Comparison of Oral Nifedipine and Vaginal Progesterone In Prolongation of Pregnancy With Preterm Labor

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ABSTRACT

Objective — *To compare the effectiveness of oral nifedipine and vaginal progesterone in prolongation of the duration of pregnancy with preterm labor.*

Study design — *Comparative study.*

Place & Duration of study — *Department of Obstetrics and Gynecology, Military Hospital Rawalpindi, from March 2016 to September 2016.*

Methodology — *A total of 90 women with singleton pregnancy, 18 to 39 years of age were included. Patients with polyhydramnios, preterm pre-labor rupture of membranes, gestational hypertension, pre-eclampsia and eclampsia were excluded. Using the lottery method, the selected patients were placed randomly assigned into two groups, Group A in which nifedipne was used and Group B where progesterone was given. Frequency of prolongation of duration of labor was noted for both the groups.*

Results — *In Group A mean age of the women was 28.31.±_5.88 year and mean gestational age 32.33.±_2.62 weeks; while in Group B mean age was 29.58± 5.11 year and mean gestational age 32.47 ± 2.24 weeks. Mean prolongation of pregnancy in nifedipine and progesterone group was 17.39.±11.71 weeks and 47.42± 12.29 weeks respectively. Prolongation of the duration of pregnancy was seen in 33 (73.33%) in group A and 42 (93.33%) in group B with p=0.011.*

Conclusion — *Effectiveness of vaginal progesterone was higher in prolongation of the duration of pregnancy with preterm labour as compared to oral nifedipine.*

Key words — *Pregnancy prolongation, Nifedipine, Progesterone.*

INTRODUCTION:

Preterm birth occurs when baby is born prior to the completion of 37 weeks of gestation. Approximately one in every ten births in the United States is a pre-term birth.[1] The significance of preterm birth is also apparent from the fact that it is the most common cause of neonatal death, while being one of the leading causes of long-term neurological disabilities children. Preterm birth is a global problem.[2] According to WHO statistics, every year, approximately 25 million preterm babies are born. Majority of preterm births are iatrogenic, however, in some cases the reasons of preterm birth include cesarean birth or an early induction of labor due to maternal disease.[3,4] Maternal causes of preterm birth include diabetes mellitus, hypertension, anemia, nutritional problems, multiple pregnancies etc.[5]

Pakistan stands 7th in the world with a rate of 15.8/100 live births.[6] An early detection of preterm labor is essential.[7] In this context, the use of several different agents has been suggested for the suppression of uterine contractions; like oxytocin receptor antagonists, nitric oxide donors,

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prostaglandin synthetase inhibitors, calcium channel blockers and beta-agonists. Treating preterm labor is a major obstetrical challenge.

The tocolytic therapy has two important objectives, firstly to address and reduce the adverse impact of idiopathic respiratory distress syndrome and secondly delaying delivery as much as possible, thereby allowing the administration of antepartum glucocorticosteroids.[7] Another important objective of the tocolytic therapy is to reduce as much as possible, both the morbidity owing to severe prematurity and perinatal mortality.[8-10]

Oral nifedipine has long been used in this regard. Progesterone is considered as natural hormone for maintaining uterine quiescence throughout pregnancy. Hence now it is being increasingly used for preterm labour suppression. There are not many studies comparing the effectiveness of these two drugs. A study conducted in 2014 showed that pregnancy could be prolonged in the nifedipine and progesterone groups, to 16.63.±. 12.64 and 40.14.±. 13.4 weeks respectively.[9] The aim of this study was to compare the effectiveness of oral nifedipine and vaginal progesterone in prolonging the duration of pregnancy in women with preterm labour.

METHODOLOGY:

It was a comparative study performed in the Department of Obstetrics and Gynaecology, Military Hospital Rawalpindi, from March 2016 to September 2016. A total of 90 women were included in this study through non-probability and consecutive sampling. Preterm labor was defined as initiation of labour that started after 24 weeks of gestation and prior to the completion of 259 days of pregnancy or 37 complete weeks.[8] The onset of labor was considered when regular palpable uterine contractions more or equal to four over 10 minutes duration noted. Documented cervical change effacement > 80% with cervical dilatation > 1 cm, increase in duration of pregnancy > 1 week prolongation was considered effective prolongation. It was hypothesized that effectiveness of vaginal progesterone was higher in prolongation of the duration of pregnancy with preterm labor as compared to oral nifedipine.

Inclusion criteria was women of age 18 to 39 years presenting with preterm labor, singleton pregnancy whose gestational age was confirmed by early dating scan and primigravida or multigravida with previous history of term deliveries. Exclusion criteria was women with polyhydramnios, gestational hypertension and pre eclampsia and eclampsia, preterm pre-labor rupture of membranes, pregnancy with fetal anomaly and history of cervical surgery. Women with preterm labor admitted through obstetrics OPD or emergency after carrying out a complete evaluation including history, examination and investigations. Institutional ethical committee approval was taken. An informed consent was obtained. The lottery method was used for random allocation of patients to either of the two groups.

In Group A, nifedipien (initial oral dose of 20 mg followed by 10-20 mg three times daily up to maximum 60 mg daily dose) was used. In Group B, 400 mg of micronized progesterone vaginally once daily was used. Patients were kept in the labor room for the monitoring. Uterine contractions were monitored every 10 minutes per hour and vaginal examination was done 06 hourly as per the protocol. Dexamethasone cover was given to each women with preterm labor. The duration of prolongation of pregnancy was documented.

Mean and standard deviation were calculated for age, gestational age, parity and time for prolongation of pregnancy. Qualitative variables like prolongation of pregnancy (yes/no) were presented by frequency and percentages. Chi-square test was used to compare the prolongation or duration of pregnancy in both the groups and the P value of 0.05 was considered statistically significant. The SPSS version 21.0 was used to enter and analyze the data. The data was stratified with respect to severity, parity, gestational age and age of participants in order to exercise control upon the effect modifiers. A Chi-square test in the post-stratification scenario was applied to observe the impact upon the outcome variables and the p-value of 0 .05 was considered significant.

RESULTS:

Total of 90 women were divided into two groups of 45 patients each. The age of the patients was from 18 years to 39 years with the mean age was 28.94 ± 5.52 year. The mean age of the study participants in Group A was 28.31 ± 5.88 year and in Group B 29.58 ± 5.11 year. Majority of the women (n=56 - 62.22%) were between 18 to 30 years. The mean gestational age of study participants in Group A was 32.33 ± 2.62 weeks and in Group B 29.58 ± 5.11 year with an overall gestational age of 24 to 36 weeks with mean age of 32.40 ± 2.43 weeks. Majority of the patients (n=70 - 77.78%) had a gestational age of 31-36 weeks.

Table I: Stratification of Frequency of Prolongation of Duration of Pregnancy According To Age Groups

Age of Patients	Group A n=45		Group B n=45		p-value
	Prolongation of the duration of pregnancy		Prolongation of the duration of pregnancy		
	Yes	No	Yes	No	
18-30 years	20 (68.97%)	09 (31.03%)	25 (92.59%)	02 (7.41%)	0.026
31-39 years	13 (81.25%)	03 (18.75%)	17 (94.44%)	01 (5.56%)	0.233

Table II: Stratification of Frequency of Prolongation of the Duration of Pregnancy According to Gestational Age

Gestational age	Group A n=45		Group B n=45		p-value
	Prolongation of the duration of pregnancy		Prolongation of the duration of pregnancy		
	Yes	No	Yes	No	
24-30 Weeks	10 (76.92%)	03 (23.08%)	06 (85.71%)	01 (14.29%)	0.639
31-36 Weeks	23 (71.88%)	09 (28.12%)	36 (94.74%)	02 (5.26%)	0.233

Table III: Stratification of Frequency of Prolongation of the Duration of Pregnancy According to Parity

Parity	Group A n= 45		Group B n= 45		p-value
	Prolongation of the duration of pregnancy		Prolongation of the duration of pregnancy		
	Yes	No	Yes	No	
Para-1	14 (82.35%)	03 (17.62%)	14 (6923%)	03 (30.77%)	1.000
Para-2	09 (60.0%)	06 (40.0%)	13 (100.0%)	00 (0.0%)	0.010
Para-3	06 (100.0%)	00 (0.0%)	08 (100.0%)	00 (0.0%)	-
Para-4	04 (57.14%)	03 (42.86%)	07 (100.0%)	00 (0.0%)	0.051

Mean parity was 2.09 ± 1.08. The mean parity in group A was 2.07 ± 1.07 and in group B 2.11 ± 1.09. Majority of the patients (n=34 - 37.78%) were of para 1. Mean prolongation of pregnancy in nifedipine and progesterone group was 17.39 ±11.71 weeks and 47.42 ±12.29 weeks respectively. Prolongation of the duration of pregnancy was noted in 33 (73.33%) women in group A and 42 (93.33%) in group B (p=0.011).

Stratification of frequency of prolongation of the duration of pregnancy between two groups according to age of patients and gestational age is given in table I & II. Table III shows the stratification of frequency of prolongation of the duration of pregnancy between the groups according to parity.

DISCUSSION:

The use of tocolytic drugs has become popular however their use has been limited.[11] The effectiveness of dugs is primarily dependent upon the timing and correct diagnosis of the preterm labor along with the fetal fibronectin and also cervical length estimation by ultrasonography.[12] Both the pregnant woman and the fetus are equally vulnerable to the drug used.[13-15] Tocolysis is aimed not only to inhibit uterine contractions, but also at allowing a safe transfer of pregnant woman to a tertiary care center.

With regards to the effective prevention of preterm labor, progesterone has been identified as one of the most promising and efficient agent. According to the recent clinical guidelines,

progesterone has been recommended as the principal prevention agent in case of singleton pregnancies with either a short cervical length or a history of spontaneous pre-term birth.[17] In our study prolongation of the duration of pregnancy was seen in 33 (73.33%) in group A (nifedipine) and 42 (93.33%) in group B (progesterone) which was statistically significant. A study conducted showed that mean prolongation of pregnancy in nididipine and progesterone group was 16.63+12.64 weeks and 40.14+13.4 weeks respectively.[9] Findings of a study showed that the frequency of preterm birth was 42.5% in the progesterone group in comparison with 35.5% in placebo group.[18]

In a meta-analysis of nine trials where progesterone and nifedipine were used for maintaining tocolysis, it was found that when tocolysis is maintained with progesterone, in contrast with the placebo treatment or no treatment at all, it can cause a significant prolongation of the gestation. It resulted in reduction of the number of pregnant women with delivery before 37 weeks. It can also lead to an increase in the birth weight of newborn.

Borna et al and Arikan et al carried out a trial using vaginal natural progesterone. The findings of their studies showed that in women with preterm labor the use of vaginal progesterone (in doses of 400 mg daily in case of Borna and Sahabi and 200 mg daily in case of Arikan et al) was highly effective in prolongation of the mean gestational age at the time of delivery or the postponement of the delivery.[19]

CONCLUSIONS:

Effectiveness of vaginal progesterone was higher in prolonging the duration of pregnancy with preterm labor as compared to oral nifedipine.

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