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# To Study the Comparison between Oral Dydrogesterone and Micronized Progesterone in Threatened Miscarriage in Terms of Pain Lower Abdomen and Bleeding Per Vaginum

Shweta Verma[1], Poonam Yadav[2]

[1]Senior Resident, Department of Obst & Gynae, RML, Delhi.

[2]Consultant, Department of Gynaecologist, Santokbha Durlabhji Memorial Hospital, Jaipur.

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**ABSTRACT**

**Background:** The present study was conducted to compare between oral dydrogesterone and micronized progesterone in threatened miscarriage in terms of pain lower abdomen and bleeding per vaginum. **Methods:** All patients were divided randomly into two groups and each containing 63 patients. Patients in Group A were given oral dydrogesterone 10 mg twice daily. Group B was given oral micronized progesterone 200 mg twice daily. Treatment continued till 12th week of pregnancy. **Results:** Growth restricted babies were 4.76% and normal weight babies were 95.24% in women who have received oral dydrogesterone and 19.05% and 80.95% in women who have received oral micronised progesterone. Patients who presented to hospital at 6-8 weeks of bleeding, had 1 abortion (2.78%) at 8-10 weeks had 1 (5%) while at 10-12 weeks had 1 (14.29%) with oral dydrogesterone. With oral micronised progesterone at 6-8 weeks patients had 6 (22.22%), at 8-10 weeks 4(16.67%) while at 10-12 weeks had 3 (25%) abortions. **Conclusion:** The dydrogesterone reduce pain in lower abdomen and bleeding per vaginum more in comparison to micronized progesterone.

***Keywords:*** Dydrogesterone, bleeding per vaginum, Abortion



## INTRODUCTION

Abortion is defined as the expulsion or extraction from its mother of an embryo or fetus weighing 500 gm or less when it is not capable of independent survival. Abortion is a common incident and it occurs in 10% to 15% of all clinically recognized pregnancies.[1] Threatened miscarriage is defined as bleeding of intrauterine origin occurring before 20th completed week, with or without uterine contractions, without dilatation of the cervix and without expulsion of the products of conception.[2] Threatened miscarriage has been reported to be present in 20% to 25% of pregnant women. The symptom of a threatened miscarriage is vaginal bleeding and pain in lower abdomen. Vaginal bleeding can vary from light spotting or brownish discharge to heavy bleeding. Pain can be diffuse to colicky in nature.[3]

Despite numerous theories, there remain a large number of miscarriage cases in which an exact cause cannot be identified.[4] Ultrasonography and histological investigations from cases of spontaneous miscarriages show that 70% is related to a defective ovum or fetus, the most common cause being chromosomal abnormalities.[5]

**Name & Address of Corresponding Author**
Dr. Shweta Verma
Senior Resident,
Department of Obst & Gynae,
RML, Delhi.

Progesterone is a female sex hormone which is essential in the maintenance of pregnancy. Progesterone is produced from the ovary (by the corpus luteum after ovulation.[6] While the corpus luteum continues progesterone synthesis up to the 10th week of gestation, the placenta concurrently begins to synthesize progesterone and by the 12th week, enough progesterone is produced to replace the corpus luteum source. Progesterone is responsible for multiple functions in the pregnancy and the insufficiency of progesterone during the luteal phase of the menstrual cycle and during early pregnancy is thought to be one of the many causes of miscarriage.[7]

Progesterone has very poor pharmacokinetics) when taken orally unless micronized. Dydrogesterone has selective progestational activity and does not inhibit ovulation.[8] The greater rigidity of dydrogesterone also positively affects its selectivity while natural progesterone is less selective.9 The present study was conducted to compare between oral dydrogesterone and micronized progesterone in threatened miscarriage in terms of pain lower abdomen and bleeding per vaginum.

## MATERIALS & METHODS

This study was carried out in the deparment of Obstetrics and Gynaecology at SDMH (Santokbha Durlabhji Memorial Hospital) Jaipur, Rajasthan, India after taking due approval from ethical committee. Patients were duly informed and consent

was obtained and a cohort of 126 patients with pain or bleeding per vaginum was included during first 12 weeks of pregnancy.

Data was collected on pre designed proforma. All patients were divided randomly (simple random technique) into two groups and each containing 63 patients. Patients in Group A were given oral dydrogesterone 10 mg twice daily. Group B was given oral micronized progesterone 200mg twice daily. Treatment continued till 12th week of pregnancy. In this study 58 patients of threatened abortion were required in each group as sample size, it was enhanced to 63 patients in each group assuming 10% attrition/drop out /lost to follow up/ received additional injectable progesterone. The diagnostic criteria for threatened miscarriage were based on documented fetal cardiac activity on USG with complain of pain lower abdomen or bleeding per vaginum in presence of closed cervix and gestational age 12 weeks or less.

On initial assessment complaints of pain and bleeding per vaginum were noted. All patient underwent a complete examination (physical and gynaecologic examination including per speculum and per vaginum examination). Included patients were being provided with drugs. On follow up, remittance of pain and bleeding per vaginum (after providing drugs) were noted. The amount of bleeding is classified as if simple spotting or used only one pad then it was considered light/mild. If similar to patient menstrual bleeding or used 2-3 sanitary pads it was considered moderate or severe. All patients were followed up at antenatal clinic and ultrasound scans were done as and when required. All patients delivered and fetomaternal outcomes were observed in terms of spontaneous abortion, preterm delivery, full term delivery, IUGR, mode of delivery and birth weight of new born at the time of delivery. Statistical analysis was done by continuous data analysis. P value less than 0.05 was considered significant.

## RESULTS

**Table 1: Age wise distribution of patients**

| Age groups | Dydrogesterone | Micronised progesterone |
|---|---|---|
| 19-21 years | 6 | 9 |
| 21-23 years | 11 | 10 |
| 23-25 years | 11 | 12 |
| 25-27 years | 12 | 8 |
| 27-29 years | 11 | 11 |
| 29-32 years | 9 | 12 |
| 32-34 years | 3 | 1 |
| Mean age | 26.08±3.47 | 25.51±3.809 |

[Table 1] shows that the mean age of patient receiving dydrogesterone was 26.08±3.47 and in patients receiving oral icronized progesterone it was 25.51±3.809.

[Table 2] shows that the percentage of abortions, pre term deliveries and full term deliveries were 4.76%, 4.76% and 90.48% respectively in women who received oral dydrogesterone.

**Table 2: Observation of pregnancy outcomes in women receiving oral dydrogesterone**

| Pregnancy outcomes | No. of women | Percentage |
|---|---|---|
| Abortion | 3 | 4.76 |
| Preterm | 3 | 4.76 |
| Term | 57 | 90.48 |

**Table 3: Observation of pregnancy outcomes in women receiving oral micronised progesterone**

| Pregnancy outcomes | No. of women(n=63) | Percentage |
|---|---|---|
| Abortion | 13 | 20.63 |
| Preterm | 10 | 15.87 |
| Term | 40 | 63.49 |

[Table 3] shows that the abortions, preterm delivery and full term delivery were 20.63%, 15.87% and 63.49% respectively in women who received oral micronised progesterone.

**Table 4: Observation of pregnancy outcome in terms of IUGR in both groups**

| Pregnancy outcomes in terms of IUGR | Group A | Group B |
|---|---|---|
| Growth restricted babies | 3 | 12 |
| Normal weight babies | 60 | 51 |

[Table 4] shows that growth restricted babies were 4.76% and normal weight babies were 95.24% in women who have received oral dydrogesterone and 19.05% and 80.95% in women who have received oral micronised progesterone.

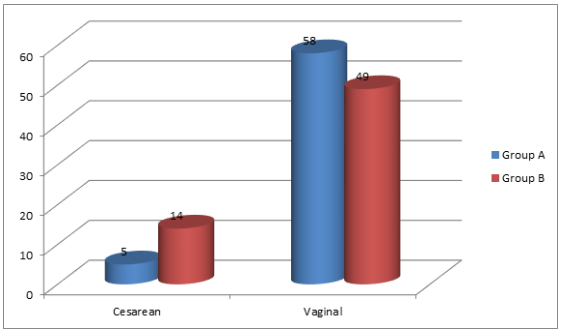


**Figure 1: Mode of delivery**

[Figure 1] shows that mode of delivery was cesarean in 5 in group I and 14 in group II and vaginal in 58 in group I and 49 in group II.

[Table 5] shows that patients who presented to hospital at 6-8 weeks of bleeding, had 1 abortion (2.78%) at 8-10 weeks had 1 (5%) while at 10-12 weeks had 1 (14.29%) with oral dydrogesterone. With oral micronised progesterone at 6-8 weeks patients had 6 (22.22%), at 8-10 weeks 4(16.67%) while at 10-12 weeks had 3 (25%) abortions.

[Table 6] shows that at 6-8 weeks gestational age, the mean birth weight in dydrogesterone was 2.686 kg with a std. deviation 0.2378 kg while in micronized progesterone group, it was 2.386 kg with

a std. deviation of 0.5416 kg and. In 8-10 weeks and 10-12 weeks gestational age, it was 2.711 ± 0.2233 kg and 2.65 ± 0.5477 kg in dydrogesterone respectively and in micronized progesterone these were 2.625 ± 0.2489 kg and 2.488 ± 0.3796 kg respectively.

**Table 5: Observation of gestational age at which first bleeding occur and number of abortions**

| Gestational Age at which first bleeding occur | Abortion | Dydrogesterone (63) | Micronized Progesterone (63) | Total |
|---|---|---|---|---|
| | | No. (%) | No. (%) | No. (%) |
| 6 Week - 8 Week | Present | 1 (2.78) | 6 (22.22) | 7 (11.11) |
| | Absent | 35 (97.22) | 21 (77.78) | 56 (88.89) |
| | Sub-total | 36 (100.00) | 27 (100.00) | 63 (100.00) |
| 8 Week - 10 Week | Present | 1 (5.00) | 4 (16.67) | 5 (11.36) |
| | Absent | 19 (95.00) | 20 (83.33) | 39 (88.64) |
| | Sub-total | 20 (100.00) | 24 (100.00) | 44 (100.00) |
| 10 Week - 12 Week | Present | 1 (14.29) | 3 (25.00) | 4 (21.05) |
| | Absent | 6 (85.71) | 9 (75.00) | 15 (78.95) |
| | Sub-total | 7 (100.00) | 12 (100.00) | 19 (100.00) |

**Table 6: Observations of birth weight of babies after receiving drugs and the gestational age at which first bleeding occur**

| Gestational Age at which first bleeding occur | Drug | N | Mean (kg) | Std. Deviation |
|---|---|---|---|---|
| 6 weeks-8 weeks | Dydrogesterone | 35 | 2.686 | 0.2378 |
| | Micronized Progesterone | 21 | 2.386 | 0.5416 |
| 8 weeks-10 weeks | Dydrogesterone | 19 | 2.711 | 0.2233 |
| | Micronized Progesterone | 20 | 2.625 | 0.2489 |
| 10 weeks-12 weeks | Dydrogesterone | 6 | 2.65 | 0.5477 |
| | Micronized Progesterone | 9 | 2.488 | 0.3796 |
| Total | Dydrogesterone | 60 | 2.69 | 0.2199 |
| | Micronized Progesterone | 50 | 2.498 | 0.4202 |

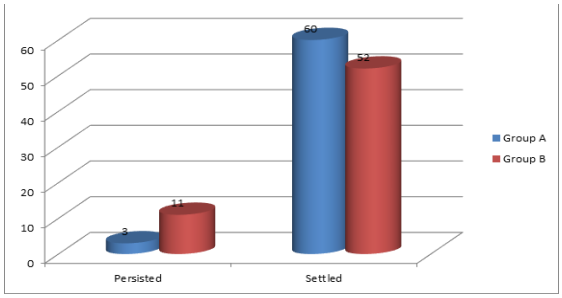


**Figure 2: Comparison of groups in terms of pain after treatment**

[Figure 2] shows that pain settled in 95.24 % of participants who have received oral dydrogesterone whereas who have received micronised progesterone it was 82.54%, significant (p<0.05) statistically significant.

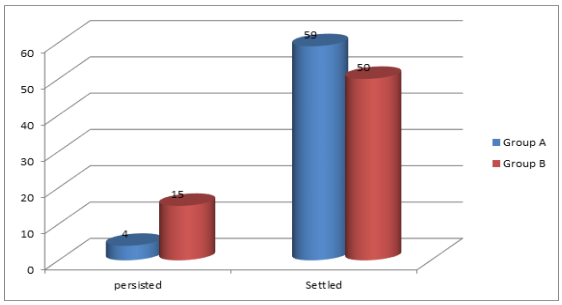


**Figure 3: Comparison of groups in terms of bleeding per vaginum after treatment**

[Figure 3] shows that in 93.65% of participants who have received oral dydrogesterone whereas it was settled in 79.37% of participants who have received micronised progesterone (p<0.05, ststistical significant).

## DISCUSSION

Each dawn brings new knowledge new thoughts and new theories to the medical sciences that help man to explore deeper into the complexities of various diseases each new day is helping us to have better insight in the treatment modalities randomised control trials are the optimum methods of assessing health care technologies and interventions.[10,11] In this study we compared the effects of oral dydrogesterone versus micronized progesterone on symptoms of threatened miscarriage and to observe the pregnancy outcomes in patients of threatened miscarriage receiving dydrogesterone and micronized progesterone. Total of 126 patients of threatened miscarriage studied in this study. All patients divided in two groups. Group A has been provided with dydrogesterone and Group B with micronized progesterone. The effects of drugs in terms of settling of pain and stoppage of bleeding p/v were compared in two groups. Also abortions in two groups were compared. We observed following findings.

We found that the mean age of patient in the group who received dydrogesterone was 26.08±3.47 and in the group who received oral micronised progesterone was 25.51±3.809 which was comparable. The percentage of abortions, pre term deliveries and full term deliveries were 4.76%, 4.76% and 90.48% respectively in women who received oral dydrogesterone and with oral

micronised progesteorne the abortions, preterm delivery and full term delivery were 20.63%, 15.87% and 63.49% respectively.

Czajkowski et al,[12] found that oral dydrogesterone decrease the abortion rate by increasing the uteroplacental flow. They provided 300 mg micronized progesterone or 30mg of oral dydrogesterone and observed the patients in three visits. In the progesterone group, 3 miscarriages followed the first visit (3/29) immediately, and another miscarriage occurred between the second and the third visit (1/26). The incidence of miscarriages in the dydrogesterone group between visits 1 and 2 and visits 2 and 3 was 1 of 24 pregnancies and 1 of 23 pregnancies. These findings also supports in our study in which we observed that dydrogesterone decrease the abortion rate.

We found that growth restricted babies were 4.76% and normal weight babies were 95.24% in women who have received oral dydrogesterone with oral micronised progesterone growth restricted babies were 19.05% and normal weight babies were 80.95%. We found that the percentage of caesareans sections (elective and emergency) was 7.94% and vaginal delivery was 92.06% in women who received dydrogesterone. The percentage of caesareans sections (elective and emergency) in patients who have received micronised progesterone was 22.22% and vaginal delivery was 77.78%.

We observed that patients who presented to hospital at 6-8 weeks of bleeding, had 1 abortion (2.78%) at 8-10 weeks had 1 abortion (5%) at 10-12 weeks also had 1 abortion (14.29%) in group who had received dydrogesterone. In group who had received oral micronised progesterone it was 6 (22.22%), 4(16.67%) and 3 (25%) respectively. R.U Pandian,[13] showed that dydrogesterone had 12/96 abortions whereas control group had 27/95 abortions. It was found that dydrogesterone was more effective than conservative treatment in maintaining pregnancy.

We found that in comparing two drugs in terms of symptoms of threatened miscarriage. Pain lower abdomen settled in 95.24% of participants who received oral dydrogesterone whereas who have received micronised progesterone pain settled in 82.54% of study participants ($p<0.05$). Bleeding per vaginum was settled in 93.65% of participants who have received oral dydrogesterone whereas it was settled in 79.37% of participants who have received micronised progesterone ($p<0.05$). El Zibdeh,[14] found that 7% were growth restricted babies who have received dydrogesterone. In our study, out of 63 who had received oral micronised progesterone 19.05% had growth restricted babies.

The shortcoming of the study is small sample size.

## CONCLUSION

In the present study the effects of oral dydrogesterone with oral micronised progesterone on symptoms of threatened miscarriage were compared and we have found that the dydrogesterone reduce pain in lower abdomen and bleeding per vaginum more in comparison to micronized progesterone.

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