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Original Research Article

## Role of oral micronized progesterone versus vaginal progesterone for prevention of preterm labour

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### ABSTRACT

**Background:** Preterm birth remains a significant problem in obstetric care, affecting women and babies world-wide. Progesterone has an essential role in maintaining pregnancy by suppression of the calcium-calmodulin-myosin light chain kinase system. This study reflects the use of progesterone in preventing preterm birth.

**Methods:** The data were collected as a retrospective study from SAMC and PGI Obstetric and Gynaecology Department.

**Results:** With the use of Oral micronized progesterone out of 15 cases, term delivery 9 cases i.e. 60% and preterm delivery 6 cases i.e. 40% and, with the use of vaginal progesterone suppository out of 15 cases, term delivery 11 cases i.e. 73.3%, preterm delivery only 4 cases i.e. 26.7%.

**Conclusions:** Progesterone appears to be safe and efficacious in reducing the risk of preterm birth as well as NICU admissions, and neonatal morbidity and mortality in high risk patients. However, there is limited information available relating to longer-term infant and childhood outcomes, the assessment of which remains a priority. Further, trials are required to assess the optimal timing, mode of administration and dose of administration of progesterone therapy when given to women considered to be at increased risk of early birth.

**Keywords:** NICU, Preterm birth, Preterm delivery, Progesterone, Vaginal progesterone

### INTRODUCTION

Preterm labour is the onset of regular uterine contractions associated with progressive cervical change between viability and 37 completed weeks of gestation.<sup>1</sup> The countries with the highest annual number of preterm births are India (3.52 million), China (1.17 million), Nigeria (773,600), Pakistan (748,100), Indonesia (675,700), and the United States (517,400).<sup>2</sup>

Preterm delivery (PTD) is due to either spontaneous preterm labor (PTL) (40%-50%), spontaneous preterm premature rupture of membranes (PPROM) (25%-40%), or obstetrically indicated PTD (20%-25%) as a result of maternal, placental or fetal complications (preeclampsia,

renal disease, diabetes mellitus with vasculopathy, placenta previa or abruptio, and fetal growth restriction.<sup>3</sup>

The generally accepted pathways of spontaneous PTB include:

- Premature activation of the fetal hypothalamic-pituitary axis,
- Infection/inflammation,
- Decidual hemorrhage or ischemia,
- Uterine overdistention, as it occurs with polyhydramnios or multiple gestations. Each of these underlying causes can initiate the cascade of events that ultimately leads to uterine activity and cervical dilation.<sup>4</sup>

Infants born preterm are over 40 times more likely to die during the neonatal period than are term infants.<sup>5,6</sup> While the risk is greatest for infants born at earlier gestational ages, this increased risk of mortality persists even for infants born between 32 and 36 weeks gestation.<sup>7</sup> For surviving infants, there are significant health implications, particularly in relation to immature lung development, with respiratory distress syndrome being a major consequence of preterm birth and the most significant cause of early neonatal mortality and morbidity.<sup>8</sup> well-documented health complications include intraventricular hemorrhage and periventricular leukomalacia, with implications for ongoing cerebral dysfunction infectious morbidity, and specific neonatal conditions associated with prematurity, including retinopathy of prematurity and necrotising enterocolitis. Infants continue to be at increased risk of hospitalization in the first year of life.<sup>9</sup>

Progesterone has an essential role in maintaining pregnancy by suppression of the calcium-calmodulin-myosin light chain kinase system.<sup>10</sup> Thus, primarily through establishing uterine quiescence. Additionally, progesterone has recognized anti-inflammatory properties, raising a possible link between inflammatory processes, alterations in progesterone receptor expression and the onset of preterm labor.<sup>11</sup>

The objectives of the study were

- This study aims to differentiate between effectiveness of oral and vaginal progesterone in cases of preterm labour.
- To study whether use of progesterone is mandatory in cases of preterm birth setting.

## METHODS

It is a retrospective study, conducted in the Shri Aurobindo medical college and PGI at obstetrics and gynaecology department 30 patients were selected which are at high risk for preterm labor and were given progesterone support from 1st trimester. 15 patients were treated with oral micronized progesterone and the rest 15 were treated with Vaginal Suppositories.

### Inclusion criteria

preterm labour upto 37 weeks of gestation, Cardiac Activity present in recent scan, previous H/o preterm labor, previous H/O abortions, and patients having H/o of infection in present pregnancy, H/o multiple gestation in present pregnancy.

### Exclusion criteria

IUFD, low lying placenta, coagulation disorders, uterine anomalies.

## Statistical analysis

Data was analyzed using Statistical Software Minitab Version 17.0 for Windows. Chi Square test was used to take out the p value. Value less than 0.05 was considered significant.

## RESULTS

With the use of Oral micronized p out of 15 cases, term delivery 9 cases i.e. 60% and preterm delivery 6 cases i.e. 40% and, with the use of vaginal progesterone suppository out of 15 cases, term delivery 11 cases i.e.73.3%, preterm delivery only 4 cases i.e. 26.7%

**Table 1: Oral micronized progesterone use.**

| Oral micronized progesterone use | No. of cases | Percent |
|----------------------------------|--------------|---------|
| Term                             | 9            | 60      |
| Preterm                          | 6            | 40      |

**Table 2: vaginal progesterone use.**

| Vaginal progesterone use | No. of cases | Percent |
|--------------------------|--------------|---------|
| Term                     | 11           | 73.3    |
| Preterm                  | 4            | 2.7     |

## DISCUSSION

In our present study with the use of vaginal progesterone suppository 26.7% had preterm delivery, our study is supported by the study of Eduardo B. da Fonseca et al 2003 out of 72 patients given progesterone 21% has preterm delivery, more women were delivered before 34 weeks in the placebo group (18.5%) than in the progesterone group (2.7%) (P <.05).<sup>12</sup>

Roberta Mackenzie initiated a randomized control trial which suggested that Progestational agents, initiated in the second trimester of pregnancy, may reduce the risk of delivery less than 37 weeks' gestation.<sup>13</sup>

SuLL et al conducted Eight studies which reviewed, involving 563 women, but only seven studies, involving 538 women, contributed data for analyses. There are some data suggesting that the use of progestational agents results in a reduction of preterm deliveries at less than 37 weeks of gestation and an increase in birthweight. The use of a progestational agent may also reduce the frequency of uterine contractions, prolong pregnancy and attenuate the shortening of cervical length.<sup>14</sup>

Dodd JM et al Thirty-six randomised controlled trials (8523 women and 12,515 infants) were included. Progesterone versus placebo for women with a past history of spontaneous preterm birth Progesterone was associated with a statistically significant reduction in the risk of perinatal mortality. Progesterone versus no

treatment/placebo for women following presentation with threatened preterm labour Progesterone, was associated with a statistically significant reduction in the risk of infant birthweight less than 2500 g (one study; 70 infants; RR 0.52, 95% CI 0.28 to 0.98). Progesterone versus placebo for women with 'other' risk factors for preterm birth Progesterone, was associated with a statistically significant reduction in the risk of infant birthweight less than 2500 g (three studies; 482 infants; RR 0.48, 95% CI 0.25 to 0.91).<sup>15</sup>

Rai P et al preterm birth occurred in 29 (39.2%) women in the oral micronized progesterone group (n=74) compared with 44 (59.5%) in the control group (n=74, P=0.002). Mean gestational age at delivery was higher in the Oral micronized progesterone group (36.1 vs 34.0 weeks, P <0.001). Fewer preterm births occurred between 28 and 31 weeks plus 6 days in the oral micronized progesterone group (RR 0.20; 95% CI, 0.05-0.73, P <0.001).<sup>16</sup>

## CONCLUSION

Preterm birth remains a significant problem in obstetric care, affecting women and babies world-wide. Progesterone appears to be safe and efficacious in reducing the risk of preterm birth as well as NICU admissions, and neonatal morbidity and mortality in high risk patients. However, there is limited information available relating to longer-term infant and childhood outcomes, the assessment of which remains a priority. Further, trials are required to assess the optimal timing, mode of administration and dose of administration of progesterone therapy when given to women considered to be at increased risk of early birth.

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