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# A comparative Study Of Oral 400 mg Natural Micronized Progesterone (OMP)Verses Vaginal 400 Mg Natural Micronized Progesterone (VMP) in Threatened Preterm Labour And Perinatal Neonatal Outcomes

**Dr. Hemant Gopal Krishna Deshpande[1], Radhika Ashok Dhedia[*2], Shriraj Katakdhond[*3]**

[1]HOD, Department of Obstetrics and Gynecology, Dr D.Y Patil Medical College Hospital and Research Centre, Pune, Maharashtra, India

Email ID: drhemantdeshpande@gmail.com

***Corresponding Author:**

[*2]Junior Resident, Department of Obstetrics and Gynecology, Dr D.Y Patil Medical College Hospital and Research Centre Pune, Maharashtra India.

Email ID: radhika.dhedia@gmail.com

[*3]Associate professor, Department of Obstetrics and Gynecology, Dr D.Y Patil Medical College Hospital and Research Centre, Pune Maharashtra India.

Email ID: drshrirajsk@gmail.com

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**ABSTRACT**

Preterm deliveries significantly contribute to neonatal mortalities and morbidities in children under the age of five. Progesterone, Tocolytics and steroid usage have been found to decrease the incidence of threatened preterm and neonatal mortality and morbidity. A prospective study was done to compare oral 400 mg natural micronized progesterone to vaginal 400 mg natural micronized progesterone and it was found that patients on OMP presented in labour earlier than patients on VMP i.e. the VMP group ended up in more term pregnancies.81.42% neonates of VMP were found to be asymptomatic as compared to smaller 72.85% neonates of OMP. Incidence of neonatal morbidity such as asphyxia was also found to be lesser in VMP as compared to OMP (10% vs 5.71%). NICU admission (4.28% vs 11.42%) was found higher in OMP group. Pertaining to the fact vaginal progesterone bypasses the first-pass metabolism, which explains its superior effectiveness in preventing preterm labour.

***Keywords:*** *Preterm labour, oral micronized progesterone, vaginal micronized progesterone, neonatal morbidity*

## 1. INTRODUCTION

Preterm birth, defined as delivery before 37 weeks or 259 days of gestation, occurs in 9 to 12 percent of pregnancies globally and is the leading cause of newborn morbidity and mortality [1]. Around 40 to 45 percent of preterm births result from preterm labour, while another 25 to 30 percent are due to preterm prelabour rupture of membranes (PPROM) [2]. Despite efforts with prophylactic and therapeutic tocolytic medications, preventing preterm birth has largely been unsuccessful. As an intention for “Prevention is better than cure” alternative strategies, including progesterone supplementation, have been explored.

In 2020, globally an estimated 13.4 million babies were born prematurely, accounting for more than 1 in 10 births. In 2019, approximately 900,000 children lost their lives due to complications related to preterm birth.[3]

As per State/ UT report under Health Management Information System for the period of 2022-23, 4.1% Pre term (< 37 weeks of pregnancy) births happened in the country. As per Cause of Death Statistics 2017-19 released by Office of the Registrar General & Census Commissioner, India; Prematurity & low birth weight is one of the leading causes of newborn mortality in India.[4]

Prematurity is the leading cause of death in children under 5 worldwide, with stark survival disparities. In low-income regions, half of babies born at 32 weeks or earlier die due to limited care, while nearly all survive in high-income countries. Middle-income settings face increased disability among surviving preterm infants.[9]

In case of High Risk factors such as shortened cervix (<15mm) some studies have showed to decrease spontaneous birth before 34 weeks of gestation.[11,12,13]

**AIM**

A comparative study of oral 400 mg natural micronized progesterone verses vaginal 400 mg natural micronized progesterone in threatened preterm labour and perinatal neonatal outcomes.

## 2. MATERIALS AND METHODS

A prospective, randomized study was conducted with 140 patients who were randomly divided into two groups receiving oral 400 mg natural micronized progesterone and vaginal 400 mg natural micronized progesterone at 10 pm[16], for 12 months, who fulfilled the inclusion criteria.

Patients were advised to take oral micronized progesterone with food as its absorption then increased 2 fold[15].

With ethical committee approval and patient consent, data were collected from women presenting with abdominal pain, uterine contractions, and cervical length under 25 mm, indicative of preterm labour (PTL). Patients were randomized into two groups (one group receiving oral progesterone and other getting vaginal progesterone) and followed biweekly for PTL detection. Pregnancies continuing beyond 36 weeks were evaluated for delivery intervention. Neonatal outcomes, including NICU admissions, were recorded for both groups. Statistical analysis was performed using unpaired t-tests, Fisher's exact test, Student's t-test, and Chi-Square test, with significance defined by a p-value < 0.05. Results were presented graphically where appropriate.

**INCLUSION CRITERIA**

1. Age: 18 to 45 years
2. Gestational age between >24 week and 1 day to <36 weeks and 6 days
3. Multiple gestations
4. Polyhydramnios
5. Past history of PTL or abortions
6. Clinical diabetes or Gestational diabetes or hypertension
7. Obese or undernourished

**EXCLUSION CRITERIA FACTORS**

1. Antepartum haemorrhage or risk of APH (such as placenta previa)
2. Foetal congenital anomalies
3. Diagnosed clotting disorders
4. Uterine anomalies

## 3. RESULTS

- **DEMOGRAPHY**

**Table 1: Demography**

| Sr No. | | OMP | | VMP | | p value | significance |
|---|---|---|---|---|---|---|---|
| | | N | % | N | % | | |
| 1.Age | 18-24 years | 14 | 20% | 16 | 22.85% | | |
| | 25-30 years | 47 | 67.4% | 50 | 71.4% | <0.05 | + |
| | 31-45 years | 11 | 15.71% | 4 | 5.71% | | |
| 2.Gestational age for usage | 24-28 Weeks | 6 | 8.57% | 2 | 2.85% | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | 29-32 Weeks | 51 | 72.85% | 11 | 15.71% | <0.05 | + |
| | 33-36 Weeks | 13 | 18.57% | 57 | 81.42% | <0.05 | + |
| 3.Smoking | Non smoker | 33 | 47.14% | 34 | 48.57% | | |
| | Smoker | 37 | 52.85% | 36 | 51.42% | | |
| 4.Parity | Primigravida | 27 | 38.57% | 28 | 40.00% | | |
| | Multigravida | 31 | 44.28% | 32 | 45.71% | | |
| | Grand multipara | 12 | 17.14% | 10 | 14.28% | | |
| 5.Mode of delivery | Vaginal | 52 | 74.28% | 56 | 80.00% | | |
| | Caesarean | 18 | 25.71% | 14 | 20.00% | | |

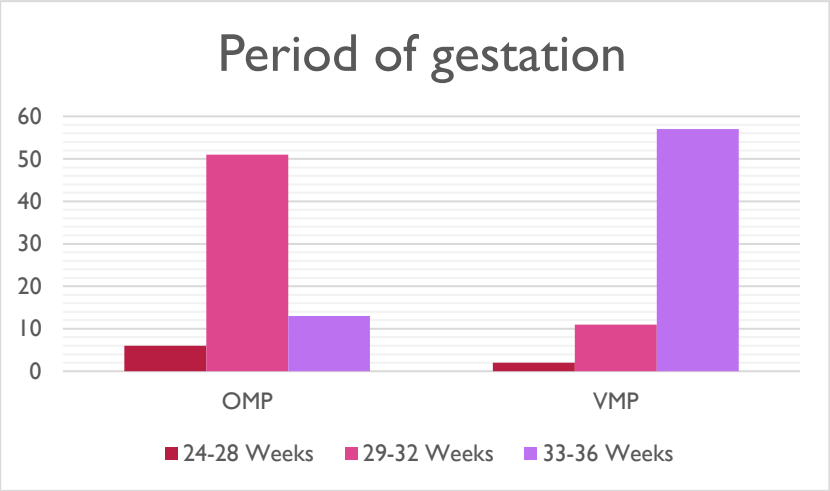



**Fig 1: The distribution of patients by gestational age highlights a higher prevalence of OMP use in earlier gestational stages compared to VMP**

- **BASED ON PERINATAL OUTCOMES**

**Table 2: Perinatal neonatal outcomes statistics**

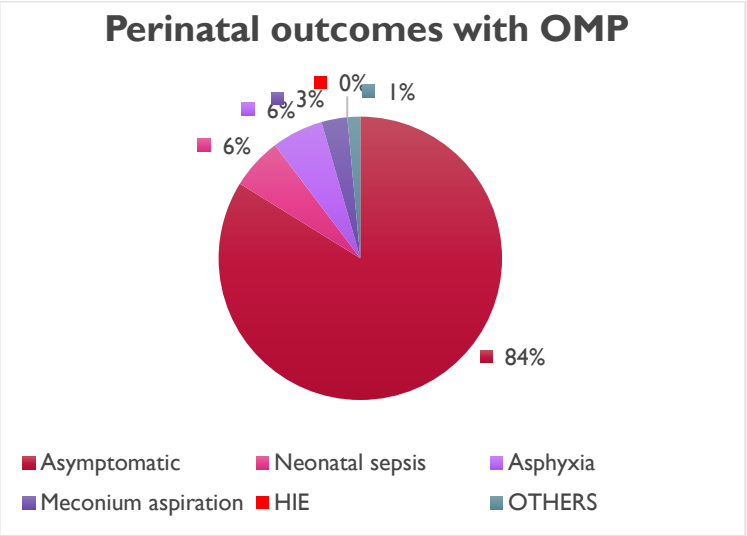
| **Perinatal outcome** | **OMP** | | **VMP** | | **P value** | **Significance** |
|---|---|---|---|---|---|---|
| | N | % | N | % | | |
| Asymptomatic | 51 | 72.85% | 57 | 81.42% | <0.05 | + |
| Neonatal sepsis | 4 | 5.71% | 4 | 5.71% | >0.05 | - |
| Asphyxia | 7 | 10% | 4 | 5.71% | <0.05 | + |
| Meconium aspiration | 4 | 5.71% | 2 | 2.86% | >0.05 | - |
| HIE | 1 | 1.43% | 0 | 0% | >0.05 | - |
| Others | 3 | 4.29% | 3 | 4.29% | >0.05 | - |

There is a statistically significant difference (P value <0.05) in the rates of asymptomatic outcomes and asphyxia between the OMP and VMP groups, with VMP having higher rates of asymptomatic outcomes and OMP having higher rates of asphyxia.

There is no statistically significant difference (P value >0.05) between the OMP and VMP groups for neonatal sepsis,

meconium aspiration, HIE, and other outcomes.

**Fig 2: Perinatal neonatal outcomes statistics with vaginal and oral micronized progesterone**



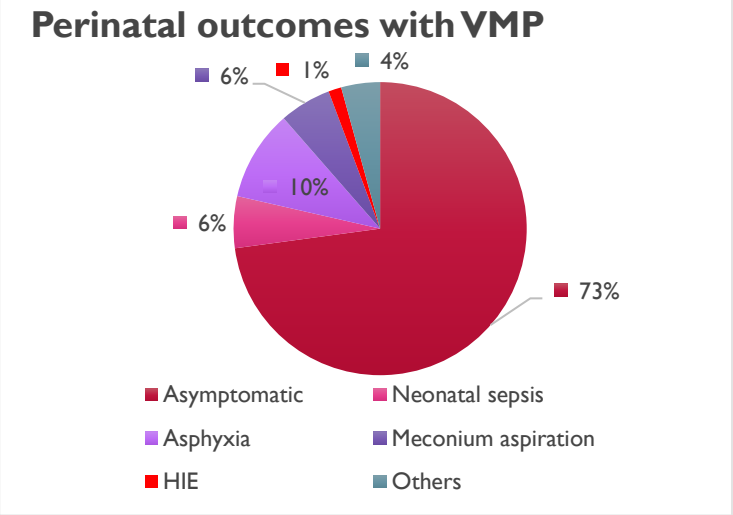




**Table 3: NICU admission with different routes of progesterone**

| Requirement of NICU | | | | |
|---|---|---|---|---|
| | OMP | | VMP | |
| | N | % | N | % |
| YES | 8 | 11.42% | 3 | 4.28% |
| NO | 62 | 88.57% | 67 | 95.71% |

In essence, the majority of babies in both OMP and VMP categories did not require NICU. However, a slightly higher percentage of babies in the OMP group required NICU compared to the VMP group (11.42% vs 4.28%).

We also observed that average duration of NICU stay of neonates of OMP patient was 5.30 days whereas VMP was 2.30 days.

**Table 4: Duration of pregnancy statistics with vaginal and oral micronized progesterone**

| Duration of delivery | | | | |
|---|---|---|---|---|
| | OMP | | VMP | |
| | N | % | N | % |
| <32 weeks | 9 | 12.85% | 5 | 7.14% |
| 32-weeks to 37weeks | 12 | 17.14% | 8 | 11.42% |
| >37 weeks | 48 | 68.57% | 57 | 81.42% |

## 4. DISCUSSION

As seen in our study, a significant proportion of patients in the OMP group (67.4%) and the VMP group (71.4%) fell within the age range of 25-30 years. The average age for patients in the OMP group was 27.12 ± 5.04 years, while in the VMP group, it was slightly higher at 28.02 ± 5.09 years. This age demographic was found to be similar with the findings of Mostafa AH [5] and Deshpande H et al. [6]. In studies by Mostafa AH [5] and Deshpande H et al. [6], mean ages for oral (28.7 ± 7.2) and vaginal (28.1 ± 8) groups, and progesterone (28 ± 4.3) and placebo (28.2 ± 4.5) respectively with study groups showing no significant differences.

In our study, 81.4% of neonates in the VMP group were asymptomatic at birth, compared to 72.85% in the OMP group. Incidence rates for meconium aspiration syndrome (2.86% vs. 5.71%), neonatal sepsis (5.71% vs. 5.71%), and hypoxemic ischaemic encephalopathy (0% vs. 1.43%) were similar in both groups. However, the OMP group had a significantly higher birth asphyxia incidence (10% vs. 5.71%; $p<0.05$).

The study indicated that 12.85% of the OMP group delivered very preterm (<32 weeks) compared to 7.14% in the VMP group. Additionally, 17.14% of the OMP group delivered preterm (32-36 weeks) compared to 11.42% in the VMP group. Lastly, 68.57% of the OMP group delivered at term compared to 81.42% in the VMP group. Similarly, Srisutham K *et al*. [7] 3-arm randomized control trial showed significantly different preterm delivery rates before 32 weeks: 16.0% (control), 12.0% (oral progesterone), 5.2% (vaginal progesterone), highlighting vaginal progesterone's effectiveness in prevention.

In our study, NICU admission was required for 11.42% of neonates in the OMP group and 4.28% in the VMP group. The mean NICU stay was significantly longer in the OMP group (5.30 days) compared to the VMP group (2.30 days; $p<0.05$). Boelig RC et al. meta-analysis revealed that oral progesterone is associated with a lower rate of perinatal death (5% vs. 17%), fewer NICU admissions, reduced respiratory distress syndrome, and higher birth weight (mean difference of 435.06 g)[8].

Similar to studies of Cheung KW *et al*. compliance of OMP was better as compared to VMP which indeed said that compliance to VMP was suboptimal [10]. Probable reasons for lower compliance of VMP are-needs privacy, clean hands, restricted mobility post application, particularity in respect to deep deposition of the drug, post application irritation. Micronized preparations have known to cause less GI symptoms [16].

Around 20-30% of deliveries occur due to PPROM, there are no studies to support usage of progesterone in present pregnancy but some studies have shown progesterone to be effective in pregnancies having past history of PPROM [14].

Similar to Hemant G *et al*. [16] study of efficacy based on time of administration of progesterone we observed there were no sedative effects of both OMP and VMP.

## 5. CONCLUSION

Our study found that VMP resulted in fewer perinatal neonatal morbidities, lower neonatal mortality, and more term births. In contrast, OMP was superior in compliance due to easier administration and no mobility restrictions. Despite these differences, both methods were equally effective in managing preterm labour.

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