

Comparative Analysis of Oral Nifedipine Versus Oral Progesterone Alone in the Treatment of Threatened Preterm Labor

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ABSTRACT

Objective: To compare the effectiveness of oral nifedipine versus oral progesterone alone in the treatment of threatened preterm labor from 24 to 37 weeks of gestation.

Study Design: Experimental Study

Place and Duration of Study: This study was conducted at the Department of obstetrics and gynecology of Al-Tibri Medical College and Hospital and Kulsoom Bai Valika Social Security Hospital, Karachi in the duration of four months from November 2020 to February 2021.

Materials and Methods: A total of 188 patients with threatened preterm labor having age 18-40 years with singleton pregnancy, gestational age between 24-37 weeks confirmed by LMP or ultrasound were included and divided into two groups. Group A (n=94) was treated with the 20mg of oral nifedipine three times for 48 to 72 hours and Group B (n=94) was treated with the 100mg oral progesterone twice daily for 72 hours. Success in stopping uterine contractions was defined as absence of any contraction after 12 hours of treatment. Data was collected into predesigned Performa.

Results: The average age of women in group A was 27.59±5.41 and in group B was 28.11±5.37 years. Mean gestational age was 33.05±3.59 weeks. Effectiveness of a drug (Success in stopping uterine contractions is defined as no contractions after 12 hours) was significantly high in group A than group B (76.8% vs. 66%; p=0.0005).

Conclusion: Nifedipine seems to be effective and safe tocolytic agent; it can be used successfully to inhibit contractions in threatened preterm labor.

Key Words: Threatened Preterm labor, Nifedipine, Progesterone

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INTRODUCTION

Preterm birth is a health and social problem, considered the leading cause of neonatal mortality worldwide. It is associated with higher rates of neurodevelopmental morbidity, sensorineural impairments and other complications. ⁽¹⁾ Approximately 70% of neonatal deaths, 36% of infant deaths and 25—50% of cases of long term neurologic problem in children can be caused by preterm birth. ⁽²⁾

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Long term morbidity comprises cerebral palsy, neurological developmental delay and chronic lung disease. Gestational age is inversely proportional to the risk of mortality and morbidity. ⁽³⁾

According to WHO definition, preterm labour refers to the onset of labour after the gestation of viability and before 37 completed weeks of pregnancy. ⁽⁴⁾ The diagnosis of onset of labour consists of documented uterine contraction, rupture fetal membrane, documented cervical change with cervical length of more than 2cm or less and / or cervical dilatation of more than 2cm, whereas threatened preterm labour comprises of only documented uterine contraction without cervical change. Every year about 15 million babies are born at preterm and this number is rising. Prematurely complications are the main cause of mortality among babies under 5 years. ⁽⁵⁾ It is estimated worldwide that the preterm birth rate ranges from 5—18% of live birth ⁽⁶⁾, while in Pakistan, preterm birth rate is 15.8/100 live birth. ⁽⁷⁾

The key element of management consists of avoiding neonatal complication though administering corticosteroid to mother and antibiotic to obviate

neonatal sepsis and during the pregnancy to reach its possible physiological term by tocolysis.⁽⁸⁾ Tocolysis is the suppression of uterine contraction and is the principal preterm birth preventive measure until the etiology of premature birth is revised.⁽⁹⁾

Progesterone administration allows the pregnancy to reach its term because at adequate level in the myometrium, it antagonizes the oxytocin effect of prostaglandin F2 α . Progesterone has been widely used in primary and secondary prevention of preterm labour⁽¹⁰⁾, so it is good for maintenance Tocolysis too. Calcium-channel Blockers block the calcium to transfer across the myometrial cell.

They reduce intracellular free calcium concentration and causes myometrial. Nifedipine is an affective agent with simple oral route and low neonatal complication. It should not be used in patients with jeopardize cardiovascular conditions. It is used for the maintenance Tocolysis is controversial.⁽¹¹⁾

The aim of this study to compare the efficacy of oral Nifedipine and oral perforation in the time of threatened preterm labour.

MATERIALS AND METHODS

This Quasi experimental study was carried at Departments of obstetrics and gynecology of Al-Tibri Medical College and Hospital and Kulsoom BaiValika Social Security Hospital, Karachi from November 2020 to February 2021. The sample size was calculated by using WHO sample size determination software⁽¹²⁾. A total of 188 patients with threatened preterm labor of age 18-40 years with singleton pregnancy, gestational age between 24-37 weeks confirmed by LMP or ultrasound were included and divided into two groups. Groups A (n=94) was treated with 20mg of nifedipine three times in a day for 48-72 hours and Group B (n=94) was treated with the 100mg progesterone twice daily for 72 hours. However, pregnant women with twins and gestational age <24 and >37 weeks were not included. Patients with comorbidities like diabetes, chronic hypertension, renal disease, cardiovascular disease, hypothyroidism, vaginal infections, cervical incompetence, placental abruption and placenta praevia were also excluded. An informed consent was taken from women before starting the recruitment process. Patients of Group A were given 20mg orally and followed by 20mg three times daily for up to 48-72 hours. The maximum dose given during study was 60 mg/day. Patients of Group B were given 100mg of progesterone twice daily for 72 hours. Uterine contraction, cervical dilation and fetal heart rate were checked before and after treatment up to 4 hours and there after 4 hourly observations for 72 hours were taken. Effectiveness of the drug was measured in term of elongation of delivery time after treatment.

Data Analysis: Data was analyzed using SPSS version 20. Frequency and percentages was calculated for

categorical variables like effectiveness and mean standard deviations were reported for continuous variables like age, gravida, parity and gestational age. Chi-square was applied to compare the efficacy in both groups taken $p \leq 0.05$ as significant.

RESULTS

Age distribution of the patients with respect to groups is shown in figure 1. The mean age of the patients in Group A was 27.59 ± 5.41 and in Group B was 28.11 ± 5.37 years. The average gravida in Group A was 3 ± 1.23 and in Group B was 3 ± 1.20 . The average gestational age in both groups was 33.04 ± 3.62 and 33.07 ± 3.59 respectively. (Table 1).

Table No.1: Mean demographic presentation of the data

Variables	Group A n=94	Group B n=94	Overall n=188
Age (Years)	27.59 \pm 5.410	28.11 \pm 5.379	27.85 \pm 5.39
Gravida	3 \pm 1.23	3 \pm 1.20	3.61 \pm 1.22
Gestational Age (Weeks)	33.04 \pm 3.62	33.07 \pm 3.572	33.05 \pm 3.59

The comparison of the effectiveness (Success in stopping uterine contractions is defined as no contractions after 12 hours) between nifedine and progesterone is presented in Table 2. Effectiveness was significantly high in group A 76.8% than group 66% ($p=0.0005$).

Table No.2: Percentage of effectiveness of oral nifedipine versus oral progesterone alone among different groups

Groups	Effectiveness	
	Yes	No
Group a (n=94)	72 (76.8%)	21 (23.3%)
Group b (n=94)	62 (66 %)	32 (34%)

Chi-square test was applied; p -value ≤ 0.05 considered significant.

With respect to gravida, effectiveness was also significantly high in group A than group B for 2 to 3 gravida women and 4 to 5 gravida women while it was insignificant for above 5 gravida women as shown in table 3.

Table No.3: Percentage of effectiveness of oral nifedipine versus oral progesterone alone with respect to gravida among different groups

Gravida	Effectiveness	Group A n=94	Group B n=94	P-Value
2 to 3	Yes	42(75.6%)	35(65.1%)	0.006
	No	14(24.4%)	19(34.9%)	
	Total	56	54	
4 to 5	Yes	23(80.6%)	20(67.5%)	0.011
	No	5(19.4%)	9(32.5%)	
	Total	28	29	
>5	Yes	8(73.2%)	7(66.1%)	0.41
	No	3(26.8%)	4(33.9%)	
	Total	11	11	

Chi-square test was applied; p -value ≤ 0.05 considered significant.

Effectiveness was significant between groups in those cases whose gestational age was ≤ 30 weeks while it was observed significantly high in group A than group B for above 30 weeks gestational age as presented in table 4.

Table No.4: Effectiveness between groups in the treatment of threatened preterm labor with respect to gestational age

Gestational age	Effectiveness	Group A n=94	Group B n=94	P-Value
≤ 30	Yes	15(72.8%)	14(68.9%)	0.54
	No	5(27.2%)	6(31.1%)	
	Total	20	20	
31 to 35	Yes	39(77.1%)	33(66.4%)	0.007
	No	11(22.9%)	16(33.6%)	
	Total	50	49	
36 to 37	Yes	19(79.4%)	16(62.9%)	0.004
	No	5(20.6%)	9(37.1%)	
	Total	24	25	

Chi-square test was applied; p -value ≤ 0.05 considered significant

DISCUSSION

In the current study the comparative analysis of oral nifedipine and oral progesterone in the treatment of threatened preterm labor was done and we have found that oral nifedipine was more effective in term of arrestation of preterm labor than oral progesterone. The Effectiveness of the drug; measured in percentage was significantly high in group A than group B (76.8% vs. 66%; $p=0.0005$). With respect to gravida, effectiveness was also significantly high in group A than group B for 2 to 3 gravida women and 4 to 5 gravida women while it was insignificant for above 5 gravida. Effectiveness was significant between groups in those cases whose gestational age was ≤ 30 weeks while it was observed significantly high in group A than group B for above 30 weeks gestational age. These findings are in the line of the previous researches indicating nifedipine was more effective and better choice of drug in the treatment of preterm labor. (13,14) However, some studies found no significant difference in the effectiveness of both drugs⁽¹⁵⁾ while other study showed contradictory finding that progesterone showed better outcomes and prevented preterm labour than nifedipine. (16)

For pregnant women and clinicians, preterm birth is a clinical challenge. It is the most common of all births, accounting for about 8%. In addition, it not only causes premature birth, but also has many fetal complications related to it. Over the years, great attention has been paid to prevent the preterm labor. However, threatened preterm labor classified as periodic uterine contractions can progress to about 25% of preterm labor. (17) It was previously observed that Terbutaline (bricanyl) has been the first line drug which used intravenously or

subcutaneously to inhibit preterm labour for over 20 years. However, there is evidence regarding failure of oral salbutamol in terms of impeding contraction. Federal Drug Association has not yet approved magnesium sulfate to use for inhibiting contraction due to high fetomaternal complications. (18) There is great evidence reporting less side effects with use of progesterone in terms of preterm pre labour and preterm babies weight. (19) Among all drugs, it is found that nifedipine has fewer side effects to mother and fetus. (11,12,18) Chawanpaiboon S et al (19) included patients of mean age of 28.3 years He concluded that progesterone and nifedipine played vital role in inhibiting contraction in 77% and 73% cases respectively. Another randomized clinical trial was conducted to determine prophylactic efficacy of nifedipine in terms of prevention of preterm labour and the finding of that study are analogous to our study. (14)

The wide variation efficacy of both drugs is to be emphasized. Areeruk W et al. in his study found no difference between both groups however our results showed significant difference in both groups. (20) In a study conducted by Nisa Su et al. she concluded that preterm labour was arrested when combination therapy of both nifedipine and progesterone was induced which is contradictory to our findings. (21) Our findings are also contradictory to an Iranian study where progesterone was equally effective as nifedipine. (22) However, Nifedipine (calcium channel blocker) is effective and safe tocolytic agent and successful treatment of preterm labor than progesterone.

CONCLUSION

Nifedipine (calcium channel blocker) is effective and safe tocolytic agent, it should be recommended to halt premature contractions. Preterm birth leads to variety of neonatal complications and to avoid this. Premature prelabour must be reducing. Nifedipine is not only effective in causing inactivity of uterine contraction; it has fewer side effects and less complication rate for perinatal morbidity and mortality.

Author's Contribution:

Concept & Design of Study: Shagufta Perveen
 Drafting: Shagufta Perveen
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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