

ROLE OF PROGESTERONE IN THE TREATMENT OF THREATENED MISCARRIAGE IN FIRST TRIMESTER

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ABSTRACT

Objective: To compare the efficacy of oral with vaginal progesterone in the treatment of threatened miscarriage in first trimester.

Material and Methos: This study was conducted at Department of Obstetrics and Gynaecology, women and children teaching Hospital Bannu. Duration of the study was one year January 2016 to December 2016. Study design was randomized controlled trial. In this study 98(49 in each group) patients were observed by women with threatened miscarriage in their first trimester (up to 12 weeks) and age group 15-45 years were included. All women were subjected to detailed history and clinical examination. Women were randomly allocated in two groups by lottery method. Women in Group A was subjected to oral progesterone (10mg twice daily) while women in group B was subjected to vaginal progesterone (400mg per vaginal for one week). All women were followed till the end of 20th week of pregnancy to determine the efficacy of either procedure. Efficacy was determined in terms of absence of bleeding per vagina and pregnancy proceeding beyond 20 weeks of gestation. All information like age, address POG and efficacy were recorded on pre designed Performa.

Results: Our study shows in oral progesterone group, mean age was 31 years with SD \pm 3.88 while in vaginal progesterone group mean age was 30 years with SD \pm 3.12. More over oral progesterone was effective in 90% patients while vaginal progesterone was effective in 71% patients.

Conclusion: Our study concludes that oral progesterone was more effective than vaginal progesterone in preventing threatened miscarriages in first trimester. .

Key Words: Oral progesterone, vaginal progesterone, threatened miscarriages.

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INTRODUCTION

Threatened miscarriage is the most common complication of early pregnancy, occurring in approximately 20% of pregnant women before 20 weeks of gestation¹. Although many women who have threatened miscarriage go on to have a successful pregnancy, there is an increase in risk of miscarriage in the same pregnancy of 2.6 times and 17% of women with threatened miscarriage go on to have further complications in the same pregnancy². The risk factors for the progression of a normal pregnancy to a complete miscarriage in

the first trimester are fairly well established. Common risk factors include increased maternal age, high pre-pregnancy body mass index (BMI) and low serum progesterone levels³. More recently, lifestyle factors such as caffeine intake, exercise, stress, exposure to cigarette smoke, and alcohol consumption have also been implicated as risk factors⁴⁻⁶.

Currently, there are no standardized clinician friendly miscarriage risk assessment tools and no standard progesterone or Progesterone-Induced Blocking Factor (PIBF) cutoff levels accepted as "low risk"⁵. Progesterone is a critical hormone during implantation^{7,8}. It sustains decidualization, controls uterine contractility and promotes maternal immune tolerance to the fetal semi-allograft⁹. Risk of miscarriage is significantly higher among women with low serum progesterone¹⁰, although cutoff levels for predicting completed miscarriage vary from 512 to 516 ng/mL among studies¹¹.

Low serum progesterone levels may be the leading cause of threatened abortion^{12,13} and progres-

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terone supplements are the conventional treatment for threatened abortion¹⁴. Studies have shown that progesterone can promote muscle protein synthesis in utero¹⁵, improve sensitivity to prostaglandin and estrogen¹⁶ and has a significant role in the prevention of early contractions of the myometrium¹⁷. Owing to the documented physiological role of progesterone in maintaining pregnancy, it has been used to treat women with threatened miscarriage for over 30 years. The historical rationale was that a progesterone deficiency would lead to miscarriage^{18,19}. The therapeutic value of progesterone in preventing or treating threatened miscarriage has not well established yet²⁰.

The success rate of oral progesterone (10mg twice daily) in prolonging pregnancy beyond 20 weeks is reported as 84.9%, 56.67% and 87%. The success rate of vaginal progesterone suppository in the prolongation of pregnancy beyond 20 weeks is reported as 80%¹⁷.

The present study is designed to determine the efficacy of oral vs vaginal progesterone in the treatment of threatened miscarriage. The studies on comparison of these two modes of administration of progesterone are very limited in literature and as mentioned above, progesterone administration is of utmost importance when the pregnancy is threatened to cope with its deficiency. This study will provide us with local comparison of oral vs vaginal progesterone in the treatment of threatened miscarriage and the results of this study will be shared with other local obstetricians and the route found successful in this study will be recommended for routine administration of progesterone for treating threatened miscarriage.

OBJECTIVE

To compare the efficacy of oral with vaginal progesterone in the treatment of threatened miscarriage in first trimester.

MATERIAL AND METHODS

This study was conducted at Department of Obstetrics and Gynaecology, Women and Children Teaching Hospital, Bannu. Duration of the study was one year January 2016 to December 2016. Study design was randomized controlled trial. In this study 98 (49 in each group) patients were observed by using the WHO software for sample size determination in health studies making use of the formula for hypothesis test of two proportion (one sided) with the following assumption: significant level = 5%, Statistical power = 80%, Anticipated efficacy of oral progesterone = 56.67. Anticipated efficacy of vaginal progesterone = 80%. More over non probability (consecutive) sampling

technique was used for sample collection. Women with threatened miscarriage in their first trimester (up to 12 weeks) and age group 15-45 years were included. While women with history of trauma during pregnancy and women with bleeding disorders on history were excluded. After the approval from hospital ethical. All women meeting the selection criteria were included in the study through OPD or ER department. All women were subjected to detailed history and clinical examination. Women were randomly allocated in two groups by lottery method. Women in Group A was subjected to oral progesterone (10mg twice daily) while women in group B was subjected to vaginal progesterone (400mg per vaginal for one week). All women were followed till the end of 20th week of pregnancy to determine the efficacy of either procedure. Efficacy was determined in terms of absence of bleeding per vagina and pregnancy proceeding beyond 20 weeks of gestation. All above mentioned information including name, age efficacy were recorded on pre designed Performa. Care was taken during extraction of information from all women to avoid responder bias. Confounders and other bias were controlled by strictly following exclusion criteria. Data was analyzed using SPSS 20.0. Quantitative variables like age was described as mean \pm SD. Categorical variables like

Table 1: Efficacy of groups (n=98)

| Efficacy | Group A | Group B |
|---------------|----------|----------|
| Effective | 44(90%) | 35(71%) |
| Not effective | 5(10%) | 14(29%) |
| Total | 49(100%) | 49(100%) |

Group A: Oral progesterone (10mg twice daily)

Group B: Vaginal progesterone (400mg per vaginal for one week) Chi Square test was applied in which P value was 0.0214

Table 2: Stratification of efficacy with respect of age

| Age | Efficacy | Group A | Group B | P value |
|-------------|---------------|---------|---------|---------|
| 20-30 years | Effective | 27 | 15 | 0.039 |
| | Not effective | 2 | 6 | |
| Total | | 29 | 21 | |
| 31-40 years | Effective | 17 | 20 | 0.270 |
| | Not effective | 3 | 8 | |
| Total | | 20 | 28 | |

Group A: Oral progesterone (10mg twice daily)

Group B: Vaginal progesterone (400mg per vaginal for one week)

efficacy was described in terms of frequencies and percentages. Chi square test was used to compare the efficacy of two groups keeping p value of ≤ 0.05 as significant. Stratification was made in age to see the effect modifiers with respect to outcome variables. Data was presented in tables and diagrams where appropriate.

RESULTS

In this study a total of 98 women (49 in each group) were observed as in Group A (Oral progesterone) 29(59%) patients were in age range 15-30 years, 20(41%) patients were in age range 31-45 years. Mean age was 31 years with $SD \pm 3.88$. Where as in Group B (Vaginal progesterone) 21(43%) patients were in age range 15-30 years, 28(57%) patients were in age range 31-45 years, Mean age was 30 years with $SD \pm 3.12$. Efficacy was determined in terms of absence of bleeding per vagina and pregnancy proceeding beyond 20 weeks of gestation so Group A (Oral progesterone) was effective in 44(90%) patients and was not effective in 5(10%) patients. Where as Group B (Vaginal progesterone) was effective in 35(71%) patients and was not effective in 14(29%) patients. (Table 1). Stratification of efficacy with respect to age is given in Table 2.

DISCUSSION

According to the Royal College of Obstetricians and Gynaecologists (RCOG) Green-top Guideline No. 17, a miscarriage can be defined as the spontaneous loss of a pregnancy before the fetus has reached viability at 24 weeks. Recurrent miscarriage is defined as three or more consecutive miscarriages before age of viability. The World Health Organization recommends that in developing countries, where gestation is often uncertain, a birth weight of 500g should be used to define viability.

Our study shows oral progesterone was more effective than vaginal progesterone in preventing threatened miscarriages in first trimester. Our study also correlated with another study conducted by Uzma Gul in which oral progesterone was effective in 62% cases while vaginal progesterone was effective in 50% in term of improvement in vaginal bleeding in threatened miscarriages in first trimester¹⁴.

Similar results were observed in another study conducted by Yassaee F in which the success rate of oral progesterone (10mg twice daily) in prolonging pregnancy beyond 20 weeks is reported as 84.9%, 56.67% and 87%. The success rate of vaginal progesterone suppository in the prolongation of pregnancy beyond 20 weeks is reported as 80%¹⁷.

CONCLUSION

Our study concludes that oral progesterone was more effective than vaginal progesterone in preventing threatened miscarriages in first trimester.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Abrar S: Concept and Design, Acquisition of Data, final approval.

Abrar T: Critical review, drafting of manuscript and data analysis.

Tahir M: Drafting, final approval.

Sayyed E: Bibliography.

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.

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