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ORIGINAL ARTICLE

Comparison of the Effectiveness of Oral Progesterone and Micronized Progesterone Pessary in Reducing the Spontaneous Preterm Birth Incidences

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ABSTRACT

Objective: The purpose of this study is to compare the effectiveness of oral progesterone and micronized progesterone pessary in reducing the spontaneous preterm births incidence.

Study Design: Randomized controlled trial

Place and Duration: Gynaecology and Obstetrics Department of Combined Military Hospital, Peshawar from January 2021 to December 2021.

Methods: Total 112 pregnant females were presented in this study. Included females were aged between 18-45 years. After taking informed written consent, detailed demographics of enrolled cases included age, BMI, parity and gestational age was recorded. Females were divided in two groups. Group I received oral progesterone in 56 females and group II received micronized progesterone pessary. Post-operative outcomes among both groups were assessed. SPSS 23.0 was used to analyze all data.

Results: Among 112 cases, 35 (31.3%) had age 18-25 years, 45 (40.2%) females had age 26-35 years and 32 (28.6%) cases had age 36-45 years. 64 (57.1%) patients had BMI <25kg/m^2 and 48 (42.9%) cases had BMI >25kg/m^2. Mean parity in group I was 2.5±1.23 and in group II parity was 1.72±3.16. Mean gestational age of the patients in group I was 33.16±10.42 weeks and in group II mean gestational age was 34.17±8.23 weeks. Frequency of c-section in both groups were higher as compared to vaginal delivery with p value <0.003. Mean time of prolongation of pregnancy in group I was 18.22±6.33 days and in group II mean time was 30.7±5.47 days. We found that micronized progesterone cyclogest pessary was effective in terms of reducing NICU admissions, maternal systemic complications, preterm C-section, tocolysis use, side effects, intraventricular haemorrhage and perinatal mortality as compared to oral progesterone.

Conclusion: Preventive micronized progesterone pessary was found to be more effective than oral progesterone (dydrogesterone) in reducing premature birth among women at high-risk of premature delivery.

Keywords: Oral Progesterone, Micronized Progesterone Pessary, Preterm Birth, Side Effects

INTRODUCTION

Obstetrics and perinatal care have a huge challenge in preventing preterm births, which can be dangerous for both mother and baby. This illness claims the lives of around one million individuals every year, placing it in the major reason of mortality among newborns and in the number two spot for the cause of death among children under the age of five [1]. At the moment, more than 1.5 billion neonates are delivered prematurely every year [2], and that figure is growing]. As a result of the immaturity of several organs, preterm neonates who are born at an early gestational age have an increased risk of morbidity and mortality [3]. Some of the conditions that preterm neonates are more likely to suffer from are respiratory distress, cerebral palsy, and graphic and neurodevelopmental impairment. Deliveries that take place before to the 37th week of a pregnant woman's gestation are referred to as "preterm births." In addition to regular uterine contractions, the clinical criteria for identifying preterm labour include a modification in cervical dilatation, effacement, or both [4]. Clinical criteria for diagnosing preterm labour].The use of progestogen chemicals has been the focus of a number of clinical studies that have been conducted with the goal of lowering the risk of having a baby too soon [5].

Up until about a decade ago, there was no medication that was proven to be consistently successful in avoiding preterm delivery in low-risk pregnancies. The fact that there were no therapies accessible contributed to this outcome. Despite this, there have been two innovations in the past ten years that have the potential to be highly significant: progestin and the pessary. In women who have attacked or established preterm labour, it has been demonstrated that progesterone can reduce the risk of preterm delivery (RR 0.63, 95% CI 0.40-0.96); however, a 2014 Cochrane systematic review concluded that the proof was inadequate to justify progestational agencies as an effective anticancer representative for females admitting with preterm labour [6]. This was because the study only comprised a limited number of trials overall. According to a recent meta-analysis of data on patients, oestrogen was found to reduce the preterm delivery rates (27% vs. 37%; OR 0.48, 95% CI 0.24-0.79) and reduced perinatal death (15percent) of the respondents vs. 17%; OR 0.69, 95% CI 0.38-1.3) in asymptomatic females to multiple or singleton pregnant women and a short cervix. These findings were discovered in women [7].

Women who are expecting twins or more babies tend to give delivery prematurely rather frequently. Women who are carrying twins have nearly twice the risk of having a premature birth as women who are carrying a single child: 1.8, 7%, and 14% of twin pregnancies end in premature birth before 28, 32, and 34 weeks of gestation, correspondingly. Females who are carrying a single child have a risk of having a premature birth that is about the same as the national average. As a direct consequence of this, 8% of births that involve twins result in perinatal death, 7% of the kids are severely harmed, and 20% are moderately affected [4]. The bacterial vaginosis, short cervix, poor socioeconomic status, bacteriuria, both high and low maternal body mass index and smoking have all been connected to premature birth. Other maternal factors that have been linked to preterm delivery include a short cervix, bacteriuria, and bacteriuria. [5].

Publicly available data indicates that no therapeutic procedure (including such antibiotics, hydration, or tocolytic treatment) can safely postpone birth for more than 24 to 48 hours. (when they admitted in preterm labour). Thus, we shifted our attention to preventative initiatives such as bed rest, pelvic rest (vaginal penetration avoidance), maternity care, intensive training, screening and managerial staff of vaginitis infections, treatment of

gingivitis, prophylactic tocolytic therapy, prevention of multiple pregnancies, evidence based broad-spectrum antibiotic therapy, smoking cessation and drug use. [8] There is new evidence suggesting that progesterone plays a vital part in the uterine quiescence maintenance (during the latter half of pregnancy). This is accomplished by limiting the generation of stimulating prostaglandins and the expression of genes that code for proteins involved in contraction. In addition, the withdrawal of functional progesterone activity has been associated to the beginning of labour in both term and preterm pregnancies (at uterus level). [9]

Clinics Specializing in Maternal and Fetal Medicine that are Part of the MFMU Network Participants were randomly randomised to receive either 17P (250 mg) or a placebo by intramuscular injection once weekly until the 36th week of pregnancy. This process began in the participant's 20th week of pregnancy and continued until the participant's 36th week. They discovered that the incidence of necrotizing enterocolitis, intraventricular haemorrhage, and the demand for supplemental oxygen at birth all went down. [10] Between the weeks 24 and 34 of their pregnancies, 142 pregnant women participated in a research project that was carried out in Brazil. The participants were given either oral supplementation or 100 mg of vaginal progesterone suppositories as their treatment of choice. In every category, the vaginal delivery group had a drop in the number of recurrent preterm births that was statistically significant (p 0.05). [11-15] There is a dearth of sufficient data in Pakistan on the efficacy of progesterone.

The purpose of this study is to compare the effectiveness of oral progesterone and micronized progesterone pessary in reducing the spontaneous preterm births incidence.

MATERIAL AND METHODS

This randomized control trial was conducted at gynaecology and obstetrics department of Combined Military Hospital, Peshawar from January 2021 to December 2021 and comprised of 112 pregnant females. After taking informed written consent, detailed demographics of enrolled cases included age, BMI, parity and gestational age was recorded. Patients <18 years of age, abnormal fetus and those did not provide any written consent were excluded.

Patients older than 18 years old, with a history of at least two prior c-sections for premature deliveries, a protracted nursery stay, and a short cervical length (between 2.5 and 3 cm) on anomaly scan. Oral progesterone (10 mg twice day) was administered to Group I, while Group B used a progesterone pessary (400 mg daily) for rectal application before night. At 32 and 37 weeks of pregnancy, patients were checked on. Maternal (respiratory distress syndrome, perinatal death, pneumonia, use of oxygen at 28days of life, neonatal sepsis, intraventricular haemorrhage, retinopathy of prematurity) and neonatal (mean gestation weeks, delivery prior to 28, 32, or 35 weeks, caesarean delivery, reason for delivery, antenatal corticosteroids used and tocolysis used) outcomes were measured. Statistical analysis was performed with SPSS 23. The quantitative variables were averaged and expressed as percentages. The percentage and frequency distributions of qualitative variables were determined. The Chi-square statistic was used. The cutoff for significance was set at a p-value of less than 0.05.

RESULTS

Among 112 cases, 35 (31.3%) had age 18-25 years, 45 (40.2%) females had age 26-35 years and 32 (28.6%) cases had age 36-45 years.(Figure-1)

We found that, 64 (57.1%) patients had BMI <25kg/m^2 and 48 (42.9%) cases had BMI >25kg/m^2. Mean parity in group I was 2.5±1.23 and in group II parity was 1.72±3.16. Mean gestational age of the patients in group I was 33.16±10.42 weeks and in group II mean gestational age was 34.17±8.23 weeks. Frequency of c-section in both groups were higher as compared to vaginal delivery with p value <0.003. Mean time of prolongation of pregnancy in group I was 18.22±6.33 days and in group II mean time was 30.7±5.47 days.(table-1)

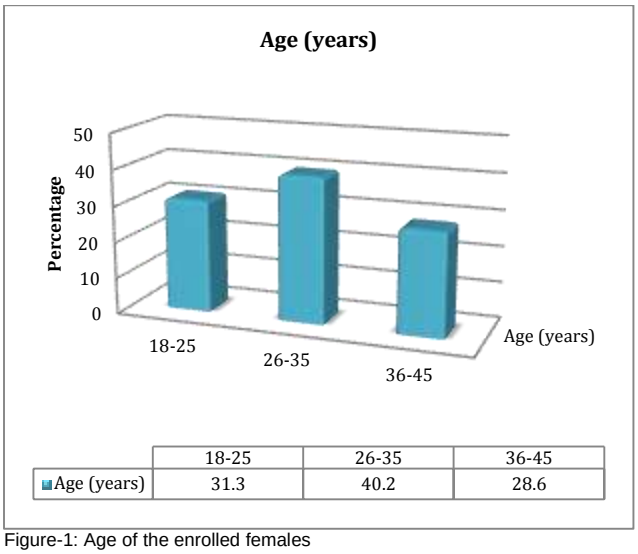

Figure-1: Age of the enrolled females

Table-1: Demographics of the enrolled females

Variables	Group I	Group II
BMI		
<25kg/m^2	32 (57.1%)	32 (57.1%)
>25kg/m^2	24 (42.9%)	24 (42.9%)
Mean Parity	2.5±1.23	1.72±3.16
Mean gestational age	33.16±10.42	34.17±8.23
Mode of Delivery		
C-section	36 (64.3%)	34 (60.7%)
Normal Delivery	20 (35.7%)	22 (39.3%)
Mean Prolong Pregnancy (days)	18.22±6.33	30.7±5.47

We found that micronized progesterone cyclogest pessary was effective in terms of reduction in preterm C-section, NICU admissions, maternal systemic side effects tocolysis use, intraventricular haemorrhage and perinatal mortality as compared to oral progesterone.(table-2)

Table-2: Post-operative outcomes among both groups

Variables	Group I	Group II
Preterm C-section		
Yes	20 (35.7%)	8 (14.3%)
No	36 (64.3%)	48 (85.7%)
NICU admissions		
Yes	23 (28.6%)	9 (16.1%)
No	33 (71.4%)	47 (83.9%)
Maternal systemic		
Yes	13 (23.2%)	7 (12.5%)
No	43 (76.8%)	49 (87.5%)
Tocolysis use		
Yes	18 (32.1%)	11 (19.6%)
No	38 (67.9%)	45 (80.4%)
Side effects		
Yes	15 (26.8%)	9 (16.1%)
No	41 (73.2%)	47 (83.9%)
Intraventricular haemorrhage		
Yes	14 (25%)	6 (10.7%)
No	42 (75%)	50 (89.3%)
Perinatal mortality		
Yes	4 (7.1%)	2 (3.6%)
No	52 (92.9%)	54 (96.4%)

We found that satisfaction rate was higher in females of group II 50 (89.3%) cases as compared to group I 42 (75%).(figure-2)

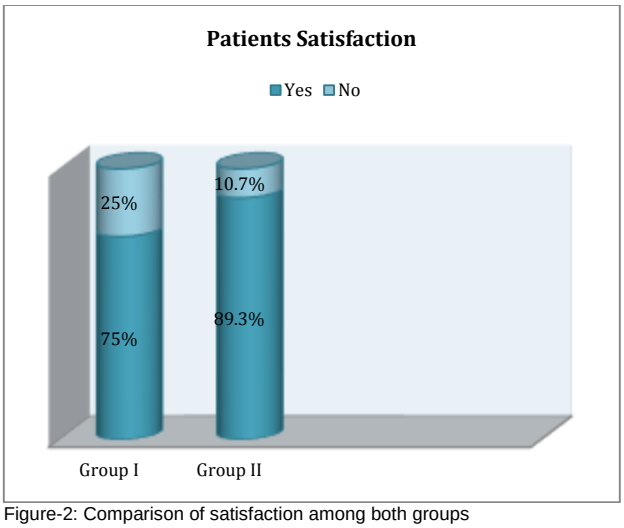

Figure-2: Comparison of satisfaction among both groups

DISCUSSION

When it concerns children younger than 5 years old, preterm birth complications are the leading cause of mortality. It is possible that current, low-cost treatments might save 75 percent of these deaths. Extremely premature birth (28 weeks), moderate to late preterm (28 to 32 weeks), and very preterm are the three subgroups of preterm birth (32 to 37 weeks). The first step in avoiding premature delivery and its risks is to have a healthy pregnancy. Having a baby prematurely means you won't have the benefit of ultrasounds to determine your due date and receive advice on how to best nourish your baby.[16]

In current study 112 pregnant females were presented. We found that 35 (31.3%) had age 18-25 years, 45 (40.2%) females had age 26-35 years and 32 (28.6%) cases had age 36-45 years. 64 (57.1%) patients had BMI <25kg/m^2 and 48 (42.9%) cases had BMI >25kg/m^2. Mean parity in group I was 2.5±1.23 and in group II parity was 1.72±3.16. These findings were comparable to the previous studies.[17,18] Pessaries and vaginal progesterone have both been proven to hold promise as preventative strategies against premature birth. Both are low-effort and may be included into standard medical practise. Other research organizations throughout the world are also conducting trials to examine the effectiveness of cervical pessaries and progesterone in preventing premature delivery. It is hoped that by combining the results of various studies, researchers would be able to determine which strategy is most effective in preventing premature births. To address this question, researchers are currently conducting a prospective, individual-participant meta-analysis of progesterone and pessaries (PROMPT) in singleton and multiple pregnancies. Currently active pessary studies have all agreed in their protocols to measure the same things.[19]

In current study, micronized progesterone cyclogest pessary was effective in terms of reduction in preterm C-section, NICU admissions, maternal systemic, tocolysis use, side effects, intraventricular haemorrhage and perinatal mortality as compared to oral progesterone. Similar studies have found that mothers who utilise vaginal progesterone are less likely to have their babies prematurely or require medical intervention. [20] Similar research also found that progesterone is linked to less maternal problems (p=0.00). [21] However, Hacket al. found that progesterone administered by rectal application was more successful in reducing maternal problems (p=0.02). [22]

No significant variations in latency periods and no significant reduction in the risk of preterm delivery were detected in randomized controlled trials using oral progesterone, vaginal progesterone, or 17-hydroxyprogesterone caproate, as reported in a previous meta-analysis by Eke et al. [23]. Results from the trial by Wood et al. [24] were similar, showing that vaginal progesterone medication did not lengthen the average time between conception and delivery. Recent research supports the hypothesis that progestogen usage extends latency periods [25]. These results were contrast to our findings.

CONCLUSION

Preventive micronized progesterone pessary was found to be more effective than oral progesterone (dydrogesterone) in reducing premature birth among women at high-risk of premature delivery.

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