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**Original Research Article**

# Use of progestogens in pregnancy and its maternal and fetal outcome

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## ABSTRACT

**Background:** Progesterone is a crucial hormone in the establishment and maintenance of pregnancy. In early pregnancy, progesterone is produced by the corpus luteum and suppresses the maternal immune system, enabling the embryo's survival. Later in pregnancy, progesterone is produced by the placenta and plays a role in the relaxation of smooth muscle cells, ensuring myometrial quiescence until delivery.
**Methods:** A prospective randomized control trial was done on 100 pregnant women attending the OPD, after written informed consent from the patient, using SPSS software and satisfying the inclusion and exclusion criteria are taken and were grouped under A -Control group (50) in whom no treatment was given and B-Study group (50) in whom progesterone was given in the form of injection or tablet and followed up till delivery at Navodaya Medical College Research Centre, Raichur, India.
**Results:** There was statistically significant difference found between group A and B with respect to outcome of miscarriage and pre-term birth with p value 0.004 and 0.025 respectively. There was no statistically significant difference found between groups with respect to NICU admission/RDS.
**Conclusions:** The study concluded that progesterone is crucial for luteal phase support and maintaining pregnancy, reduces uterine contractility, thus preventing miscarriage, preterm birth and neonatal morbidity and mortality.

**Keywords:** Luteal phase support, Miscarriage, Neonatal morbidity and mortality, Preterm birth, Progesterone

## INTRODUCTION

Progesterone, rightly called the "pregnancy hormone", is crucial in the maintenance of pregnancy as it is involved in modulation of the maternal immune response, suppression of inflammatory response, reduction of uterine contractility, improvement of utero-placental circulation, and luteal-phase support.[1] Particularly in early pregnancy, progesterone is responsible for preparing the endometrium for implantation and maintenance of the gestational sac in the uterus.[2] Labor is triggered by increased production of prostaglandin by amnio-chorion-decidua and promoted by estrogen.[3] Progesterone counteracts this effect in several ways: adequate progesterone concentrations in myometrium inhibits prostaglandin stimulatory activity, decreases the concentration of myometrial oxytocin receptors and gap junctions.[4]

Progesterone is an endogenous 21-carbon steroid hormone synthesized from cholesterol by way of pregnenolone and is a major gonadal hormone synthetized in the corpus luteum of the ovaries and also by the placenta during pregnancy.[5] To a lesser extent, progesterone is also produced at much lower levels by the adrenal cortex, adipose and other tissues. It has a half-life of about 5 minutes and is metabolized mainly by the liver to pregnanediol, bound mostly to albumin in the blood stream.[6]

The anti-inflammatory effects of progesterone is appreciable. If there is sufficient progesterone, pregnancy

lymphocytes secrete the so called progesterone-induced-blocking factor (PIBF), a protein with inhibitory effects on cell-mediated immune reactions. It induces the suppression of T-cell reactions and inhibits NK cells.[7] Progesterone was shown to have a tocolytic effect in the myometrium. Adequate concentrations in the myometrium are able to counteract the stimulatory activity of prostaglandin and oxytocin.[8] It is also believed to act as an immunomodulatory agent via a specific locally produced protein (PIBF) in three ways: (1) by inducing a pregnancy-protective shift from pro-inflammatory Th1 cell-dependent cytokines, (2) by suppressing NK-cell activity in the pregnant uterus, and (3) by increasing the synthesis of asymmetric, anti-abortive antibodies.[9] It facilitates blastocyst nesting and is essential in the maintenance of pregnancy, through progesterone intracellular receptors it stabilizes endometrial activity.[10]

Progesterone treatment reduces the incidence of composite neonatal morbidity and mortality, low birth weight, respiratory distress syndrome, admission to neonatal intensive care unit, and requirement for mechanical ventilation, and has no effect on the incidence of adverse maternal events or on congenital abnormalities.[11]

## METHODS

### *Study site*

This study was conducted at Navodaya Medical College Research Centre, Raichur.

### *Study design*

This was a prospective randomized controlled trial.

### *Study period*

This study conducted for 12 months (From January 2023 to December 2023). Total 100 patients were included.

### *Inclusion criteria*

Women were eligible for enrollment in the trial were women confirmed with pregnancy and intrauterine cardiac pole or gestational sac visible on USG. Presented with vaginal bleeding/PV spotting and pain abdomen. Pregnant women with history of abortions. Pregnant women with previous history of pre term delivery. Pregnant women between 25 weeks to 34 weeks period of gestation complaining of pain abdomen or having >/= 2 contractions in 10 minutes

### *Exclusion criteria*

Participants were excluded if at the time of presentation the fetal crown-rump length was 7 mm or longer with no visible heartbeat. Gestational sac was a mean of 25 mm or greater in diameter with no visible fetal pole on ultrasonography or blighted ovum. Had evidence of ectopic pregnancy; if they had life-threatening bleeding. Had contraindications to progesterone therapy (i.e., a history of liver tumors; current genital or breast cancer, severe arterial disease, or acute porphyria; or a history during pregnancy of idiopathic jaundice, severe pruritus, or pemphigoid gestations).

Thorough history taking, general and obstetric examination, routine investigations were done on 100 women who fit into inclusion criteria and were grouped under,

Group A - 50 patients as Control group who didn't receive any treatment. Group B - 50 patients as Study group who received progesterone treatment in the form of injection or tablets.

Out of 50 patients in both the groups, 30 patients had high risk for abortion or had threatened abortion, and 20 patients had risk for preterm labour.

50 patients in Group A (Control) received a placebo. In Group B (Study group), out of 50 patients, 30 patients with per vaginal spotting, pain abdomen in early weeks and previous history of miscarriages received Injection maintane 500mg IM weekly till NT scan was done followed by tablet duphaston 10mg twice daily orally till 36 weeks POG and were followed up regularly with serial scans. 20 patients with pain abdomen and previous history of preterm birth received progesterone in the form of tablets i.e. Tablet susten 200mg twice daily orally from 13weeks till 36 weeks of pregnancy and regular follow-up, steroid coverage for fetal lung maturity and monitoring for uterine contractions and pain abdomen was done.

### *Statistical analysis*

Both the group outcomes were compared and analysed by SPSS software.

## RESULTS

P value 0.004, there was statistically significant difference found between Control and study groups with respect to outcome. Only 33.3%patients continued pregnancy in Group A (Control group) when compared to 70% in Group B (Study group (Table 1).

**Table 1: Distribution of subjects those who had H/o miscarriage/ threatened abortion, PV spotting in 1st trimester according to outcome among Group A (Control-30) and Group B (Study group-30).**

| | Group A/ Control group (30) | | Group B/ Study group (30) | |
|---|---|---|---|---|
| | N | % | N | % |
| **Spontaneous miscarriag** | 20 | 66.7 | 9 | 30 |
| **Continued pregnancy** | 10 | 33.3 | 21 | 70 |

P value 0.025, there was statistically significant difference found between groups with respect to outcome. Only 25% patients had term delivery in Group A (Control)when compared to 60% in group B (Study group) (Table 2).

**Table 2: Distribution of subjects those who had c/o pain abdomen, H/o preterm delivery according to outcome among group A (Control-20) and group B (Study-20).**

| | Group A/Control group (20) | | Group B/Study group (20) | |
|---|---|---|---|---|
| | N | % | N | % |
| **Preterm delivery** | 15 | 75 | 8 | 40 |
| **Term delivery** | 5 | 25 | 12 | 60 |

P value 0.074, there was no statistically significant difference found between groups with respect to NICU admission /RDS in the neonates (Table 3).

**Table 3: Distribution of subjects according to NICU admission/RDS among the neonates in Control and study groups (50 each).**

| | Group A/Control group (50) | | Group B/Study group 50) | |
|---|---|---|---|---|
| | N | % | N | % |
| **NO NICU admission** | 37 | 74 | 44 | 88 |
| **NICU admission** | 13 | 26 | 6 | 12 |

## DISCUSSION

Progesterone is an essential hormone in the process of reproduction. In early pregnancy, before the placenta starts to produce progesterone, corpus luteum production is vital for the survival of the fetus. Luteal phase defect is associated with both implantation failure and miscarriage.[12]

Table 1 shows the outcome of pregnancies with h/o PV bleeding/spotting in early weeks and previous history of miscarriages in treatment group and placebo group where p value (0.004) is significant showing progesterone supplementation is useful to prevent miscarriages. Out of 30 patients only 10 (33.3%) continued pregnancy in placebo group whereas 21 patients (70%) continued pregnancy in treatment group.

In a study by El-Zibdeh and Yousef, 146 women presenting with mild-to-moderate vaginal bleeding during the first trimester were randomized to 10 mg oral dydrogesterone twice daily (n = 86) or no treatment (n = 60). The incidence of miscarriage was found to be 17.5% with dydrogesterone versus 25% with no treatment ($p<0.05$).[13]

Progesterone has been shown to exert a tocolytic effect on the myometrium during pregnancy. It has been shown to be concentration dependent; only high doses of progesterone exert a tocolytic effect in early pregnancy, with optimal dosage ranging from 100 to 200 mg/day depending upon maternal weight.[14]

Table 2 denotes preterm birth occurred in 40% cases of the progesterone group compared with 75% in placebo group ($p<0.025$).

Cetingoz et al reported similarly positive results from a study in 150 Turkish women with high-risk pregnancies (prior spontaneous preterm birth, twin pregnancy, uterine malformation) randomized to micronized progesterone prophylaxis (100mg/day) or placebo. Preterm labor occurred in 25.0% of women in the progesterone group compared with 45.7% in the placebo group ($p<0.05$).[15]

Table 3 shows NICU admissions and RDS occurred in 12% of the progesterone group neonates as compared to 26% in the placebo group. The meta-analysis by Romero et al supported earlier findings that progesterone treatment reduces the incidence of composite neonatal morbidity and mortality, low birth weight, respiratory distress syndrome, admission to neonatal intensive care unit, and requirement for mechanical ventilation. The authors also confirmed that progesterone treatment has no effect on the incidence of adverse maternal events or on congenital abnormalities.[16]

Limitation of this study was that progesterone cannot be used if the pregnancy is extrauterine.

## CONCLUSION

The study concluded that progesterone is crucial for luteal phase support and maintaining pregnancy before placental development by creating a favorable environment, thus preventing miscarriage. It increases uterine blood flow and reduces uterine contractility, preventing preterm birth. Progesterone is a safe drug that can be used until the third trimester to maintain pregnancy and prevent complications of pregnancy. Progesterone treatment reduces the incidence of composite neonatal morbidity and mortality, low birth weight, respiratory distress syndrome, admission to neonatal intensive care unit, and requirement for mechanical ventilation in neonates.

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