

# Role of Progesterone in the Management of Threatened Miscarriage

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## ABSTRACT

**Objective:** To find out the efficacy of Progesterone in the management of threatened miscarriage.

**Study design:** A Quasi Experimental study.

**Duration & settings of study:** The study was conducted in the Department of Obstetrics & Gynaecology, Bahawal Victoria Hospital, Bahawalpur from 01-1-2010 to 31-12-2010.

**Materials & methods:** A Total of 60 patients admitted with threatened miscarriage at gestational age 5-14 weeks having viable pregnancy were studied. The diagnosis was made on history, examination and viability was confirmed on ultrasonography.

Patients were divided into two groups; A and B. Group-A was given Progesterone & Group-B was given no treatment, only the bed rest was advised to patients of Group B. It was observed whether the vaginal bleeding stopped, abdominal discomfort/pain settled and pregnancy continued to second trimester or not.

**Results:** Basic parameters such as age, BMI, gravidity and period of gestation at the start of treatment did not differ between the two groups. Vaginal bleeding settled in Group-A in 16 (53.33%) and in Group-B 12(40%) patients. Abdominal pain / discomfort settled in Group-A 15(50%) of the patients and in Group B 12(40%). The most important variable was persistence of pregnancy up to 2<sup>nd</sup> trimester. Group-A showed persistence of pregnancy up to 2<sup>nd</sup> trimester in 16(53.3%) and in Group-B 11(36.7%).

**Conclusion:** The use of progesterone in the management of threatened miscarriage improves the outcome to some extent but not significantly.

**Key words:** Threatened miscarriage, Progesterone, Vaginal bleeding, abdominal discomfort.

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## INTRODUCTION

Threatened abortion is a common occurrence that complicates at least a quarter (25%) of clinically diagnosed pregnancies<sup>1,2</sup>. Different types of miscarriage and early pregnancy failure along with ectopic pregnancy and gestational trophoblastic disease account for the bulk of early pregnancy problems<sup>1</sup>.

Miscarriage is associated with chromosomal abnormality of the conceptus in over 50% of cases<sup>3,4</sup>. Other risk factors for miscarriage include maternal age over 34 years<sup>5</sup>, maternal infection such as genital herpes simplex, human immunodeficiency virus-1 and vaginal colonization of group B streptococci<sup>6</sup>. Maternal endocrine abnormalities such as uncontrolled diabetes mellitus<sup>7</sup> and insufficient production of progesterone by the corpus luteum<sup>3</sup>, polycystic ovary syndrome, maternal autoimmune factors such as phospholipids antibodies, and a previous history of two or more miscarriages<sup>8</sup> are other suggested factors associated with miscarriage. In many cases, the cause of miscarriage cannot be identified in a large number of women

Miscarriage is associated with considerable physical and psychological morbidity. Bleeding can be excessive, leading to shock<sup>3</sup> and death, a known complication in developing countries but very rare in developed countries<sup>9,10</sup>. The emotional response to miscarriage can be profound; it includes depression, sleep disturbance, anger and marital disturbances<sup>3</sup>.

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<sup>3</sup>. The therapeutic value of progesterone in preventing or treating threatened miscarriage has not been well established yet<sup>11</sup>. But there are few studies which showed that corpus luteal support with dydrogesterone (progesterone) reduce the incidence of pregnancy loss in threatened abortion<sup>12</sup>. The importance of progesterone on the maintenance of pregnancy was demonstrated by the successful use of progesterone antagonists, such as mifepristone (RU 486) in the elective induction of abortion<sup>13</sup>. But there is no sufficient evidence to support the routine use of progestogens for the treatment of threatened miscarriage.

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Threatened miscarriage is a common health problem, and miscarriage can cause serious morbidity among childbearing women. Any treatment which might prove to be effective is worth investigation. Keeping in view this problem, we have conducted the current study which will help to find out the effectiveness of progesterone in threatened miscarriage

**MATERIALS & METHODS**

It was a quasi experimental study conducted in the department of Obstetrics & Gynecology unit-I at Bahawal Victoria Hospital Bahawalpur. The duration of study was one year from January 2010 to December 2010. A total of 60 patients with threatened miscarriage fulfilling inclusion/exclusion criteria were studied to determine the efficacy of progesterone in the management of threatened abortion. All patients (non hypertensive & non diabetic) admitted with threatened miscarriage at gestational age 5-14 weeks having viable pregnancy were included. The diagnosis was made on history, examination and viability was confirmed on ultrasonography.

A proforma was used to collect data from patients admitted in Gynecology Unit-I after taking verbal consent; patients were fully informed about the side effects of drugs. Patients were divided into two groups; A and B whereas age, parity and gestational age was matched so as to make two comparable groups. Group-A was given Progesterone (tab. Duphaston-10mg twice daily) till 14 weeks. Group-B was given no treatment only bed rest was advised.

It was observed whether the vaginal bleeding stopped, abdominal discomfort / pain settled and pregnancy continued to second trimester or not. The collected data was entered in SPSS version 10 for analysis. Frequencies were determined for the cessation of vaginal bleeding, settlement of abdominal pain and the number of patients reaching the second trimester in each group. Mean and S.D was calculated for gestational age. Tables were formed, percentages were calculated to know the statistical significance between two groups. Chi square test was applied to compare the outcome.

**RESULTS**

Majority of the patients (38%) belonged to age group between 31-35 years. Regarding comparison of gestational age, majority of the patients (65%) were found between 5-8 weeks of gestation. In Group-A, gestational age between 5-8 weeks was found in 19 (63.33%) and in Group-B, 20(66.67%) and the mean

gestational age in both groups was  $8.07 \pm 2.55$  and  $7.45 \pm 1.99$  respectively. (Table No. 1).

Among main variables of this study one was vaginal bleeding and comparison of this variable is shown in Table No. 2. In Group-A 16 (53.33%) and in Group-B 12 (40%) patients the bleeding settled. This shows no significant difference in both groups (P value=0.301).

Another outcome variable was abdominal discomfort / pain (Table No.3), it was also analyzed and chi-square test was applied which showed that in Group-A 15(50%) and in Group-B 12(40%) of the patients, the pain settled (P value =0.436).

Among other study variables, the most important variable was persistence of pregnancy up to 2<sup>nd</sup> trimester. In this study (Table No.4), Group-A showed persistence of pregnancy up to 2<sup>nd</sup> trimester in 16 (53.3%) and in Group-B 11(36.7%) which was statistically insignificant (P value = 0.194).

Table 1: A comparison in gestational age (before treatment) in both groups

Duration of gestation (weeks)	Group A (Progesterone)		Group B (No treatment)	
	n=	%age	n=	%age
5-8	19	63.33	20	66.67
9-11	08	26.67	09	30
12-14	03	10	01	3.33
Total	30	100	30	100
Mean/S.D	$8.17 \pm 2.48$		$7.80 \pm 1.97$	

P value = 0.977

Table 2: A comparison of per vaginal bleeding in both groups (after treatment)

Bleeding status	Group A (Progesterone)		Group B (No treatment)	
	n=	%age	n=	%age
Settled	16	53.3	12	40
Persisted	14	46.7	18	60

P value = 0.301

Table 3: A comparison of abdominal discomfort/ pain in both groups (after treatment)

Abdominal discomfort /pain	Group A (Progesterone)		Group B (No treatment)	
	n=	%age	n=	%age
Settled	15	50.	12	40
Persisted	15	50	18	60

P value = 0.436

Table 4: A comparison of pregnancy outcome in both groups (after treatment)

Pregnancy outcome	Group A (Progesterone)		Group B (No treatment)	
	n=	%age	n=	%age
Persisted	16	53.3	11	36.66
Aborted	14	46.66	19	63.33

P value = 0.194

## DISCUSSION

Miscarriage is pregnancy loss before 24 weeks' gestation based on the first day of the last menstrual period. Threatened miscarriage is manifested by vaginal bleeding, with or without abdominal pain, while the cervix is closed and the fetus is viable and inside the uterine cavity<sup>14</sup>.

Doctors often prescribe bed rest and progesterone for women with symptoms of threatened miscarriage. Progesterone's are a group of hormones, which bind to the progesterone receptors; they include both the natural female sex hormone and the synthetic forms. Progesterone is secreted during early pregnancy from the ovary by corpus luteum. The functional corpus luteum is essential for the implantation and maintenance of early pregnancy through the production of progesterone. In humans, increasing amounts of progesterone are produced during pregnancy. Initially, the source is the corpus luteum that has been "rescued" by the presence of human chorionic gonadotrophin (hCG) from the conceptus. However, after the 8th week production of progesterone shifts to the placenta. The placenta utilizes maternal cholesterol as the initial substrate, and most of the produced progesterone enters the maternal circulation.

In a retrospective study of 226 women who were hospitalized for threatened miscarriage, 16% of 146 women who were bed resting eventually miscarried, compared with a fifth of women who did not follow this option<sup>15</sup>.

Although progesterone has been prescribed for many years for the treatment of threatened miscarriage, a study conducted by Hayfaa A Wahabi and colleagues<sup>3</sup> concluded that there is no evidence to support the routine use of progesterones for the treatment of threatened miscarriage. Information regarding the potential harm to the mother or child, or both, with the use of progesterone in the treatment of threatened miscarriage is lacking.

In another prospective study no significant difference was found in the outcome in patients presented with threatened miscarriage who were prescribed dydrogesterone<sup>12</sup>. Our study is also in the view that whether the use of progesterone in threatened miscarriage improves the outcome or not.

In this study, the incidence of threatened miscarriage was higher in elderly age and increased body mass index in both groups which is comparable to international studies conducted by Everett C. Ashurst H, Chalmers I<sup>16</sup>.

The current study shows that body mass index in both groups was almost equal and the mean was 27.12±3.84. Gestational age was also similar in both

the studies with 8.17 and 7.80 weeks mean in both groups respectively. These results are also in agreement with the studies mentioned above<sup>3,12,16</sup>, where the mean gestational age was 7 weeks, which is very close to our findings.

The main outcome of this study was based on three variables i.e. per vaginal bleeding; abdominal pain and persistence of pregnancy up to 2<sup>nd</sup> trimester. Settlement of per vaginal bleeding in patients administered with progesterone alone was 53.33%) while in the patients who were not given progesterone it settled in 40% cases. Abdominal pain in Group-A was settled in 50% of the patients while 40% of the patients in Group-B got rid of it. Persistence of pregnancy up to 2<sup>nd</sup> trimester (>14 weeks) was the most important and considerable outcome which was 53.3% with progesterone while in group B 36.7%.The results of my study also show that there is no significant improvement observed by the use of progesterone in treatment of threatened miscarriage which are comparable to the other studies<sup>3,12,16</sup>.

## CONCLUSION

The use of progesterone in the management of threatened miscarriage improves the outcome to some extent but not significantly.

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