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A COMPARISON OF DYDROGESTERONE AND MICRONIZED PROGESTERONE ON THE EFFECT OF THREATENED ABORTION

Gynaecology

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ABSTRACT

Background: Threatened abortion is defined as bleeding during the first 20 weeks of pregnancy while the cervix is closed. Low serum progesterone and progesterone -induced blocking factor have been associated with miscarriage. Thus women with threatened miscarriage are given progesterone . These progesterone can be natural like micronized progesterone or synthetic like dydrogesterone.

Objective: This study aims to compare the effectiveness of dydrogesterone with micronized progesterone on threatened abortion

Material and methods: This is a prospective study done in patients who came to MGM MEDICAL COLLEGE AND HOSPITAL , JAMSHEDPUR from December 2016 to December 2017. Patients with threatened abortion were randomised into two groups. Group1(G1) received dydrogesterone as treatment and group2(G2) received micronized progesterone.

Results: 88 patients were included in these study who could be followed for the subsequent duration. More successful pregnancy was observed in G1 who received dydrogesterone than in G2 who received micronized progesterone($P<0.05$). Duration of vaginal bleeding was also less in G1 but this was not statistically significant.

Conclusion: Dydrogesterone is found to be superior to micronized progesterone in the continuation of pregnancy and thus decreasing miscarriage rate.

KEYWORDS

Introduction:

Abortion is the most common complication of pregnancy(1).Threatened abortion is diagnosed when a vaginal bleeding appears in the presence of a viable fetus and a closed cervical os before 20 weeks of gestational age(2). While threatened abortion occurs in about 20% of pregnancies in the first trimester 50% of that lead to complete abortion (3,4). It is worth noting that the risk of abortion doubles in pregnant women who have mild vaginal bleeding than women without bleeding during pregnancy, and this possibility will be increased to four times in the presence of heavy vaginal bleeding (3). Among women who experienced vaginal bleeding in the first trimester of pregnancy without complete abortion; so the risk of antepartum hemorrhage, preterm labor and low birth weight will be increased (2). Several risk factors can increase the rate of complete abortion such as older women, increased pre-pregnancy maternal body mass index (BMI), maternal serum Progesterone levels and living habits (like caffeine, some exercises, stress, smoking and alcohol consumption) (5). In the case of threatened abortion, the following measures are necessary; a pelvic exam to check the inevitable abortion, ultrasound to prove the presence of live fetus and laboratory testing to evaluate of fetal growth (6). Threatened abortion may occur for many reasons such as placental dysfunction (which can lead to preterm delivery, preeclampsia, placenta previa and IUGR), ineffective vascularization and chronic decidual inflammation(7).

The outcome of threatened abortion can be predicted by some biochemical markers including serum β hCG, Progesterone, pregnancy-associated plasma protein A (PAPP-A), inhibin A and activin A (8, 9). Progesterone is a steroid hormone that is secreted from ovarian granulosa cells; and it causes decidual changes in endometrial, and prepares the uterus and it causes decidual changes in endometrial and prepares the uterus for implantation of the blastocyst (8). Progesterone is secreted from the corpus luteum during pregnancy (10). This hormone inhibits the contraction of smooth muscle and production of prostaglandins, also blocks the mother's cellular immune responses (9). Progesterone stimulates the production of particular substance from the lymphocytes of mice that are known as the anti-abortion (10). Oral administration of Progesterone does not have effective blood levels and also some side effects occur such as nausea, drowsiness and headaches (11). Dydrogesterone is structurally and pharmacologically similar to the natural Progesterone with higher bioavailability and fewer side-effects, so it can be used instead of Progesterone (11). Dydrogesterone has high specificity for Progesterone receptor and it is different with other synthetic Progesterone because it does not have androgenic and anabolic properties or hormonal effects like estrogen and corticoid.

The purpose of the current study is to compare the effects of dydrogesterone and Progesterone in pregnant patients who were referred because of threatened abortion and also to evaluate and compare between Dydrogesterone drug and micronized Progesterone in maintaining pregnancy in patients with threatened abortion.

MATERIALAND METHODS:

This randomized clinical trial study was performed on 88 pregnant women at gestational age ≤ 12 weeks who were referred due to threatened abortion to MGM HOSPITAL,Jamshedpur. The study treatment conducted on non- hospitalized women, but in the case of long distance between patients' living locations to the hospital, they were hospitalized to follow-up treatment. All study population was randomly divided into two equal groups - considering the amount of vaginal bleeding (mild to moderate). Group I (received Dydrogesterone tablet) and group II (received Progesterone vaginally).

Patients included were pregnant women at the first trimester with symptoms of threatened abortion, having an ultrasound report that confirmed a viable fetus, no history of uterine anomalies and mullerian defects, having a closed cervical os, and no history of smoking and alcohol. Exclusion criteria included the presence of underlying diseases such as hypertension, diabetes, severe hepatic impairment, antiphospholipid syndrome, fever, disorders of the cervix and cervical length are less than 3 cm, allergy to components of prescribed drug, severe bleeding, absence of a normal gestational sac in 5th week, the absence of fetus at the 6th weeks of gestation, and absence of heart activity in 7th weeks of pregnancy.

After history-taking and preliminary examinations, an ultrasound examination was performed for confirming a live fetus in the uterus; then patients received their treatment protocol according to their group. The participants' data such as age, last menstruation age (LMP) and gestational age, history of previous pregnancies, the history for vaginal bleeding in previous pregnancies, the amount of vaginal bleeding, history of previous abortion, etc. were collected in the researcher- made questionnaire. For each patient BMI was assessed and reported in her questionnaire. Patients attending the clinic on Saturday, Monday or Wednesday were allocated to dydrogesterone and those attending on Sunday, Tuesday or Thursday were allocated to

the Progesterone suppository group. Group I (Dydrogesterone group) received 40 mg Dydrogesterone stat followed by 10mg daily, which was continued one week after stopping bleeding. The group II (Progesterone group) was given vaginally Progesterone 200 mg each night and was continued until the end of vaginal bleeding. During treatment, patients were examined and evaluated weekly. Patients were re-examined and also re-evaluated by ultrasound after stopping vaginal bleeding.

The obtained results from two groups were compared like the number of days of vaginal bleeding, the amount of bleeding, the number of hospitalization days, and continuation of pregnancy after 20 weeks of gestational age and the side effects of prescribed drug such as burning and vaginal discharge. The amount of bleeding was evaluated by the number of pads consumption: 1-2 pads was as mild bleeding, 3-4 pads medium and more than 4 pads, or if there was blood clots was severe bleeding. All patients received standard supportive treatments include iron supplements, folic acid and multivitamins.

For continuous variables, data were presented as means ± standard deviation (SD) and for categorical variables; as number with frequency. The comparisons of variables between the two groups were made using the Fisher's exact or Chi-square methods for categorical variables. The Mann-Whitney and t- test were used for the continuous variables. Statistical analysis was performed using SPSS version 20 and STATA 11, and data with $P<0.05$ were significant.

RESULTS AND DISCUSSION:

A total number of 88 pregnant women at gestational age ≤ 12 weeks with threatened miscarriage, participated in the study. The mean ages (± SD) in Dydrogesterone and Progesterone groups were 26.75 ± 5.47 and 25.64 ± 5.12 years, respectively. T-Test did not show significant difference between two groups (P = 0.89). The mean BMI in the Dydrogesterone group was 26.45 ± 2.16 kg /m^2 and in the Progesterone group 25.62 ± 2.54 kg /m^2. According to the T- test; there was no significant difference between study groups (P=0.21). The two groups were similar about history of previous pregnancy. While in Dydrogesterone group, 24 women (54%) had a history of previous pregnancy, this figure in Progesterone group was 20 women (46%). According to Fisher's Exact test; it was not observed significant difference between two groups regarding the history of previous pregnancy (P=0.44). In Dydrogesterone group, only 8 women (8%) had a history of vaginal bleeding in previous pregnancy, and in Progesterone group 7 women (7%). The two groups were also similar about history of vaginal bleeding in previous pregnancy. According to Fisher's Exact test; there was no significant difference between two groups about history of vaginal bleeding (P=0.50). The first ultrasound showed that the mean gestational age was 9.28 ± 2.68 and 9.41 ± 3.45 weeks in the Dydrogesterone and Progesterone groups, respectively. There was no significant difference between study groups, according to the T- test (P=0.76

In this study, the amount of vaginal bleeding was evaluated according to the numbers of pad consumption. In Dydrogesterone group, 23 women (53%) were recorded in the mild vaginal bleeding group and 21 women (47%) in the medium group. In Progesterone group, these records were 20(46%) and 24 (54%), respectively. According to Fisher's Exact test; it was not observed significant difference between two groups regarding the amount of vaginal bleeding (P=0.19). The mean duration of vaginal bleeding in the first and second group was 2.61± 1.50 and 2.70 ±1.61 days, respectively.

According to T- test; there was no significant difference between two groups about duration of bleeding (P=0.4). Among group I; three patients were hospitalized for 3 ± 1.73 days and in the group II only one woman was hospitalized but for 4 days. There was no significant difference between study groups, according to Mann- Whitney test (P=0.56). In the first group, pregnancy was continued among 36 women (84 %) but in 8 women (16 %) was aborted. In the second group, these figures were 32(72%) and 12 (28%), respectively. According to Chi- square test; significant difference was observed between two groups regarding the continuation of pregnancy (P=0.31) . The obtained results showed that, there was not any side effect of prescribed drug (Dydrogesterone oral tablet) in the group I.

In the group II (Progesterone suppository) 7 women (15%) showed some side effects, while 37 women (85%) in this group did not have any side effects. Most patients in the group II complained from burning and itching of the vagina, and 1 woman complained from vaginal discharge. According to Fisher's Exact test; there was a significant difference between two groups regarding the side effect of prescribed drug (P=0.000). The aim of this study was to investigate and compare Dydrogesterone oral tablet with Progesterone suppository to prevent miscarriage in the cases of threatened abortion. According to our results in the two groups there was significant difference in pregnancy continuation was reported (P=0.31). In a comparative study in women who were referred because of threatened abortion, the rate of continuing pregnancy by administered Dydrogesterone was more than control group who did not receive any medication (P< 0.05). This study showed no difference between the two groups regarding to preterm delivery, preeclampsia, low birth weight and congenital anomalies (12). The same results were reported in a study about Dydrogesterone administration in women with threatened abortion as compared to control group (11). In a systematic review study was indicated that the administration of Dydrogesterone reduced 47% of the miscarriage risk in women with threatened abortion (11)

CONCLUSION:

The study demonstrated significant differences were found between the two groups in terms of continuing the pregnancy. Also because of the use of oral Dydrogesterone are more convenient for patients than vaginal Progesterone, it is recommended that Dydrogesterone tablets are more prescribed for threatened abortion patients.

S.No.	Participant Features	G1(Dydrogesterone)	G2(Progesterone)
1.	Age in years	26.75 +/-5.47	25.64 +/-5.12
2.	BMI (kg/m2)	26.45 +/- 2.16	25.62 +/-2.54
3.	H/o Previous pregnancy	24(54%)	20(46%)
4.	H/o Previous Vaginal bleeding	4(8%)	3(7%)
5.	Gestational age at first Ultrasound	9.28 +/- 2.68	9.41 +/- 3.45
6.	Amount of Vaginal bleeding Mild Moderate	23(53%) 21(46%)	20(46%) 24(54%)
7.	Duration of Vaginal bleeding	2.61 +/- 1.50	2.70 +/- 1.61
8.	Duration of hospitalisation	3+/-1.73	4
9.	Successful pregnancy Yes No	36(84%) 8(16%)	32(72%) 12(28%)
10.	S/E drugs Yes No.	7(15%) 37(85%)	44(100%) 0

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