# OUTCOME OF USING TAMOXIFEN WITH MISOPROSTOL IN FIRST TRIMESTER PREGNANCY TERMINATION

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## ABSTRACT

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

**Materials & Methods:** This study was a case series and conducted at Department of Gynaecology & Obstetrics from 1st April ,2018 to 30th September 2018 at Nishtar hospital Multan. Over the 6 months period .163 patients, 18 to 40 years of age with fetal demise or missed abortion confirmed on ultrasonography in 1st trimester (<12 gestational weeks) of pregnancy were included in the study. All the enrolled patients received 20 mg tamoxifen orally for 4 days then it is 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" is a 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 loss of a fetus spontaneously before the 20th week of pregnancy.[3] It can be spontaneous or therapeutic. Most providers consider all terminations of pregnancies to be elective and a voluntary decision by the patient. There are some medical factors, both fetal and maternal that contribute in decision making. These factors have been termed therapeutic termination of pregnancy, that is the pregnancy termination based on medical indications, includes following: Any medical disease effecting the mother if the pregnancy is continued, it can have the potential risk to the life or wellbeing of the mother. Consider the present medical disease status as well as the pregnancy consequences as it progresses.[4] It is estimated that approximated 1.3 to 1.4 million pregnancy terminations occur annually in US.[5,6] According to an estimate ,annually in Pakistan, about 890,000 induced abortions are performed .To determine, the precise prevalence of abortions is not possible, because maximum miscarriages occur before the established pregnancies and before women become aware of their pregnancies.[8] Medical terminations are done by abortifacient drugs. Medical termination of pregnancy became an alternative method of miscarriage in which prostaglandin analogs became available in 1970s and the antiprogestogen, mifepristone in the 1980s. Although this idea of utilizing medications to start a late menses or for terminatiom of early pregnancy dates back centuries, Regimens that are medically proven are only found from 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 oral misoprostol (synthetic prostaglandin) after 24-48 hour, having success rate 93.6%.[14-16] Early studies oabout mifepristone attempted to find out its optimal dose and dosing schedule to achieve acceptable miscarriage rate. The outcome of oral therapy was almost same within a dose range of 50 to 400 mg given

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daily in single dose or divided doses over a 4 days period. For gestations up to 7 weeks, complete miscarraige occurred in about 60% to 80% cases, incomplete miscarriage in 6% to 30% cases, and intact continuing pregnancies in about 7% to 40%.[17-19]

Tamoxifen when used in Guinea pigs and hamsters was found to cause spontaneous miscarraige which led to several human studies.[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 combines use of Tamoxifen and Misoprostol is about 94% effective for termination of pregnancy. It is almost 100% effective in patients less than 6 weeks.[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 study is a case series study that was conducted at Department of Gynaecology & Obstetrics,Nishtar hospital ,Multan, from 1st April to 30th September , 2018 over 6 month period .Total 163 primigravida and multigravida of 18–40 years of age, having fetus less than 12 weeks confirmed on USG, undergoing termination of pregnancy medically were included in this study.

Patients with cardiac or cerebrovasular 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 (pregnancy outside uterine cavity) and hemodynamically unstable (blood pressure ≤ 80/40 mmHg) women excluded from the study.

Approval of study was taken from the ethical committee and informed written consent was taken from every woman.

All the enrolled patients received 20 mg tamoxifen orally for 4 days then it is followed by 800 mcg oral misoprostol for 1- 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 SPSS version 10. Descriptive data (age and gestational age) was applied to calculate mean and standard deviation. Percentages and Frequencies were calculated for outcome (i.e. complete abortion).Stratification is used to control effect modifiers like age, gestational age and parity and chi-square test was applied to see their effect on outcome. P ≤ 0.05 was considered as significant.

## RESULTS

Mean age in this 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). Patients were divided into four equal groups i.e. age group 18-25, 26-30, 31-35 and 36-40 years.

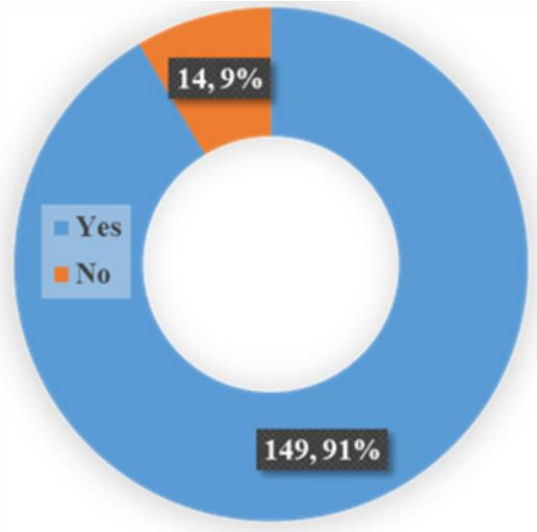


**Fig. 1:** Frequency of complete abortion

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. There was Statistically insignificant association of complete abortion with age groups with p value of 0.950. (Table 1) Patients were equally divided in two groups according to gestation 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 according to age groups.

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

**Table 2:** Stratification of outcome according to gestational age.

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

**Table 3:** Stratification of outcome according to parity.

| | **Complete Abortion** | | Total | |
|---|---|---|---|---|
| **Parity** | Yes | No | | **p-value** |
| **Nulliparous** | 74 (91.36%) | 07 (8.64%) | 81 (49.69%) | |
| **Primiparous** | 44 (91.67%) | 04 (8.33%) | 48 (29.45%) | |
| **Multiparous** | 24 (92.31%) | 02 (7.69%) | 26 (15.95%) | **0.980** |
| **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 tamixifen 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]3 Wiebe ER et al[24] compared methotrexate to tamoxifen, both followed by misoprostol. The trial was conducted in 2 phases: in first phase low dose tamoxifen (40mg) and in second phase high dose (160mg) given. In the initial phase, 198 women admitted for medical termination of pregnancy at <7 weeks were randomized and they received either 40 mg of tamoxifen, followed 2 - 3 days accompanied by 800 μg of misoprostol self-administered through vaginal route,then it is accompanied by the same dose of misoprostol 5 to 7 days later. In the second phase, 200 women were randomized and they received 20 mg tamoxifen two times a day for 4 days,accompanied by 800 μg of misoprostol. The main measure of outcome was success rate that is determined by the number of women having complete miscairaige without surgical intervention. In first phase , the success rate was 85.7%. In the second phase , the success rate was 84.7%. Jain JK et al[25] 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 al[26] in which they selected 50 pregnant women range from 41 to 48 days gestational age used 20 mg tamoxifen orally

for 4 days then accompanied by 800 mcg oral misoprostol for 1 or 2 day. This study has shown that complete abortion occurred in 88% women. In another study, the combination of both drugs is found 94% successful for termination of pregnancy. It is about 100% effective for less than 6 weeks pregnancies. [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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