ORIGINAL ARTICLE

Comparison between Oral Nifedipine alone Vs Oral Nifedipine plus Progesterone as Tocolytic Agent in the Treatment of Threatened Preterm Labor

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ABSTRACT

Aim: To compare the efficacy of oral nifedipine alone vs oral nifedipine plus progesterone as tocolytic agent in the treatment of threatened preterm labour

Methods: A total of 60 patients of threatened preterm labour, 16 to 38 years of age with singleton pregnancy of gestational age between 28 to 36 weeks (calculated from LMP) were included in the study. Patients with severe pre-eclampsia, diabetes mellitus, h/o renal and hepatic diseases, severe intra-uterine growth retardation (IUGR), fetal distress, cervix >2cm dilated and to whom nifedipine was contraindicated were excluded. The selected patients were placed randomly into two groups i.e. Group A (oral nifedipine alone) & Group B (oral nifidipine plus progesterone), by using lottery method.

Results: The mean age of women in group A was 24.43±4.98 and in group B was 24.66±4.87 years. Mean gestational age was 31.88±2.32 weeks. Efficacy was noted in 19 (63.33%) patients of Group A and 23 (76.6%) of Group B. Significant (P = 0.001) difference between the efficacy of both groups was noted.

Conclusion: This study concluded that oral nifedipine plus progesterone is associated with higher efficacy for tocolysis (stoppage of uterine contractions) of threatened preterm labor as compared to oral nifedipine alone. So, we recommend that oral nifedipine in combination with progesterone should be used as a first line tocolytic agent in tocolysis of threatened preterm labor to achieve benefits from prolongation of pregnancy and significant reduction in perinatal morbidity and mortality.

Keywords: Threatened preterm birth, tocolytic agents, stoppage, contractions.

INTRODUCTION

Preterm labor (PTL) is defined by the World Health Organization (WHO) as the onset of labor after the gestation of viability and before 37 completed weeks of gestation. The conditions which determine the onset of labor include documented uterine contractions (at least 1 every 10 min), ruptured fetal membrane, documented cervical change with cervical length of about 1cm or less and/or cervical dilation of more than 2cm. Considering this, threatened preterm labor can be diagnosed when there are documented uterine contractions with no cervical changes[1].

Worldwide preterm delivery accounts for more than 9% of all births. Prematurity is the direct cause of 28% of all neonatal deaths.[2,3] In Pakistan the perinatal mortality rate is 96 / 1000 total births while the percentage of perinatal deaths due to prematurity is 8.81%[4]. There are many risk factors and causes of preterm labor and delivery. However, the majority of preterm deliveries occur in women without any known risk factors. Several medications, typically beta-sympathomimetics, calcium channels blockers, prostaglandin inhibitors, or magnesium sulphate ($MgSO_4$), are regularly used to treat acute preterm labor. These are administered to decrease the probability of delivery within 24 – 48 hours allowing time to administer corticosteroids for fetal benefit[2,5].

Due to poor health facilities and limited resources, parinatal morbidity and mortality rate is very high in Pakistan. The commonest cause of this is prematurity and low birth weight. The purpose of this study was to find effective and better drugs with minimum side effects to reduce the risk of preterm labor by enabling corticosteroid administration to accelerate fetal lung maturation which would help us to reduce perinatal mortality and morbidity.

MATERIALS AND METHODS

This randomized controlled trial was conducted at Department of Obstetrics and Gynecology Bahawal Victoria Hospital Bahawalpur from July 2015 to January 2016. Total 60 patients with Threatened Preterm Labor having age 16 to 38 years, gestational age between 28-36 weeks (according to last menstrual period), single normal fetus with cephalic presentation (assessed on per abdominal examination and confirmed with obstetrical ultra

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sonography) and regular painful uterine contractions (1 in 10 minutes) assessed on per abdominal and cervical dilatation ≤ 2cm with intact membranes on per vaginal examination were selected for this study.

Patients having age <16 to >38 years, gestational age <28 and >36 weeks (according to last menstrual period), history of pre-eclampsia, cardiac disease, diabetes, hepatic dysfunction, concurrent use of $MgSO_4$, patients who have severe intra-uterine growth retardation (confirmed on discrepancy between the period of gestation according to last menstrual period or booking obstetrical scan and serial growth scans), fetal distress (30 minutes admission CTG showing suspicious or pathological CTG tracings), cervix >2 cm dilated(on vaginal examination), preterm rupture of membranes(on per speculum examination), congenital fetal malformations(on anomaly scan or recent obstetrical USG), multiple pregnancy (confirmed on obstetrical USG), contraindication to nifedipine (allergy to nifedipine, maternal cardiac disease, hypotension <90/50 mmHg).

Threatened Preterm Labor was defined as: the occurrence of regular painful uterine contractions, 1 in 10 minutes on per abdominal and cervical dilatation ≤2cm with intact membranes on per vaginal examination, before 37 completed weeks of pregnancy according to last menstrual period or booking obstetrical scan.

Each patient was informed about the case study and after explaining the aims, methods, reasonably anticipated benefits, and potential hazards of the study; a written consent was taken from them. Subjects were informed that their participation is voluntary and that they may withdraw consent to participate at any time during the study. They were also informed that choosing not to participate will not affect their care.

After taking a written consent from the patients, all patients were offered to pick up a slip from total mixed up slips (half-slips were contained letter 'A' and other half slips were contained letter 'B') and she was placed in that respective group. Base line investigations like complete blood count, random blood sugar, Urine Complete Examination, Renal functions tests and ECG (where needed) were done in every patient on admission. Similar procedure was applied on all cases.

Procedural detail: In group A, nifedipine was given as 30 mg tablet stat orally and then 20 mg twice daily till 36 weeks. For patients in group B, nifedipine was given as 30 mg tablet stat orally along with progesterone pessary 400mg vaginally stat. After this, nifedipine tablet 20 mg twice daily along with progesterone pessary 200 mg was given vaginally twice weekly till 36 weeks.

After the start of the treatment, all patients were evaluated for prolongation of gestation at 36 weeks. If uterine contractions were remained stopped till 36 weeks after the start of treatment, it was regarded successful otherwise was labelled as unsuccessful. Data was collected through predesigned Performa.

Data was entered and analyzed using SPSS version 14.0. Mean and standard deviation was calculated for quantitative variables like age and gestational age. Frequencies and percentages were calculated for qualitative variables like parity, efficacy of oral nifedipine and oral nifedipine plus vaginal progesterone. Efficacy of both treatment regimens were compared in two groups by applying chi square test. P value < 0.05 was taken as significant.

RESULTS

In this study, the age range was from 16 to 38 years with mean age of 24.55±4.88 years. The mean age of women in group A was 24.43±4.98 and in group B was 24.66±4.87 years.

Comparison of efficacy between both treatment groups was done. Efficacy was 36.66% in group A (oral nifedipine) and 76.6% in group B (oral nifedipine plus progesterone) and statistically significant (P = 0.001) difference between the efficacy of both groups was noted (Table 1).

Comparison of efficacy between treatment both groups for age group 16-20 years, age group 21-30 years and age group 30-38 years was done. The difference of efficacy between Group A and Group B was statistically significant (P=0.048, 0.032) for age group 16-20 years and 21-30 years and difference was insignificant (P=0.196) for age group 31-38 years (Table 2).

Gestational age was from 28 to 36 weeks with mean gestational age of 31.88±2.32 weeks. The mean gestational age in group A was 31.73±2.49 weeks and in group B was 32.03±2.18 weeks. Patients were divided into three gestational age groups, gestational age group 28-30 weeks, 31-33 weeks and 34-36 weeks. Comparison of efficacy between treatment both groups for gestational age was done. The difference of efficacy between Group A and Group B was statistically insignificant (P=0.202) for gestational age group 28-30 weeks and significant (P=0.040, 0.045) for gestational age group 31-33 weeks and 34-36 weeks (Table 3).

Comparison of efficacy between both treatment groups for parity was also done and statistically significant (P=0.023, 0.034) difference for Primiparous and Multiparous was noted between the efficacy of both groups A & B (Table 4).

Table 1: Comparison of Efficacy between both Groups

Group	Efficacy		Total
	Yes	No	
A	11(36.66%)	19(63.33%)	30
B	23(76.6%)	7(23.4%)	30

P value = 0.001

Table 2: Stratification for age

Age (Yrs)	Group A (n=30)		Group B (n=30)		p-value
	Efficacy		Efficacy		
	Yes	No	Yes	No	
16-20	2(28.57%)	5 (71.42%)	5 (83.33%)	01 (16.66%)	0.048
21-30	7(38.8%)	11 (61.11%)	14 (73.78%)	05 (26.31%)	0.032
31-38	2 (40%)	3 (60%)	04 (80%)	01 (20%)	0.196

Table 3: Stratification for gestational

Gestational age	Group A (n=30)		Group B (n=30)		p-value
	Efficacy		Efficacy		
	Yes	No	Yes	No	
28-30 weeks	04 (40%)	06 (60%)	05 (71.4%)	02 (28.5%)	0.202
31-33 weeks	05 (41.66%)	07(58.33%)	12(80%)	03(20%)	0.040
34-36 weeks	02 (25%)	06 (75%)	06 (75%)	02 (25%)	0.045

Table 4: Stratification for parity

Parity	Group A (n=30)		Group B (n=30)		p-value
	Efficacy		Efficacy		
	Yes	No	Yes	No	
Primiparous	08 (44.4%)	10 (55.5%)	16 (80%)	04 (20%)	**0.023**
Multiparous	03 (25%)	09 (75%)	07 (70%)	03 (30%)	**0.034**

DISCUSSION

Present was planned to compare the efficacy of oral nifedipine alone vs oral nifedipine plus progesterone as tocolytic agent in the treatment of threatened preterm labour. In our study, there was stoppage of uterine contractions in 11 (36.66%) and no stoppage in 19(63.3%) patients in Group A while in Group B, it was seen in 23 (76.6%) and 7 (23.4%) patients respectively. So, efficacy was 36.66% in group A (oral nifedipine alone) and 76.6% in group B (oral nifedipine plus progesterone) with p-value of 0.001.

In a study, Chawanpaiboon S et al[6] have compared the efficacy of progesterone and nifedipine in inhibiting threatened preterm labor in Siriraj Hospital. They found that progesterone and nifedipine were successful in inhibiting uterine contractions in threatened preterm labor 77% and 73% respectively.

Kamat S et al[7] have observed that a total of 10% of the patients in the nifedipine group and 61% of the patients in the progesterone group delivered at term. In a study by Naz S et al[4] showed that the efficacy of oral nifedipine as a tocolytic agents in stopping uterine contractions at 48 hours was 74.1%. In another study, Regmi et al[8] has shown the reduction in recurrent preterm labor with the use of progesterone which shows the efficacy of 64%.

Dodd JM et al[9] have studied prenatal administration of progesterone for preventing preterm birth. They have included thirty six randomized controlled trials involving 8523 women. Progesterone was associated with statistically significant increase in pregnancy prolongation.

King JF et al[10] have reviewed 12 randomized controlled trials involving 1209 women and showed that nifedipine was associated with a reduction in the number of delayed delivery for 7 days and before 34 weeks of gestation.

Dodd et al[9] concluded that women who received progesterone were statistically significantly less likely to give birth before 37 weeks.

CONCLUSION

This study concluded that oral nifedipine plus progesterone is associated with higher efficacy for tocolysis (stoppage of uterine contractions) of threatened preterm labor as compared to oral nifedipine alone. So, we recommend that oral nifedipine in combination with progesterone should be used as a first line tocolytic agent in tocolysis of threatened preterm labor to achieve benefits from prolongation of pregnancy and significant reduction in perinatal morbidity and mortality.

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