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Research Article

**EFFECT OF TOCOLYTIC AGENTS AND BED REST ON
PRETERM LABOUR**¹ Dr. Amna Jabbar, ² Dr. Iqra Habib, ³ Sahar Waraich¹ Werribee Mercy Hospital, Australia. PMDC #: 88083-P, meon.rind@gmail.com² Doctor at Sialkot, iqrahabib76@yahoo.com³ Sheikh zayed hospital**Abstract:**

Objective: To compare the success rate of nifedipine administration as a tocolytic agent and bed rest for preventing uterine contraction of pregnant women with threatened preterm labour. Methods: A total of 188 pregnant women with threatened preterm labour between 26-35 weeks were enrolled in this study. Cervical measurement was performed in all patients. All women in each group (94 cases) were randomly inhibited uterine contraction with nifedipine administration and bed rest intervention. Results: Nifedipine took the shorter time than bed rest for contraction inhibition in threatened preterm labour with statistical significance. (nifedipine: 2.31 ± 1.19 hours, bed rest: 2.54 ± 0.71 hours) From subgroup analysis, the success rate of nifedipine inhibition and bed rest in the patients with cervical length < 3 cm were 83.9% (26 cases) and 55.2% (16 cases), respectively, which was different with statistical significance.

Conclusions: Nifedipine can be used successfully to inhibit contractions in threatened preterm labour. However, if the cervical length was ≥ 3 cm, bed rest should be firstly applied to avoid unnecessary medical intervention.

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INTRODUCTION:

The preterm birth rate in Mayo Hospital, about 12.8% while the threatened preterm labour rate is about 1.3% in the year 2017 [1]. The higher rate of preterm birth is related to the higher rate of perinatal morbidity and mortality. The best way to decrease preterm birth is to prevent uterine contraction which is the early sign of preterm labour. Bed rest is the primary intervention which was recommended to use in women with threatened preterm labour. However, threatened preterm labour, which is classified as regular uterine contractions, following with bed rest intervention, can progress to preterm birth in about 2530% of cases and undergo delivery subsequently [2-4]. Halting the process of uterine contraction could reduce preterm birth rate and also perinatal morbidity and mortality.

Even though no definite intervention is strongly proved to inhibit uterine contraction, nifedipine is the oral medication which was successfully reported for uterine contraction inhibition in preterm labour. Therefore nifedipine compared with bed rest was a noteworthy topic to study for inhibiting uterine contraction in women with threatened preterm labour. The hypothesis of the study is to prove the efficacy of nifedipine comparing to bed rest intervention for inhibiting uterine contraction in threatened preterm labour.

MATERIAL AND METHODS:

This study was approved by Ethics Committee of the Faculty of Medicine Mayo Hospital, Lahore. The sample size, using a power and precision analysis formula, was calculated by the incidence of threatened preterm labour at Mayo Hospital, Lahore which was about 1.3%/year [1]. One hundred and eighty-eight pregnant women with threatened preterm labour between 1st December 2016 and 31st December, 2017, were enrolled in this study. All women with singleton pregnancies presenting to the labor ward with painful and regular uterine contractions at 26-35 weeks of gestation were diagnosed as threatened preterm labour. In all cases gestation was calculated from the menstrual history and by a transvaginal ultrasound [5-7] scan in early pregnancy.

Women in active labor, defined by the presence of cervical dilatation ≥ 3 cm, those with cervical insufficiency, and those with ruptured membranes were excluded. Classic cervical insufficiency is a diagnosis, based on an obstetric history of recurrent second- or early third-trimester fetal loss, following painless cervical dilatation, prolapse or rupture of the membranes, and expulsion of a live fetus despite minimal uterine activity [8].

If causes of threatened preterm labour including bacterial vaginosis and urinary tract infection were found, they were treated according to their causes. The patients with threatened preterm labour that occurred spontaneously were included in this study. Maternal demographic datas including age, gravida, parity, abortion, gestational age of admission and cervical length were recorded. The patients in each group were randomly inhibited uterine contraction with either nifedipine administered or bed rest. Nifedipine administered and bed rests were randomly allocated 94 persons in each group.

A loading dose of nifedipine 20 mg orally every 30 minutes for 3 times, then maintained with nifedipine SR 20 mg every 12 hours was used [3,4,9]. Contractions were recorded every 1 hour until 12 hours. Successful cessation of uterine contractions was defined as no contractions after inhibition for 12 hours by nifedipine or bed rest. Unsuccessful cessation of uterine contraction was defined as continuing contractions during and after inhibition for 12 hours.

If the inhibition succeeded, the same intervention in each group was continued until 34 weeks. If the inhibition failed and there was no contraindication to use bricanyl intravenously, then bricanyl was used [9]. When any complication or contraindication of nifedipine was found, the contraction inhibition was changed to be bricanyl intravenous and the patient was excluded from the study. Maternal vital signs and fetal heart rate monitoring were recorded during the intervention. The QUOROM statement flow diagram of patients' selection was also presented (Figure 1).

SPSS version 14 (for windows) was used to analyze data. Fisher's exact; Chi-square and one-way ANOVA tests were used to compare the data. Results were reported as means, standard deviations (SD) or percentages. The level of statistical significance was <0.05 .

RESULTS:

A total of 188 pregnant women with the diagnosis of threatened preterm labour were admitted at labour room, Mayo Hospital, Lahore, during 1st December 2016 to 31st December, 2017. Nifedipine administration for uterine contraction inhibition and bed rest intervention were applied in the 94 pregnant patients designated in each group.

There was no statistical significance in maternal age, mean gestational age of admission, mean gravida, parity, abortion, mean gestational age of admission and cervical length at admission among the patients in the 2 groups (Table 1). Nifedipine and bed rest were used to inhibit contraction with the patients in both groups. The success rates of nifedipine inhibition and bed rest of the patients were 97.9% (92 cases) and 78.7% (74 cases), respectively (Table 2). Nifedipine took the shorter time than bed rest for contraction inhibition in threatened preterm labour with statistical significance. (nifedipine: 2.31 ± 1.19 hours, bed rest: 2.54 ± 0.71 hours) (Table 3).

Gestational age of delivery, mean neonatal body weight and mean APGAR score between the patients in 2 groups were significant in statistical analysis (Table 4). Income and educational level of the

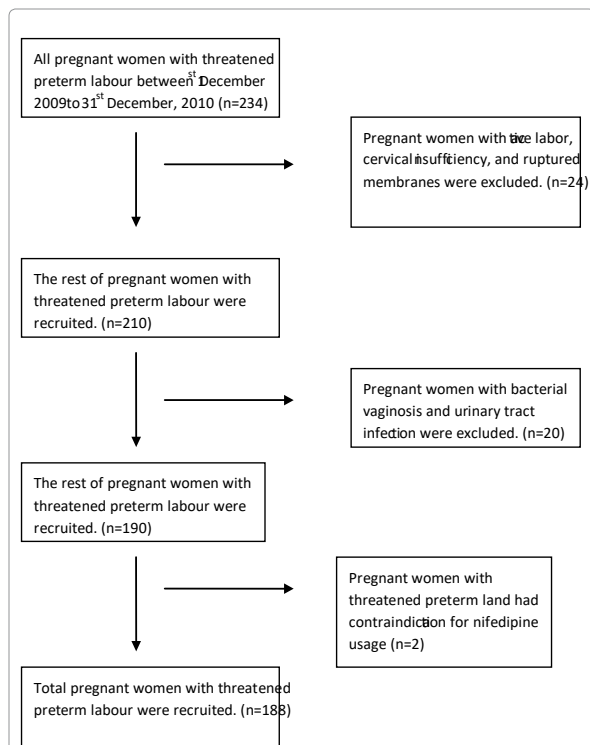


Figure 1: The QUOROM statement flow diagram of patients selection.

patients were not significantly different between the 2 groups. The patients who failed from nifedipine and bed rest inhibition were later inhibited with bricanyl. The patient with nifedipine inhibition and bed rest had normal vaginal delivery in 84 and 86 cases; caesarean section was performed in 10 and 8 cases, respectively. The indications of caesarean section were previous caesarean section (12 cases) and Cephalo-Pelvic Disproportion (CPD) (6 cases).

From subgroup analysis, the success rate of nifedipine inhibition and bed rest in the patients with cervical length <3 cm were 83.9% (26 cases) and 55.2% (16 cases), respectively, which was different with statistically significant difference. For the patients with cervical length ≥ 3 cm, there was no statistical significance between nifedipine inhibition and bed rest groups (Table 5).

DISCUSSION:

Nifedipine has been used and strongly recommended to inhibit uterine contraction for over 30 years [10-12]. Maternal and fetal complications and side effects of nifedipine were presented to be lower than those of magnesium sulfate [10,13,14]. The oral administration form of nifedipine is also more favorable than the intravenous or subcutaneous administration forms of magnesium sulfate or bricanyl [13-15]. Therefore the pregnant patients with threatened preterm labour who have no indication for

Table 1: Demographic data before delivery of the patients with uterine contraction inhibition by nifedipine and bed rest.

Outcome	Type of inhibition		P-value
	Nifedipine n=94	Bedrest n=94	
Success	92 (97.9%)	74 (78.7%)	0.035
Failure	2 (2.1%)	20 (21.3%)	

admission can be treated at home with oral nifedipine.

From the author's previous study, nifedipine, proluton depot and bed rest interventions were successful inhibiting contraction in threatened preterm labour at about 80%, 66% and 64%, respectively [16]. This study strongly reassures that nifedipine usage can stop uterine contraction in threatened preterm labour with a shorter time than bed rest intervention. However, cervical length may influence the efficacy of bed rest for the treatment of threatened preterm.

At the present time, no strong evidence supports the use of bed rest to inhibit uterine contraction in threatened preterm labour. If cervical length is long among threatened preterm labour patients, the labour must take time to proceed. From the subgroup analyzed result of this study, nifedipine and bed rest interventions were successful inhibiting contraction in threatened preterm labour with cervical length ≥ 3 cm without statistically significant difference between those interventions. Therefore bed rest intervention can be firstly applied to patients in those groups for stopping uterine contraction in order to avoid unnecessary administration of medication which may be accompanied with side effects and complications.

From this study, threatened preterm labour with cervical length <3 cm was successfully inhibited uterine contraction by nifedipine with a statistical significance comparable to those inhibited by bed rest. Therefore if the cervical length was lesser than 3 cm, nifedipine should be used instead of bed rest intervention in order to prevent true labour.

Mean gestational age at delivery, neonatal body weight and mean APGAR score between the patients in the 2 groups were statistically significant. However, clinical significance was not apparent. Complications of nifedipine were not detected.

The tocolytic agents were presented to be more effective than placebo or no therapy for delaying delivery 48 hours or 7 days. However, overall rates of respiratory distress syndrome or neonatal death were not significantly decreased [17]. The result of this study could not show validity of these interventions to minimize the risk of preterm labour and to improve neonatal outcome, but appropriate intervention to stop uterine contraction was related to the low risks of medical intervention in case of cervical length ≥ 3 cm.

Table 2: Type of inhibition and outcome of treatment in pregnant women.

Type of inhibition	Mean time (Hour)	Median (Min,max)	P-value
	Mean \pm SD		
Nifedipine n = 94	2.31 \pm 1.19	2 (0.5,4)	0.032
Bed rest n = 94	2.54 \pm 0.71	3 (1,6)	

Table 3: Mean and median time of succession after inhibition with nifedipine and bed rest.

	Intervention		p-value
	Nifedipine n=94	Bed rest n=94	
Gestational age of delivery in week (mean \pm SD)	37.31 \pm 2.05	35.88 \pm 2.45	0.021
Birth weight (mean \pm SD)	2,845.70 \pm 504.59	2,687.84 \pm 707.86	0.040
APGAR at 1 minute Mean \pm SD (min,max)	8.88 \pm 0.47 (6,10)	8.58 \pm 0.76 (6,10)	0.002
APGAR at 5 minute Mean \pm SD (min,max)	9.86 \pm 0.44 (7,10)	9.58 \pm 0.72 (7,10)	0.003

Table 4: Demographic data after delivery of the patients with uterine contraction inhibition by nifedipine and bed rest.

Cervical length	Outcome	Type of inhibition		Total (cases)	P-value
		Nifedipine (cases) (%)	Bedrest (cases) (%)		
<3 cm.	Success	26 (83.9)	16 (55.2)	42	0.016
	Failure	5 (16.1)	13 (44.8)	18	
Total		31 (100)	29 (100)	60	
\geq 3 cm.	Success	62 (98.4)	65 (100)	127	0.894
	Failure	1 (1.6)	0	1	
Total		63 (100)	65 (100)	128	

Intervention			p-value
	Nifedipine n = 94	Bed rest n = 94	
Age (mean \pm SD)	27.3 \pm 5.5	26.5 \pm 5.0	0.311
Gravida			0.463
81 (86.2%)	82 (87.2%)		
11 (11.7%)	10 (10.6%)		
2 (2.1%)	2 (2.1%)		
Parity			0.312
88 (93.6%)	90 (95.7%)		
6 (6.4%)	4 (4.3%)		
Abortion			0.352
79 (84.0%)	81 (86.2%)		
15 (16.0%)	13 (13.8%)		
Gestational age of admission in week (mean \pm SD)	31.53 \pm 1.58	32.42 \pm 1.54	0.061
Cervical length of admission in mm (mean \pm SD)	34.07 \pm 6.37	33.14 \pm 8.42	0.048

By Fisher's Exact test was significant in <3 cm group
In conclusion, nifedipine can be used to inhibit uterine contraction in threatened preterm labour, especially with cervical length <3 cm. Those patients with cervical length \geq 3 cm should be firstly prescribed bed rest. Therefore, unnecessary medical intervention and complication from tocolytic drugs can be reduced.

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