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A COMPARATIVE STUDY OF DYDROGESTERONE AND MICRONIZED PROGESTERONE ON EARLY PREGNANCY LOSS IN THREATENED ABORTION AND RECURRENT PREGNANCY LOSS

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ABSTRACT

Background: Progesterone is mandatory for maintenance for healthy intrauterine pregnancy. High risk pregnancies like early pregnancy loss,threatened abortion,recurrent pregnancy loss needs supplementation of progesterone for continuing pregnancy as production of endogenous progesterone is not sufficient. So, different forms of progesterone are given as adjuvant to support pregnancy to enhance uterine quiescence and immuno-modulation to prevent rejection of embryo and leading to successful implantation. **Methodology:** This prospective study was done at Nalanda Medical College, Patna which included 50 patients with history of early pregnancy loss in threatened abortion and recurrent pregnancy loss and coming with either complaint of pain abdomen and bleeding per vaginum within 9-24 weeks of gestation. These patients were divided into two groups GROUP A and GROUP B of 25 patients each. GROUP A were given DYDROGESTERONE of 10 mg BD and GROUP B were given MICRONISED PROGESTERONE 200 mg BD till 24 weeks . **Results :** Patients presented with history of vaginal bleeding was 16% in group A and 20.83% in group B. Miscarriage rate was 4% in group A whereas 12.5% in group B and successful pregnancy was 96% in group A and 87.5% in group B. **Conclusion:** Dydrogesterone is a retro-progesterone with better tolerability, bioavailability with no androgenic,mineralocorticoids and estrogenic properties and more effacious in cases of early pregnancy loss,threatened abortions and recurrent pregnancy loss.

KEYWORDS

Dydrogesterone, Micronized Progesterone,threatened Abortion,recurrent Pregnancy Loss

INTRODUCTION

Progesterone is known as "pregnancy hormone".

1) It induces secretory changes in the lining of uterus and leads to successful Implantation of the embryo.
2) It modulates the immune response of the mother to prevent rejection of embryo.
3) Enhance uterine quiescence

Luteal phase defect is a disorder in which sufficient endogenous progesterone are not produced to preserve a functional endometrium which later leads to early pregnancy loss, threatened abortions and recurrent pregnancy loss.

Early pregnancy loss is non-viable,intra-uterine pregnancy within first $12^{6/7}$ weeks of gestation. It is diagosed by -

1) USG showing empty cavity followed by bleeding.
2) Diagnostic finding of pregnancy loss-

a) CRL of 7mm or greater with no heartbeat.
b) Mean sac diameter of 25 mm or greater and no embryo
c) Absence of embryo with heartbeat 11 days or more after a scan that showed gestational sac with yolk sac.

Follow-up USG at 7-10 days done for assessing pregnancy viability. Threatened abortion is defined as bleeding that occurs before 24 weeks of gestation.

Recurrent pregnancy loss leads to significant negative impact on life of a couple.

Recurrent Pregnancy Loss Diagnostic Criteria Are:

	ESHRE2017	ASRM2013	RCOG2011
PREGNANCY	Serum or urine HCG;ectopic and molar pregnancies not to be included in the definition	Clinical pregnancy documented by USG or histopathological examination	All pregnancy loss not further defined
WEEKS OF GESTATION	Upto 24 weeks	Only mentions that majority is lost prior to 10th week	Upto 24 weeks
RECURRENCE	2	2	3
CONSECUTIVE	Consecutive or nonconsecutive	consecutive	consecutive

Latest definitions of recurrent pregnancy loss is two or more failed pregnancies confirmed by sonographic or histopathological examinations.

Etiopathologies:

a) chromosomal aberrations
b) hormonal and metabolic disorders
c) antiphospholipid syndrome
d) cytogenetic abnormalities

These causes are excluded by screening for antiphospholipid antibody,TSH and TPO antibodies and assessing uterine anomaly by 3D USG.

Natural progesterone are made from a chemical called diosgenin which is isolated from wild yam or soy. There are various limitations of natural progesterone like:

a) Lower bioavailability
b) Poor oral absorption
c) High first-pass metabolism
d) Higher side effects
e) Patient compliance

There are various formulations of progesterone like Dydrogesterone and micronized progesterone.

	Micronized Progesterone	Dydrogesterone
Source	Progesterone undergoes Processing to become micronized progesterone	Progesterone under light technology bends it into curved retro-steroid structure
Progesterone Induced Blocking Factor (pibf)	Not produced	Produced by blocking cascade reaction by shifting to T-HELPER type 2 and immunomodulation
Nitric Oxide Production	Not increased	Increased leading to increase uterine and endometrial blood flow during luteal phase and early pregnancy
Specific Features	Has less affinity for progesterone receptors and also for androgen,mineralocorticoid,glucocorticoid,and estrogenic receptors	Has high specific affinity for progesterone receptors and no affinity for androgen,mineralocorticoid,glucocorticoid ,and estrogenic receptors

Bioavailability	Less	More

AIM OF STUDY

To compare the efficacy of dydrogesterone and micronized progesterone on early pregnancy loss in threatened abortion and recurrent pregnancy loss.

Study Design

This is a prospective clinical study.

Selection Of Cases

This study was conducted on 50 patients in Nalanda Medical College, Patna during time period of December 2019 to December 2021 who were presented with history of threatened abortion and recurrent pregnancy loss and complaint of pain abdomen and bleeding per vaginum between 9-24 weeks of gestation.

Sample Size

A total of 50 patients were selected and studied.

Inclusion Criteria

Women presented with A) history of early pregnancy loss B) history of recurrent pregnancy loss C) pain in abdomen and bleeding per vaginum between 9-24 weeks.

Exclusion Criteria

The following were excluded from the study-

1. Patients documented with chromosomal aberrations like trisomies and monosomy X. Trisomy 16 is most commonly associated with early pregnancy loss.
2. Uterine anomalies
3. Antiphospholipid syndrome
4. chronic diseases like hypertension,diabetes,hepatic impairment
5. drug allergy
6. Patient not willing to go for study

MATERIAL AND METHODS

This is a prospective study. The selected patients were divided into 2 groups A and B of 25 patients each. History taking such as age, parity, last menstruation period, gestational age was done. History of vaginal bleeding in previous pregnancy and its amount and previous abortions were taken. General and clinical examinations were done. Gestational age and viability of foetus were confirmed by ultrasonography. After routine antenatal checkup Group A was given Dydrogesterone 10 mg BD and oral micronized progesterone 200 mg BD from 9-24 weeks gestations. Follow up of these patients were done routinely.

RESULTS AND ANALYSIS

Initially, 25 patients in each GROUP A and GROUP B were observed during this study but 1 patient from Group B went to loss of follow-up.Following observations were made:

Table 1: Distribution Of Patients In Both Groups According To Gestational Age

Gestational Age(in Weeks)	Group A (dydrogesterone 10mg Bd)	Group B (micronized Progesterone 200 Mg Bd)	Total N=49 1 Patient Loss To Follow-up)
12-14	9 (36%)	8 (32%)	17
15-17	8 (32%)	7 (28%)	15
18-20	5 (20%)	6 (24%)	11
21-24	3 (12%)	4 (16%)	6

Table 2: Distribution According To Gravida

GRAVIDA	GROUP A	GROUP B
PRIMI	3 (12%)	2 (8%)
G2-G3	12 (48%)	14 (56%)
>G4	10 (40%)	9 (36%)

Table 3: Distribution Of Patients According To Treatment Variables

TREATMENT GROUP VARIABLES	GROUP A N=25	GROUP B N=24 (1 LOSS TO FOLLOW-UP)
BMI (MEAN±SD)	25.2 ± 2.20	23.4 ± 3.1
HISTORY OF PREVIOUS VAGINAL BLEEDING	4 (16%)	5 (20.83%)
MISCARRIAGE RATE	1 (4%)	3 (12.5%)
SUCCESSFUL PREGNANCY	24 (96%)	21 (87.5%)
SIDE EFFECT YES	2 (8%)	4 (16.66%)
NO	23 (92%)	20 (83.33%)

24 patients delivered out of 25 from dydrogesterone group while 21 delivered out of 24 patients from micronized progesterone group.

Miscarriage rate was slightly higher in oral micronized progesterone group.

There was significant difference in both groups (p value <0.001) .

However,tolerance and safety profile were same in both groups, there was no Significant difference in dissatisfaction among the study groups.

DISCUSSION

In both groups, maximum multiparous women were prescribed with 2 forms of progesterone therapy. 48% belonged to gravida 2 and gravida 3 in group A whereas 56% belonged to group B. Grandmultipara was 40% in group A whereas 36% in group B. Primigravida was 12% in goup A whereas 8% in group B. In group A BMI (MEAN±SD) was 25.2 ± 2.20 and in group B was 23.4 ± 3.1. History of previous vaginal bleeding was 16% in group A and 20.83% in group B. Miscarriage rate was higher 12.5% in group B and 4% in group A. Higher rate of successful pregnancy 96% were with group A and 87.5% with group B.Side effect of drug was 8% with group A and 16.66% with group B.

CONCLUSION

In this comparative study, we found that oral dydrogesterone was more effective in preventing miscarriage rate. But, there is need of larger trial with more number of patients for establishing superiority in high risk pregnancies like threatened abortion,early pregnancy loss and recurrent pregnancy loss where the exact cause cannot be determined. Dydrogesterone is a retroprogesterone; here hydrogen at C9 is in beta position and methyl group at C10 is in alpha position. This leads to improved oral activity, metabolic stability and lacks estrogenic, androgenic and mineralocorticoid properties.

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