ORIGINAL ARTICLE

# SAFETY OF MISOPROSTOL IN SECOND TRIMESTER MISCARRIAGES IN PATIENTS WITH PREVIOUS UTERINE SCARS

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## ABSTRACT

**Objective:** To assess the safety of Misoprostol in mid-trimester miscarriages in patients with previous scars.

**Materials and Methods:** This was a cross-sectional comparative study conducted in the Department of Gynaecology and Obstetrics, Lady Reading Hospital, from January 2021 to December 2021. Two-hundred patients with second-trimester miscarriages were included in the study. They were divided into two groups, 100 patients with no previous scar as the control group and another 100 patients with a previous scar as the study group. Patients having an incomplete abortion, gestational trophoblastic disease, and more than one scar were excluded from the study. Misoprostol doses were kept vaginally in both groups. The doses were kept according to the gestational period of 13 to 24 weeks following the local protocol which was comparable with the FIGO protocol. Data analysis was done using SPSS-24.

**Results:** The Demographic features of patients of the two groups, were comparable for maternal Age (26±5.3 Years versus 25±4.9 years), Gestational Age in weeks of (18±1.3 weeks versus117±1.6 weeks) Gravidity (4.5±1.6 versus 4.9±1.2) and of Parity (3.4 ±1.4 versus 3.6 ±1.1) which showed no significant difference with respect to age, parity and gestational age. The period needed for successful TOP was 18 hours in the control group whereas it was 36 hours in the scarred uterus with half doses. Successful termination was observed in 61% of the study group with the scared uterus and 72% in the control group.

**Conclusion:** Our study concluded that misoprostol is safe and effective in the termination of second-trimester miscarriages with a scarred uterus.

**Keywords:** Misoprostol, Miscarriage, Previous Uterine Scar

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## INTRODUCTION

It is of great importance in modern obstetrics to diagnose cases of missed miscarriages and structural abnormalities and offer Termination of pregnancy (TOP) in these cases. [1] Two options are there to offer termination of pregnancy: one medical and the second surgical termination. Surgical termination has a higher risk of maternal morbidity and mortality. [2] Misoprostol is a prostaglandin analog PE1 and one of the safest methods for medical termination of pregnancy and priming the cervix before surgical termination. According to the American College of Obstetrics and Gynaecology, misoprostol is the treatment of choice for ripening of the cervix. [3] There are many risk factors involved in the termination of pregnancy. The most important of these is the previous uterine scar which leads to serious complications like uterine rupture, infections, fistulas, severe blood loss, and death. So, the method of termination should be carefully selected to avoid such complications. [4] Some studies have reported serious complications with misoprostol before the third trimester while other studies have reported safety with the use of misoprostol. [5]

The safety of the use of misoprostol has been questioned in women with previous uterine scars. The data on the safety of misoprostol in the second trimester with previous scar is limited and no local studies have been done to date, so this study was planned. The conclusion of the study will render with local statistics and will pave the way for further research.

## MATERIALS AND METHODS

This was a descriptive cross-sectional comparative study conducted in the Department of Gynaecology and Obstetrics, Lady Reading Hospital, from January 2021 to December 2021. The ethical approval of the study was taken from the hospital's ethical committee. Written informed consent was taken from all the couples included in the study. Patients were admitted and a detailed Proforma was filled regarding the history of the patient, including demographic features, period of gestation, high-risk factors,

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and previous surgeries, clinical examination was done and routine Laboratory investigations and ultrasound were performed. The sample size was 200 calculated with the WHO formula taking the prevalence of miscarriages in pregnancy as 7%, confidence interval 95%, and margin of error 5%. The patients were distributed in the two groups by lottery consecutive sampling.

100 patients with no previous scar were put in the control group and another 100 patients with previous scar were put in the study group. The patients having incomplete miscarriages, with gestational trophoblastic disease and more than one scar were excluded from the study. Misoprostol doses were kept vaginally in both groups. The doses were kept according to the gestational period of 13 to 24 weeks following the local protocol which was comparable with the FIGO protocol. Full doses of 200 micrograms 6 hourly were kept from 13 to 17 weeks and doses of 100 micrograms 6 hourly were kept from 18 to 24 weeks for 24 hours and half of these amounts were kept in the study group with previous scar according to local ward protocol which has also been recommended by FIGO as shown in table 1 (FIGO recommends to alter the dose according to local protocol for patients with scarred uterus).

Data was entered in SPSS 24; Mean ±SD was calculated for continuous variables like age, period of gestation, and parity. Post-stratification analysis was done using a paired independent t-test to calculate the p-value which was taken as ≤ 0.05 to be significant. The primary outcome was success rate observed in both groups in terms of doses used and period for termination and the secondary outcome was the complication rate in both groups.

## RESULTS

A total of 200 patients were included in the study. They were divided into two groups. One group had 100 patients as control with no scarred uterus and the other group included 100 patients with scarred uterus. The demographic features of patients of the two groups with the control and study group were comparable for maternal Age (26±5.3 Years versus 25± 4.9 years with a p-value of 0.860), Gestational Age in weeks of (18±1.3 weeks versus17±weeks+1.4 with a p-value of 0.554) Gravidity (4.5 ± 1.6 versus 4.9 ± 1.2 with a p-value of 0.844) and of Parity (3.4 ±1.4 versus 3.6±1.1 with a p-value of 0.842) and showed no significant difference concerning age, parity and gestational age as can be seen in Table 2. Successful termination was observed in 61% of the study group with the scared uterus and 72% in the control group. The p-value of 0.03 showed that TOP was more successful in patients in the control group without previous C-sections as compared to the study group, which was attributed to half doses taken in the control group hence these patients were subjected to a second cycle as shown in Table 3. The time period needed in hours for expulsion was 18±2.3 hours in the control group and 36±3.5 hours in the scarred uterus with a p-value of 0.04 showing almost double the time needed for expulsion in the scarred uterus with half doses. The doses needed for the control group were 3 doses per cycle and for the study group were 6 doses as shown in table 4.

Surgical intervention was needed in 18% of the control group and 19% in the study group due to vaginal bleeding and incomplete abortion as can be seen in Table 3. Side effects rates in the two groups were comparable with no significant difference with no major complication of uterine rupture seen in both groups.

**Table 1: Departmental protocol for per vaginal dose administration of Misoprostol comparable with the FIGO protocol**

| Gestational Age | Misoprostol Without Previous Scar | Misoprostol With Previous Scar |
|---|---|---|
| 13-17 weeks | 200 μgm 6 hourly | 100 μgm 6 hourly |
| 18—24 weeks | 100 μgm 6 hourly | 50 μgm 6 hourly |

**Table 2: Demographic features of patients (n=200)**

| Variable | Control group (n=100) | Study group (n=100) | P value |
|---|---|---|---|
| Age | 26±5.3 Years | 25±4.9 years | 0.860 |
| Gestational Age | 18 ±1.3 weeks | 17.3±1.4 weeks | 0.554 |
| Gravida | 4.5±1.6 | 4.9±1.2 | 0.844 |
| Parity | 3.4±1.4 | 3.6±1.1 | 0.842 |

**Table 3: The Outcome of Misoprostol in Termination of Pregnancy**

| Outcomes | Control group | Study group | P value |
|---|---|---|---|
| Successful Termination | 72% | 61% | 0.03 |
| Surgical Intervention | | | |
| Excessive PV bleeding | 12% | 13% | 0.832 |
| Incomplete Abortion | 6% | 6% | 0.722 |

**Table 4: Efficacy parameters in termination of pregnancy**

| Efficacy Parameters | Control group (hours) | Study group (hours) | P value |
|---|---|---|---|
| Time period | 18±2.3 | 36±3.5 | 0.04 |
| Doses | 3.44±1.04 | 6.06±0.96 | 0.05 |

**Table 5: Complications**

| Complications | Control group | Study group | P value |
|---|---|---|---|
| Uterine rupture | 0 | 0 | 0 |
| Heavy vaginal bleeding | 18% | 19% | 0.09 |
| Failed induction | 1o% | 2o% | 0.06 |

## DISCUSSION

According to WHO, the cesarean section (CS) rate is on the rise in both developed and developing countries. Mid-trimester miscarriage makes up 10 -15 % of all miscarriages. [6]

For termination of pregnancy, both medical and surgical methods are available. A lot of work has been done in the past 10 years on misoprostol use in miscarriages but its safety in previous C-sections in mid-trimester through the vaginal route needs further large trials for its safety to be proven. [7]

In this study, we compared the two groups, the success rate was 72% in the control group and 61% in the study group with the previous C-section.

Our results showed similar findings to the study by Ashraf and Gulec and his colleague which showed a high success with no significant rates of complications. [7,8] In contrast to this Iftikhar B et al. noted high rates of complications like abdominal pain, heavy uterine bleeding, and failure of induction rate in mid-trimester miscarriage terminations. [9] In a meta-analysis done by WUHL et al. concluded that termination of miscarriages in the second trimester is safe with misoprostol but in special cases like previous C-sections the doses can be altered for patient safety which is also recommended by FIGO. [10] The success rate of mid-trimester abortion with misoprostol decreases with an increase in the number of previous CS. A systemic review by Berghella et al. showed that termination in more than one CS decreases the success rate with the increase in complication rate whereas the success rate is high with the prior one CS. [11]

The decision for the mid-trimester abortion in patients with previous CS should be on a case-to-case basis, and careful monitoring should be done during such a procedure. Uterine rupture is a drastic complication of abortion in scar uterus, with an incidence of 0.4%, however, no comparative study is done to date to confirm this. [11] In our study, uterine rupture was not observed. Our findings were similar to Shah et al. in which no uterine rupture or other major complication was noted. [12] It has been suggested by many studies that low-dose misoprostol can be used in women with scarred uterus however case reports have been published in which silent ruptures had taken place in primigravida patients but in those cases, higher doses had been kept in. [13]

The period from administration to the expulsion of products was significantly different in both groups. The time period for the control group was 18 hours and for the study group with the previous scar was 36 hours which is attributed to half doses used in the scar group. This was comparable with studies done by Mauzani et al. [14] In another study done by Shah N, the expulsion time was reduced to 13 hours as doses were given frequently at 3 hours intervals. [15]

FIGO recommends adjusting misoprostol doses in cases with previous C section according to local protocols but in a systemic review by Andrikopaulaou M et al. when routine doses with misoprostol were given in cases of second-trimester miscarriages with previous scar there was no increase in uterine rupture and the incidence of uterine rupture remained 0.47% same as in cases with no scar. [16] Also, a study done by El Sharkwy IA revealed the safety of misoprostol in patients with more than one C-section. [17]

## CONCLUSION

Our results showed that the use of low-dose misoprostol is safe and effective in second-trimester miscarriages in patients with scarred uterus, taking double time to achieve success but is not associated with increased morbidity. This study will lead the way to further local research and protocols in patients with the scarred uterus in which previously low thresholds for hysterotomies were kept and hence were exposing the patients to further scars.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

**Sabir SA:** Concept, Critical appraisal, and Discussion Writing

**Sultan S:** Data collection, compilation of results, formatting of the article

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.