Original Article

Comparison of Nitroglycerine VS Nifedipine for Preterm Labour

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ABSTRACT

Objective: The objective of this study is to compare outcome of Nitroglycerine versus Nifedipine to delay the time of preterm delivery.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Obstetrics and Gynaecology Department, Hayatabad Medical Complex, Peshawar, from July, 2016 to January, 2017.

Materials and Methods: This study was carried out over 154 women with preterm delivery who were divided into two groups equally through lottery method. One group, group A, was subjected to treatment with Nifedipine and the other group, group B, to nitroglycerine. After informed consent, all the females were followed until the delivery of baby and the complications were noted in predesigned Performa. The subjects were selected through non-probability purposive sampling. Entry and analysis of the data was done in SPSS (version 10).

Results: A total of 154 patients were observed, who were divided in two equal groups. Average age was 29.58 years ±7.75SD with range of 16-42 years. In group A, out of 77 patients, there was 1 day prolongation of pregnancy in 18 (23.4%),in 42 (54.5%) there was 2 days prolongation of pregnancy followed by 17(22.1%)in whom pregnancy was prolonged for more than 2 days. While in-group B in 19(24.7%) there was 1 day prolongation of pregnancy,in 46(59.7%)there was 2 days prolongation of pregnancy followed by 12(15.6%) patients in whom pregnancy was prolonged for more than 2 days. Although the difference in prolongation of pregnancy in both the groups was insignificant with p-value 0.585 but it was prolonged in Group A. Post-treatment headache occurred to 15(19.5%) patients in group A and to 20(26%)patients in group B, however it did not reach statistical significance with p- value 0.336. Of the neonates born to mothers in group A 15(19.5%) were admitted in NICU while in group B 25(32.5%) were admitted in NICU with p-value 0.066.

Conclusion: Nifedipine is better treatment as compared to Nitroglycerine for preterm delivery.

Key Words: Nifedipine, preterm delivery, prolongation of pregnancy, headache, NICU and Nitroglycerine.

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INTRODUCTION

Pre-term labor is one of the most common complications of pregnancy and has a major role in neonatal mortality and morbidity.[1]Across 184 countries, the rate of preterm birth ranges from 5% to 18% of new born babies.[2]Almost 15 million infants are born preterm every year all over the world.[3]It affects around 9% of births in high income countries and an estimated 13% of births in low and middle income countries.[4]

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Preterm labouris the occurrence of uterine contractions of sufficient strength to bring about effacement and dilatation of the cervix before full term gestation and it occurs at 20-37 weeks.[5] Preterm labour is responsible for 50% of preterm births. It occurs in approximately 12% of pregnancies and is the leading cause of neonatal mortality in the United States.[6]Various drugs and strategies have been used for the treatment of preterm labor however mixed results have been reported.[7] Tocolytic drugs used commonly as a therapy for preterm labour are magnesium sulfate (MgSO4), Nifedipine and indomethacin.[8] Nifedipine has proved to be a safe drug in managing preterm labour.[9]As compared with other tocolytic agents, Nifedipine is more effective in prolongation of pregnancy, leading to fewer number of admissions to NICU and lesser occurrence of necrotizing enterocolitis, RDS and intraventricular hemorrhage.[9] Nifedipine and Nitroglycerine have been used globally for preventing preterm labour ,however no local data is available to confirm supremacy of either drug.[7]

This study is designed to compare outcome of Nitroglycerine and Nifedipine in females presenting with preterm labour to prolong their gestational age.

Until now, no local study is published and global data supports Nifedipine for prevention of preterm delivery till 48 hours but there is controversy regarding need for NICU care and maternal headache.[7] This study will help us to verify the role of Nitroglycerine and Nifedipine for the prolongation of pregnancy and know exact statistics regarding need of neonates stay in NICU and maternal headache. After completing this study superior drug will be used in future as first line treatment for managing preterm labour.

MATERIALS AND METHODS

Obstetrics and Gynaecology Department, PGMI Hayatabad Medical Complex, Peshawar was the place where the study was conducted from Jul 20, 2016 To Jan 19, 2017. Total sample size was 154 (77 in each group). Sampling technique was Consecutive (Non-Probability) Sampling. Design of the study was Randomized controlled trial. A total of 154 pregnant females aged 16-42 years presenting with preterm labour, as per definition described above were included in this study. These females had a cervical dilatation of> 1 cm and cervical effacement of $\geq$ 50%. All had singleton pregnancy(confirmed on USG). To avoid confounding factors, patients with ruptured membranes were excluded from the study. Patients having maternal and fetal indications for termination of pregnancy were also excluded from the study.

154 females(77 females in each group) were enrolled from labour ward of Obstetrics and Gynaecology department PGMI, HMC. After approval from hospital ethical committee all pregnant females fulfilling the required criteria were included in the study. An informed consent was taken and their basic demographic information (such as name and age), contact details and gestational age (weeks) were taken. All females were divided randomly using lottery method in two groups (Group-A and Group-B). In Group-A females were given 20mg Nifedipine orally as a loading dose. This could be repeated after 1 hour. If successful, a maintenance dose of 20 mg was started 6 hours from the last dose and continued Q.I.Dfor further 48 hours. The therapy for women in group-B was administration of transdermal Nitroglycerin patch Nitroderm 10, abdominally, which provides 10 mg nitroglycerin over 24 hours. Additional patch was applied in case contractions did not cease at the end of one hour. At one point in time no more than 2 patches were administered together. After 24 hours a fresh patch was applied. Patches were not removed until 12 hours after cessation of contractions. All females were followed up until the delivery of the baby; maternal headache and neonates admission to NICU as per operational definition were noted. All data were collected in an attached proforma by the researcher herself.

All the data was entered and analyzed in SPSS (version 10). Frequencies and percentages were calculated for categorical variables like prolongation of pregnancy and complications (post treatment headache, admission of NICU). Mean± SD was calculated for numerical variables like age, gestational age, parity and gravida. For comparing the prolongation of pregnancy and complications in both the groups, Chi-Square test applied. Prolongation of pregnancy and complications in both groups were stratified among the age, gestational age, parity and gravida to see the effect modifiers. P value of less than 0.05 was taken as significant. Post stratification chi square test was applied. All the results were presented as tables and charts.

RESULTS

Average prolongation of pregnancy in Group A was 40.09 hours ± 26.26SD. Out of 77 patients; in 42(54.5%) there was 2 days prolongation of pregnancy followed by 18(23.4%) patients who had 1 day prolongation in pregnancy in Group A.In Group B out of 77 patients; in 46(59.7%) there was 2 days prolongation of pregnancy followed by 19(24.7%) patients who had 1 day prolongation in pregnancy.In group A, 17(22.1%) patients had more than 2 days prolongation of pregnancy while in group B pregnancy was prolonged in 12(15.6%) patients for more than 2 days. Although the difference in prolongation of pregnancy in both the groups was insignificant with p-value 0.585 but it was prolong in Group A.

Table No.1: **Prolongation of pregnancy in both the groups**

		Groups		Total	P-Value
		A	B		0.5854
Prolongation of Pregnancy (in days)	1 Day	18 23.4%	19 24.7%	37 24.0%	
	2 Days	42 54.5%	46 59.7%	88 57.1%	
	> 2 Days	17 22.1%	12 15.6%	29 18.8%	
Total		77 100%	77 100%	154 100%	
Mean +- SD		40.09+ -26.26	36.93+ -23.64	38.51+ -24.96	0.4338

Group-B showed a higher rate of complications than group-A. Group A showed 19.5% post treatment headache. While in Group B, it was 26% of the patients. Admission in NICU in group A was 19.5% patients, while 32.5% found in Group B.

Table No.2: Comparison of complications in both the groups

		Groups		P- Value
		A	B	
Post Treatment Headache	Yes	15	20	0.336
		19.5%	26%	
	No	62	57	
		80.5%	74%	
Admission in NICU	Yes	15	25	0.066
		19.5%	32.5%	
	No	62	52	
		80.5%	67.5%	

DISCUSSION

Preterm birth remains one of the main causes of perinatal mortality and long term morbidity. More than 70% of the total perinatal mortality can be attributed to preterm birth.[10]

Preterm birth is becoming more and more common across low and middle income countries. In such countries the rate of preterm birth ranges from 7.4-13.3% while it is 8.6% in high income countries.[11] Multiple causes of perinatal morbidity including intraventricular haemorrhage, cerebral palsy, chronic lung disease and respiratory distress syndrome are due to Preterm birth .[12]

The performance of numerous tocolytic agents has been demonstrated by a number of studies but comparison between tocolytic agents of the same group has been made by only a few studies. Multiple drugs have been used to treat preterm labour but the choice for first line tocolytic drug still remains controversial.[13]

Code-Aqudelo et al., agrees with the authors who proposed that acalcium channel blocker, like Nifedipine can be administered as a first line therapy for tocolysis.[14-17] A Cochrane review about calcium channel blockers (CCBs) for acute tocolysis in preterm labor including 12 randomized controlled trials showed that when Nifedipine therapy is started, the preterm delivery risk before 34 weeks is decreased within 7 days, and neonatal outcomes are improved.[18]The differences in the result of this study is due to the fact that our sample comprised of local population.

When Nitroglycerin and Nifedipine were compared by Amorim et al., it was demonstrated that the rate of preterm labour within 48 hours of their administration was15.4% and 12.5% respectively.[19]A study by Dhawle et al.[20],showed that beyond 48 hours labour prolongation was significantly greater in the Nifedipine arm 88.4% as compared to Nitroglycerin 68.3%. Nifedipine prolonged pregnancy for 7 days in 72.1% and 14 days in 62.8% cases. This was not significantly different as compared to NTG which prolonged pregnancy for 7 days in 65.9% and for 14 days in 58.6% cases.[21,22] Our study took into consideration the complications too in terms of NICU admissions and maternal headache which showed significant results.

In this study, delivery was delayed for beyond 2 days by Nifedipine in 76.6% and by NTG in 75.3%, which was not significantly different. The average prolongation in pregnancyin the current study was 36.93 Hour +23.64 in the NTG group against 40.09hours+26.26 in the Nifedipinearm. This is same as the conclusionof Papatsonis et al[21] 39.2 in Nifedipinearm as compared to 22.1% in Ritodrine arm& Lees et al[22] 35.8 in NTG as compared to Ritodrine36.9.

CONCLUSION

To conclude, oral Nifedipine is more effective in delaying delivery beyond 48 hours as compared to transdermal NTG. Tocolysis was more frequently failed with transdermal NTG patch. This study also shows that the complication rate was higher with nitroglycerine as compared to Nifedipine in terms of post treatment headache and admissions of neonates to ICU. However to arrive at a final conclusion, further studies need to be conducted with a larger sample size and ones in which preterm labour is more precisely defined in terms of cervical length measurement using transvaginal ultrasound or fetal fibronectin assay.

Author's Contribution:

Concept & Design of Study:	Maryam Khan Badshah
Drafting:	Naeem Utman, Jehan Ara
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Revisiting Critically:	Maryam Khan Badshah, Naeem Utman
Final Approval of version:	Maryam Khan Badshah

Conflict of Interest: The study has no conflict of interest to declare by any author.

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