

Research Article

**Success rate of tamoxifen with misoprostol in first
trimester pregnancy termination**

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ABSTRACT

Objective: To determine the success rate of using tamoxifen with misoprostol in first trimester pregnancy termination.

Materials & Methods: This case series study was conducted at Department of Gynaecology & Obstetrics DHQ Teaching Hospital, Sahiwal from June 2016 to December 2016 over the period of 6 months. A total of 163 patients, 18 to 40 years of age with fetal death or missed abortion on ultrasonography in 1st trimester (<12 gestational weeks) of pregnancy were included in the study. All the enrolled patients were given 20 mg tamoxifen oral daily for 4 days followed by 800 mcg oral misoprostol for 1 or 2 days orally (maximum 80 mg) and the outcome (in terms of complete abortion) was assessed after 7 days.

Results: Mean age in our study was 24.89 ± 5.23 years. Mean gestational age was 7.07 ± 3.67 weeks. Majority of patient i.e. 49.69% were nulliparous. Complete abortion after tamoxifen with misoprostol therapy was seen in 149 (91.41%) cases.

Conclusion: This study concluded that tamoxifen with misoprostol in first trimester pregnancy termination is very effective and useful with 91.41% rate of complete abortion.

Keywords: Medical abortion, complete abortion, prostaglandins.

INTRODUCTION

The term “abortion” comes from the Latin word “aboriri” which means “to miscarry”.¹ Missed abortion is the condition in which the fertilized ovum dies within the uterus but is retained in the uterus for unknown reasons. Most of the missed abortions terminate spontaneously. But if there is a delay of 5-6 weeks in expulsion, there is a risk of developing coagulation disorders. Therefore uterus is to be evacuated as soon as the diagnosis of missed abortion is made.²

A miscarriage is the spontaneous loss of a fetus before the 20th week of pregnancy.³ It can be spontaneous or therapeutic. Most providers consider all terminations to be elective, or a voluntary decision made by the patient herself. There are medical factors both maternal and fetal that contribute to the decision. These factors have been termed therapeutic abortion, defined as the termination of pregnancy for medical indications, including the following: Medical

illness in the mother in which continuation of the pregnancy has the potential to threaten the life or health of the mother is a factor. Consider the present medical condition and a reasonable prediction of future circumstances, as well as the consequences of the pregnancy as it progresses.⁴ It is estimated that approximated 1.3 to 1.4 million abortions occur annually in US.^{5,6} We estimate that 890,000 induced abortions are performed annually in Pakistan.⁷ Determining the precise prevalence of miscarriage is not possible, because a large number of miscarriages occur before pregnancies become established and before women are aware they are pregnant.⁸ 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 antiprogesterone mifepristone in the 1980s. Although the idea of using medications to induce a late menses or cause abortion dates back centuries, medically proven regimens have only been found in the last 50 years.¹²

More than 40% pregnancies are aborted by medical methods, for which different regimens used depending on gestational age and on women desire.¹³ Widely used method for termination of pregnancy is oral mifepristone (anti progesterone) 200 mg followed by 800 mcg buccal misoprostol (synthetic prostaglandin) after 24-48 hour, having success rate 93.6%.¹⁴⁻¹⁶ Initial studies of mifepristone attempted to configure the optimal dose and dosing schedule to achieve acceptable rates of expulsion. The outcome of oral therapy was no different within a dose range of 50 to 400 mg daily in single or divided doses over 4 days. For gestations up to 49 days, complete abortion occurred in approximately 60% to 80%, incomplete abortion in 6% to 30%, and continuing pregnancies in 7% to 40%.¹⁷⁻¹⁹

Tamoxifen was found to cause spontaneous abortion in Guinea pigs and hamsters which led to several studies on humans.²⁰ Tamoxifen produced significant impairment of decidual development, making it useful in termination of pregnancy.²¹ In Orlando women center it is noted that the combination of Tamoxifen and Misoprostol is 94% effective in causing the termination of pregnancy. It is nearly 100% effective for patients less than 6 weeks from their last menstrual period.²²

Therefore this study was done to evaluate the outcome of tamoxifen with misoprostol in first trimester pregnancy termination so that on the basis of the results, the decision for its use in our routine practice could be taken in future.

OPERATIONAL DEFINITIONS:

- **Outcome:** outcome of using tamoxifen with misoprostol in first trimester pregnancy termination was measured in terms of complete abortion which was confirmed on ultrasound immediately and after 7 days.
- **First trimester Pregnancy Termination:** Termination of pregnancy within 12 weeks of gestation.
- **Miscarriage:** A miscarriage is the spontaneous or therapeutic loss of a fetus before the 20th week of pregnancy (diagnosed on ultrasound showing no products of conception inside uterine cavity).
- **Incomplete evacuation** means that uterine cavity still contains products of conception after procedure. It was diagnosed by pelvis scan.

MATERIALS & METHODS

This case series study was conducted at Department of Gynaecology & Obstetrics DHQ Teaching Hospital, Sahiwal from June 2016 to December 2016 over the period of 6

months. Total 163 primigravida and multigravida having age 18–40 years, having gestational sac less than 12 weeks confirmed on USG, undergoing medical abortion were selected for this study.

Patients with cardiac or cerebrovascular disease, patients with known allergy or contraindications to misoprostol and tamoxifen use, complete miscarriage (ultrasound showing empty uterine cavity), molar pregnancy (abnormal pregnancy with abnormally swollen placental villi with or without embryo presentation), ectopic pregnancy (implantation of fertilized ovum outside uterine cavity) and hemodynamically unstable (blood pressure \leq 80/40 mmHg) women excluded from the study.

Study was approved by the ethical committee and written informed consent was taken from every woman.

All the enrolled patients were given 20 mg tamoxifen oral daily for 4 days followed by 800 mcg oral misoprostol for 1 or 2 days orally (maximum 80 mg). During termination the time period of termination was noted. All patients were advised to contact with emergency Gynaecological Department in case of any problem on 24 hours basis. Pregnancy termination was measured in terms of complete abortion which was confirmed on ultrasound immediately and after one week. The outcome (in terms of complete abortion) was assessed after 7 days and noted on the proforma.

The collected data was entered and analyzed in computer software SPSS version 10. Descriptive statistics was applied to calculate mean and standard deviation for the age of the patient and gestational age. Frequencies and percentages were calculated for outcome (i.e. complete abortion). Effects modifiers like age, gestational age and parity were controlled by stratification and chi-square test was applied

Fig. 1: Frequency of complete abortion

to see the effect of these on outcome. $P \leq 0.05$ was considered significant.

RESULTS

Mean age in our study was 24.89 ± 5.23 years. Mean gestational age was 7.07 ± 3.67 weeks. Out of 163 patients, complete abortion was noted in 149 (91%) patients. (Fig. 1) Selected patients were divided into four equal groups i.e. age group 18-25, 26-30, 31-35 and 36-40 years. Total 78 (47.85%) patients belonged to age group 18-25 years followed by 44 (26.99%) patients to age group 26-30 years, 27 (16.56%) patients to age group 31-35 years and 14 (8.59%) patients to age group 36-40 years. Complete abortion was noted in 72 (92.31%) patients, 40 (90.91%) patients, 24 (88.89%) patients and 13 (92.86%) patients respectively. Statistically insignificant association of complete abortion with age groups was noted with p value 0.950. (Table 1) Patients were divided into two equal groups according to gestational age i.e. <6 weeks group and ≥ 6 weeks group. Total 91 (55.83%) patients were belonged to <6 weeks group and 72 (44.17%) patients belonged to ≥ 6 weeks group. Complete abortion was noted in 86 (94.51%) patients and 63 (87.5%) patients respectively. Insignificant association of complete abortion with gestational age was noted with p value 0.113. (Table 2) Nulliparous were 81 (49.69%), Primiparous were 48 (29.45%), Multiparous were 26 (15.95%) and Grand Multiparous were 8 (4.91%). Complete abortion was noted in 74 (91.36%) Nulliparous followed by 44 (91.67%) in Primiparous, 24 (92.31%) paras and 07 (87.5%) in Grand Multiparous. But complete abortion was insignificantly associated with parity with p value 0.980. (Table 3)

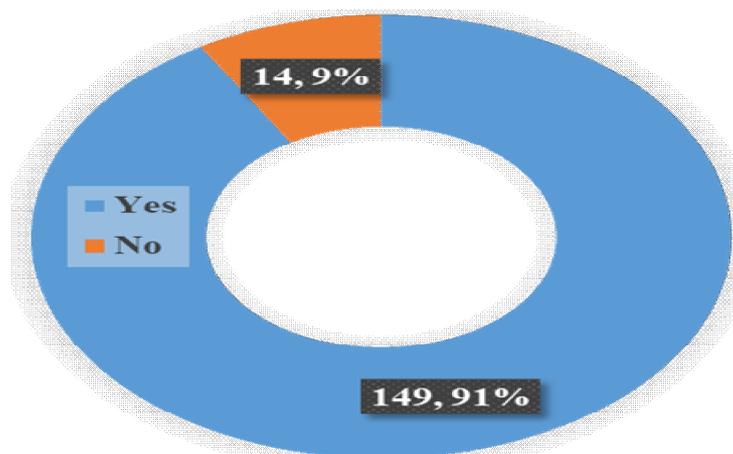


Table 1: Stratification of outcome with respect to age groups.

Age (in years)	Complete Abortion		Total	p-value
	Yes	No		
18-25	72 (92.31%)	06 (7.69%)	78 (47.85%)	0.950
26-30	40 (90.91%)	04 (9.09%)	44 (26.99%)	
31-35	24 (88.89%)	03 (11.11%)	27 (16.56%)	
36-40	13 (92.86%)	01 (7.14%)	14 (8.59%)	

Table 2: Stratification of outcome with respect to gestational age.

Gestational Age	Complete Abortion		Total	p-value
	Yes	No		
<6 weeks	86 (94.51%)	05 (5.49%)	91 (55.83%)	0.113
≥6 weeks	63 (87.5%)	09 (12.5%)	72 (44.17%)	

Table 3: Stratification of outcome with respect to parity.

Parity	Complete Abortion		Total	p-value
	Yes	No		
Nulliparous	74 (91.36%)	07 (8.64%)	81 (49.69%)	0.980
Primiparous	44 (91.67%)	04 (8.33%)	48 (29.45%)	
Multiparous	24 (92.31%)	02 (7.69%)	26 (15.95%)	
Grand Multiparous	07 (87.5%)	01 (12.5%)	8 (4.91%)	

DISCUSSION

In our study, it was seen that complete abortion after tamoxifen followed by oral misoprostol occurred in 91.41% cases of first trimester pregnancy. These findings are similar to findings of a study in which tamoxifen followed by intravaginal misoprostol was given and this combined approach was found effective in 92% cases for complete abortion in pregnancies less than 56

days.²¹ Wiebe ER et al²⁴ compared methotrexate to tamoxifen, both followed by misoprostol. The trial was conducted in 2 phases: phase 1 low dose tamoxifen (40mg) and phase 2 high dose (160mg). In the first phase, 198 women presenting for medical abortion at <7 weeks gestation were randomized to receive either 40 mg of tamoxifen, followed 2 to 3 days later by 800 µg of misoprostol self-administered vaginally,

followed 5 to 7 days later by the same dose of misoprostol. In the second phase, 200 women were randomized to receive 20 mg tamoxifen twice daily for 4 days, followed by 800 µg misoprostol. The main outcome measure was success rate determined by the number of women who aborted without surgery. In phase 1, the success rate was 85.7%. In phase 2, the success rate was 84.7%. Jain JK et al²⁵ undertook a study on 150 women with pregnancies <156 days of gestation, complete abortion occurred in 93.3% in tamoxifen group and 90.7% in placebo group.

In a recent study done by Nabila Atta et al²⁶ in which they selected 50 pregnant women range from 41 to 48 days gestational age used 20 mg tamoxifen oral daily for 4 days followed by 800 mcg oral misoprostol for 1 or 2 day. This study has shown that complete abortion occurred in 88% women. In another study, this combination of Tamoxifen and Misoprostol is found 94% effective in causing the termination of pregnancy. It is nearly 100% effective for patients less than 6 weeks from their last menstrual period.²²

CONCLUSION

This study concluded that tamoxifen with misoprostol in first trimester pregnancy termination is very effective and useful with 91.41% rate of complete abortion (complete expulsion of products of conception). So, we recommend that tamoxifen with misoprostol should be used as a first line medical method in the therapeutic termination of 1st trimester pregnancy in order to achieve rapid and safe results and avoid surgical methods.

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