or decreasing the dose of the drug [13]. However, in our study there were about 15 cases of late second trimester pregnancy managed according to the usual

protocol and 93.3% has expelled in less than 48 hrs without any complications. But the number of cases in our study is small so as to make any strong conclusions on the efficacy and safety of combined use of mifepristone/misoprostol for late second trimester pregnancy termination.

Another observation of the study was the expulsion time in relation to the elapsed time since the start of mifepristone and the start of misoprostol in which about 62.76% had elapsed time of 36 to 48 hrs. This finding is also consistent with other studies done previously. WHO, FIGO and ACOG also recommend to use the combination of mifepristone and misoprostol in second trimester termination of pregnancy with an interval of preferably more than 24 hrs to have very successful treatment as the greater the interval between mifepristone and misoprostol the shorter the time of expulsion [13,19].

The observed complication rate in this study was comparable to most previous studies [15-17] but much lower compared to the study done in Portugal which reported complication rate of 25.2% including excessive blood loss, need for transfusion, placental retention [14]. But similar to our study there were no cases of uterine rupture or need for hysterectomy. The difference in the complication rate might be attributed to the fact that only major complications were reported in our study.

One important practical implication of the study findings in developing countries context is that: Second trimester pregnancy termination with mifepristone and misoprostol can be provided with low level health workers with back up of Gynecologists. But there might be some logistic challenges too in developing countries. Most of the public hospitals have high turnover rate and lack of beds for emergency gynecologic conditions is a common place. Hence in such facilities practitioners might prefer to perform surgical evacuation of the products of conception and discharge patients early rather than starting medical termination and keeping them in wards until fetal expulsion occurs.

One important limitation of the study is that there were no adequate cases of medical treatment failure to make comparison of success based on different characteristics in the two groups (success vs. failure).

Conclusions

Mifepristone and misoprostol is a safe and effective combination for second trimester termination of pregnancy with few complications in a developing country, Ethiopia.

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Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from St. Paul's Hospital Millennium Medical College.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no any competing interests.

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Authors Contributions

OK was involved in the inception, data analysis, draft manuscript write up. WG collected resources and revised the manuscript. BN revised the study protocol and the manuscript. All authors have read and approved the manuscript.

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