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COMPARISON OF MICRONIZED PROGESTERONE VERSUS NIFEDIPINE IN PREVENTION OF PRETERM LABOR.

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ABSTRACT

BACKGROUND: The definition of preterm labor is when a woman gives birth before completing 37 weeks of gestation, which is calculated from the last menstrual cycle date **OBJECTIVE**: To determine the effectiveness of micronized progesterone versus nifedipine in the prevention of preterm labor.**METHODOLOGY:** A randomized controlled trial was conducted by the Department of Obstetrics and Gynecology at Peoples University of Medical & Health Science for Women Nawabshah during the period of September 2019 to October 2020. Eighty-three women were treated with micronized progesterone (group 1) and 83 women were treated with nifedipine (group 2). Nifedipine tocolysis was initiated orally. Prior to administering the treatment, the blood pressure, pulse, uterine contractions and fetal heart rate of the mother were assessed. Documentation was conducted every thirty minutes within the initial hour and then hourly for up to four hours. Following this, documentation took place every four hours until a final outcome was reached at twelve hours. **RESULTS:** Mean age of group 1 and group 2 was 29.01 ± 5.59 years and 28.06 ± 6.18 years, respectively. The mean parity was 2 ± 0.73 in group 1 and 2 ± 0.64 in group 2. There were 39 (46.99%) primigravida and 44 (43.01%) multigravida in group 1 while 21 (25.30%) primigravida and 62 (74.70%) multigravida in group 2. Effectiveness was significantly high in group 1 as compared to group 2 (77.1% vs. 57.8%; p=0.008). **CONCLUSION:** It is concluded that treatment with micronized progesterone resulted in a substantial reduction in the rate of recurrent preterm delivery among women who were at particularly high risk for preterm delivery and reduced the likelihood of several complications in their infants.

KEY WORDS: Preterm delivery, Micronized progesterone, Nifedipine,

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INTRODUCTION

The definition of preterm labor is when a woman gives birth before completing 37 weeks of gestation, which is calculated from the last menstrual cycle date.[1] Preterm labour is multifactorial, and preterm labour typically accounts for around six to seven percent of births.[1, 2] In the United States, the incidence of preterm delivery is about 11.5%.[3] While in Europe, the incidence is around 5.8%, while in Turkey, the incidence is about 5.6%.[3] In Pakistan, the frequency of preterm labor was 13.4%.[4] The preterm labour processes are also uncertain. Either premature initiation of the physiological contracting mechanism or a pathological cause responsible for uterine contractions may be associated with it, leading to premature delivery.[4] A effective tocolytic medicine includes the avoidance of preterm labour. Progesterone, nifedipine, and β adrenergic receptor agonists are the most widely used tocolytics; however sadly, no placebo-controlled trials are required to support this.[5]

During the first eight weeks of gestation, progesterone is a steroid hormone secreted by the corpus luteum and the placenta. The concentration of intracellular calcium and the synthesis of prostaglandins are directly impacted, resulting in uterine quiescence. [6] Several clinical trials conducted on individuals who are at risk and treated with either intramuscular 17-alpha-hydroxyprogesterone caproate on a weekly basis or vaginal micronized progesterone daily have indicated a small reduction in the incidence of preterm labor between the 24th and 34th weeks. Yet in terms of perinatal mortality and morbidity, these therapies showed little benefit.[7-9] Nifedipine is an efficient tocolytic agent with a simple oral route, few adverse effects, and the least risk of neonatal complications. However, in patients with weakened cardiovascular disorders, it should be used with caution, since they could be at risk of pulmonary oedema and heart failure.[10]

We designed this study to know the effects of progesterone and nifedipine in prevention

of preterm labor so prevention strategies could be made and applied to women with preterm labour. The present study determined the effectiveness of micronized progesterone versus nifedipine in prevention of preterm labor.

METHODOLOGY

Between September 2019 and October 2020, the department of Obstetrics and Gynecology at PMCH Nawabshah conducted a randomized controlled trial after obtaining ethical approval.

A non-probability convenience sampling technique was used to recruit the patients. A sample size of 83 was determined using the OPENEPI calculator, by keeping the power of 80%, type I error as 5%, P1= 77.8% [11] and P2= 72.2%. Women of age between 18-40 years, parity 1-3 presenting with preterm labor. Preterm labour was defined as the ≥ 1 contractions within 10 minutes along with cervical dilatation < 3 cm during 28-35 weeks of gestational age assessed on ultrasonography. Following women were excluded: multiple pregnancy, diabetes, chronic hypertension, renal disease, cardiovascular disease or hypothyroidism.

The trial was conducted on 166 pregnant females presenting in the labor room and fulfilling the inclusion criteria. The informed consent was obtained and demographics were noted. The randomization was done by using computer-generated simple random numbers. Patient was assigned to receive intervention if the last digit of random number is odd (micronized progesterone) group 1 and was considered as a control participant if the last digit of random number is even (nifedipine) group 2.

Nifedipine tocolysis was initiated orally. If uterine contractions persisted beyond 30 minutes, another equivalent amount of medication was given after the same amount of time had passed. If the contractions continued after the second dosage, a third amount of 20mg was given at intervals of 30 minutes, up to a maximum total dose of 60 mg during the first hour of treatment. After receiving three doses of nifedipine, patients were given a dose of 20mg every 3-8 hours as needed for 48 to 72 hours. The mother's blood pressure, pulse rate, and uterine contractions were checked before and after treatment initiation. A chart was created to record this information every half-hour for the first hour, then hourly up to four hours and subsequently every four hours until final outcomes were measured at twelve hours. The oral micronized progesterone was given in 100mg twice daily until delivery. Uterine contractions were monitored by using Cardiotocography (CTG). Treatment was considered as effective when there was successful stoppage to the uterine contraction i.e. no contractions after inhibition of 12 hours.

Data was entered and analyzed using the statistical package for social sciences (SPSS v. 19). Frequency and percentage were calculated for qualitative variables like effectiveness while mean standard deviation were reported for continuous variables like age, gravida, parity and gestational age. Chi-square test was used to compare categorical variables like effectiveness. A p-value of < 0.05 was set as cut off for statistical significance.

RESULTS

In this study, 83 patients who were randomized to group 1 had mean age of 29.01 ± 5.59 years, while mean age of patients in group 2 was 28.06 ± 6.18 years. The mean gestational age was 32.03 ± 2.30 weeks in group 1 and 31.67 ± 2.59 weeks in

group 2. The mean parity was 2 ± 0.73 in group 1 and 2 ± 0.64 in group 2. There were 39 (46.99%) primigravida and 44 (43.01%) multigravida in group 1 while 21 (25.30%) primigravida and 62 (74.70%) multigravida in group 2 Table-1.

Table 1: Characteristics of Patients

Variables	Group		Total
	Group 1	Group 2	
n	83	83	**166**
Age (Years)	29.01 ± 5.59	28.06 ± 6.18	**28.54 ± 5.90**
Gestational Age (Weeks)	32.03 ± 2.30	31.67 ± 2.59	**31.99 ± 2.46**
Parity	2 ± 0.73	2 ± 0.64	**2 ± 0.69**
Primigravida	39 (46.99%)	21 (25.30%)	**60**
Multigravida	44 (43.01%)	62 (74.70%)	**106**

Effectiveness in terms of successful stop uterine contraction was assessed between groups. Effectiveness was significantly high in group 1 as compared to group 2 (77.1% vs. 57.8%; p=0.008) Table-2.

Table 2: Comparison of Effectiveness between groups

Effectiveness	Group		Total	P-Value
	Group 1	Group 2		
Yes	64(77.1%)	48(57.8%)	112(67.5%)	0.008
No	19(22.9%)	35(42.2%)	54(32.5%)	
Total	83	83	166	

DISCUSSION

Delivery that occurs before 37 weeks of gestation is known as preterm delivery and has a significant impact on infant mortality in developing nations. It occurs in 7-12% of all births and contributes to over 85% of perinatal morbidity and mortality. While all births prior to 37 weeks of gestation are described as preterm, most accidents and deaths occur in babies prior to 34 weeks. The rate of survival has improved with advances in neonatal treatment, but the high cost of handling preterm babies remains a huge economic burden, and is very complicated for the population of our world, where most families cannot fulfil their basic requirements. In this scenario, the prenatal treatment of patients and the burden of infant care, particularly premature, is very complicated and many families cannot afford it and results in neonatal mortality as well.[11-14]

Delaying the process of labor and delivery has two-fold benefits: First it has to be made sure to ensure enough time for administering antepartum glucocorticosteroids in order to reduce the occurrence and intensity of respiratory distress syndrome in newborns. This should be done while also making arrangements for transferring the mother to a specialized facility that can handle extreme prematurity cases. Another objective is to lower the number of perinatal complications and deaths associated with severe prematurity.

The key goal of tocolytic treatment is to boost perinatal performance by suppressing pre-term labour.[15] Tocolytic agents can prolong the pregnancy by 2 to 7 days and are recommended for short-term use to provide time for the administration of antenatal corticosteroids and transition to the appropriate neonatal unit.[16] The results obtained from this study suggest that administering hydroxyprogesterone on a weekly basis until the gestational period reaches 36 weeks or upon delivery can effectively diminish the preterm delivery rate before the 36th week of gestation in women who are at greater risk of preterm delivery. The effects of prematurity may also be minimised in babies of women undergoing progesterone therapy. The drawback of our research is that we have not set up a control panel for a more rigorous comparison to assess the disparity in the reduction in premature babies.

According to the American College of Obstetricians and Gynecologists, administering progesterone supplements is a viable option for women who have previously experienced spontaneous preterm delivery due to premature membrane rupture or labour in cases where they are currently experiencing a single-tone pregnancy. In addition, pregnant women with limited cervical duration (less than 15 mm) during mid-quarter ultrasound screening may also benefit from considering this treatment option.[17] The Society of Obstetricians and Gynecologists of Canada has recommended the utilization of progesterone replacement therapy, specifically either 17 OHP-C 250 mg intramuscular weekly or regular micronized progesterone 100 mg vaginally for women with a history of spontaneous preterm birth. For those with limited cervical duration (<15 mm) at 22-26 weeks of childbirth, a daily dose of micronized progesterone 200 mg vaginally is advised. The initiation of this therapy should take place after the 20th week of conception and should be discontinued once the risk of prematurity is minimal.[18]

CONCLUSION

It is concluded that treatment with micronized progesterone led to the substantial decrease in the frequency of recurrent preterm delivery in females who had higher risk of preterm delivery in subsequent pregnancy and decreased the probability of many complications for their neonates.

ETHICS APPROVAL: The ERC gave ethical review approval

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin

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CONFLICT OF INTEREST: No competing interest declared.

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