



CODEN [USA]: IAJ PBB

ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES<http://doi.org/10.5281/zenodo.3625753>Available online at: <http://www.iajps.com>

Research Article

**COMPARING THE EFFICACY OF NIFEDIPINE AND
NITROGLYCERINE AS TOCOLYTIC AGENT IN PRETERM
LABOR PATIENTS**

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Article Received: November 2019 **Accepted:** December 2019 **Published:** January 2020**Abstract:**

Objective: To compare the efficacy of nifedipine with nitroglycerine when used in preterm labor or pregnancy prolongation.

Methodology: This randomized control trial was conducted in the department of Gynecology and Obstetrics, Services Institute of Medical Sciences, Lahore, Pakistan from August 2016 to January 2017 and None probably consecutive sampling technique was used. Patients were divided into two groups; group N (nifedepine) and group NG (nitroglycerine). Blinding was done by lottery method. The main outcome variable of our study was efficacy of drug. Data were analyzed through SPSS version 23.

Results: A total 72 females were included in the study. The mean age and gestational age of the patients was 25.36±3.8 years and 32.09±1.78 weeks. Efficacy of drug used in group N was 88.9% and in group NG, efficacy was 61.1%. In group N, prolongation of pregnancy for 48 hours seen in 88.9% patients while in group NG this frequency was 61.1%. **Conclusion:** Nifedipine was a better tocolytic agent than nitroglycerin for the preterm patients when used for pregnancy prolongation. (Rawal Med J 201;43:280-284).

Keywords: Nifedipine, nitroglycerine, preterm labor, tocolytic agent.

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Please cite this article in press Mustafa Awais et al., *Comparing The Efficacy Of Nifedipine And Nitroglycerine As Tocolytic Agent In Preterm Labor Patients.*, Indo Am. J. P. Sci, 2020; 07(01).

INTRODUCTION:

Delivery of fetus before thirty seven weeks (259 days) is labeled as preterm birth.¹ Preterm birth is multifactorial and its incidence has increased one and half fold in last few years and is a leading cause of fetal mortality worldwide.² About 75% mortality and morbidity of fetus and mother occurs during preterm birth. Pattern and mechanism of preterm labor is unknown but in all cases force full uterine contractions are common.³ Uterine contractions may be physiological and pathological that ends with preterm delivery of fetus.

Preterm labor is an unresolved issue in obstetrical profession and has lot of challenges for fetal and maternal outcomes. Preterm labor can be stopped with use of tocolytic medication, antibiotics and corticosteroids; in cases of preterm labor progesterone can be used for maintenance of tocolytic effect.^{6,7} Many techniques have been used and recommended to stop the preterm labor. Use of excessive water to prevent dehydration and complete bed rest are famous but do not have any effect in inhibition of preterm labor.⁸ It has been shown that parenteral tocolytic agents have better outcome as compared to oral.⁹ In preterm babies, corticosteroids are used for fetal lung maturity.¹⁰ Not multiple but a single dose of corticosteroids reduced the incidence risk of respiratory distress and parental mortality rate. Efficacy of transdermal nitroglycerine has been observed in 64% tocolysis successfully within 48 hours. In another study, Nifedipine showed less incidence neonatal jaundice, respiratory distress, enterocolitis and vascular hemorrhage as fetal outcomes.¹¹ A number of cross sectional studies available on efficacy of nitroglycerine and nifedipine as tocolytic agents but few comparisons of two regimes (Nifedipine vs Nitroglycerine) have been published. This study aimed to investigate the efficacy of these two regimes as tocolytic agents.

METHODOLOGY:

This randomized control trial was carried out in the department of Gynecology and Obstetrics, Services Institute of Medical Sciences, Lahore, Pakistan from March 2016 to March 2017. Study was started after ethical approval from hospital ethical board and an Informed consent was taken from all patients. Sample size was calculated with WHO sample size calculator using following figures: CI 95%, Power of study 80% proportion of outcome variable (p1) 21%. Patients with multiple gestation, obstetric bleeding, fetal anomaly, allergic reactions, intrauterine death and patients who refused to participate in the study were excluded. Successful tocolysis was labeled as prolongation of

pregnancy for minimum 48 hours (corticosteroids were given in this time for fetal lung maturity) after therapy of tocolysis. Failed or unsuccessful tocolysis was labeled when delivery occurred within 48 hours.

All patients were admitted and all fetal and maternal monitoring was started. Pelvic examination was done and then continuous monitoring of contractions started. To overcome the nitroglycerine induced hypotension, 500 ml of normal saline was infused. Patients were divided into two equal groups; group N and group NG. Patients were allocated in two groups by using lottery method. After confirmation of diagnosis and initial investigations, tocolytic therapy was started in group N with 20 mg Nifedipine oral stat, if contractions persisted, 20 mg was given after 30 minutes for two further doses; maximum 160 mg can be given safely as stated and approved by Royal Hospital for women. Tocolysis in group NG was done with 10 mg patch of nitroglycerine applied at abdomen. If there was no improvement observed another patch was applied; never used more than 2 patches.

All data were analyzed using SPSS version 23. Post stratification chi square test was applied to see effect modification. P? 0.05 was considered as significant.

RESULTS:

A total of 72 female patients were included in the study. Mean age and gestational age of the patients was 25.36 ± 3.8 years and 32.09 ± 1.78 weeks. 56.9% (n=41) patients had 15-25 years of age and 43.1% (n=31) patients fell in age group 26-40 years. Gestational age distribution showed that majority of the patients i.e. 58.3 (n=42) had gestational age 29-32 weeks and 41.7% (n=30) had 33-36 weeks of gestational age (Table 1).

Mean age and gestational age of patients in group N was 25.33 ± 2.49 years and 31.13 ± 1.55 weeks, respectively. Mean age and gestational age of patients in group NG was 25.38 ± 4.8 years and 33.05 ± 1.47 weeks, respectively. Mean age and gestational age of the patients in which the drug was found to be affective was 26.42 ± 3.27 years and 32.01 ± 1.83 weeks, respectively while the mean age and gestational age of the patients in which the drug was ineffectuated was 22.16 ± 3.53 and 32.33 ± 1.64 weeks, respectively (Table 2).

The main outcome variable of our study was efficacy of drug. Efficacy of drug used in group N was 88.9% and in group NG, efficacy was 61.1% (Fig. 1). It was also noted that, in group N,

prolongation of pregnancy for 48 hours presented in 88.9% (n=32) patients while in group NG this frequency was 61.1% (n=22) (Table 2). When Chi-Square was applied to check the association, it was noted that efficacy of drug was significantly

associated with age in both groups (p=0.006 and 0.039). But efficacy of drug was not significantly associated with gestational age (p=0.053) (Table 3).

Table 1. Demographic variables (n=72).

Characteristics	Frequency	Percentage
Stratified Age		
15-25 years	41	56.9
26-40 years	31	43.1
Total	72	100.0
Stratified Gestational Age		
29-32 Weeks	42	58.3
33-36 Weeks	30	41.7
Total	72	100.0
Descriptive Statistics		
	Mean±S.D	
Age	25.36±3.8 years	
Gestational Age	32.09±1.78 weeks	

Table 2. Demographic variables in groups.

Prolongation of Pregnancy for 48 Hours			
Groups	Presence	Frequency	Percent
N	Yes	32	88.9
	No	4	11.1
	Total	36	100.0
NG	Yes	22	61.1
	No	14	38.9
	Total	36	100.0
Descriptive Statistics			
Groups	Variable	Mean±S.D	
N	Age	25.33±2.49 years	
	Gestational Age	31.13±1.55 Weeks	
NG	Age	25.38±4.8 years	
	Gestational Age	33.05±1.47 weeks	
Descriptive Statistics With respect to Efficacy of Drugs			
Efficacy of Drug	Variable	Mean±S.D	
Yes	Age	26.42±3.27 Years	
	Gestational Age	32.01±1.83 weeks	
No	Age	22.16±3.53 years	
	Gestational Age	32.33±1.64 weeks	

Fig. 1. Efficacy of drugs in groups.

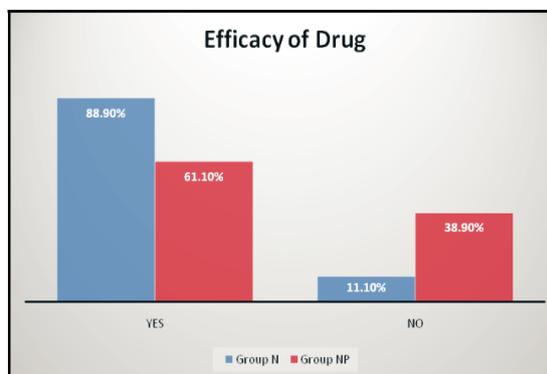


Table 3. Association of efficacy of drug with effect modifiers (n=72).

Effect Modifiers		Efficacy of Drugs		Total	P-value
		Yes	No		
Groups	N	32	4	36	0.006*
	NG	22	14	36	
Total		54	18	72	
*P-value is statistically significant with Pearson Chi-Square value = 7.40, d.f=1					
Stratified Age	15-25 Years	27	14	41	0.039*
	26-40 Years	27	4	31	
Total		54	18	72	
*P-value is statistically significant with Pearson Chi-Square value = 4.25, d.f=1					
Stratified Gestational Age	29-32 Weeks	35	7	42	0.053*
	33-36 Weeks	19	11	30	
Total		54	18	72	
*P-value is statistically insignificant with Pearson Chi-Square value = 3.73, d.f=1					

The main outcome variable of our study was efficacy of drug. Efficacy of drug used in group N was 88.9% and in group NG, efficacy was 61.1% (Fig. 1). It was also noted that, in group N, prolongation of pregnancy for 48 hours presented in 88.9% (n=32) patients while in group NG this frequency was 61.1% (n=22) (Table 2). When Chi-Square was applied to check the association, it was noted that efficacy of drug was significantly associated with age in both groups (p=0.006 and 0.039). But efficacy of drug was not significantly associated with gestational age (p=0.053) (Table 3).

DISCUSSION:

The main outcome variable of our study is efficacy of drug. Efficacy of nifedipine was 88.9% and that of nitroglycerine was 61.1%. A study concluded that nifedipine was a better tocolytic drug when used in preterm labor as compared to nitroglycerine.¹² Efficacy of nifedipine was reported 74% and 52% in nitroglycerine cases. Due to their adverse effects and short outcomes these drugs were replaced with oxytocin, ca⁺ channel openers and blockers. A new drug nifedine has

been introduced for reduction of uterine contractions. It is a Ca⁺ channel antagonist that blocks the Ca⁺ influx in cells of myometrium and oral intake gains peak plasma level within 45 minutes and has half life 2-3 hours.¹³

In another study, Parveen et al observed the tocolytic efficacy of nifedipine as 87.5% and similar finding for nitroglycerin 87.5%.¹⁴ Tocolytic agents like betamimetics have globally accepted efficacy but at the same time lot of adverse effects like cardiac arrhythmias and increase in fetal heart rate reduced their use. In our study, we observed that in nifedipine 88.9% patients had prolonged pregnancy while in nitroglycerine 61.1% patients had prolong pregnancy. Conde-Agudelo et al conducted a study in 2011 on comparison between nifedipine and magnesium sulphate in management of preterm labor. They reported that nifedipine was more effective in β -adrenergic agonist as Mg sulphate is also. There was no significant difference in two drugs when assessed on basis of tocolysis.¹⁵ Results of our study are again comparable with this

study. Hangekar et al conducted a study on efficacy of nifedipine and concluded that it was a safe and effective medicine in inhibition of preterm labor.¹⁶ Results of his study showed success rate of nifedipine 84.92%. Our findings were similar.

Spirlet et al conducted a study on tocolytic effect of different doses of nitroglycerine and reported that it was not effective in inhibition of uterine contractions in case of severe preterm labor. They reported that at maximum dose of 1.2 mg/h success rate is only 54% and also had complications like hypotension and headache.¹⁷ In our study, we also observed lower success rate of nitroglycerine as compared to nifedipine. Several reports concluded that nitroglycerine was sufficient tocolytic agent to prolong pregnancy till 48 hours.¹⁸⁻²⁰ However, in comparison nifedipine provided these effects on very low doses, this being the advantage of nifedipine over nitroglycerine.²¹

CONCLUSION:

The observations of our trial suggest that nifedipine is a better tocolytic agent than nitroglycerin for the preterm patients, when used for pregnancy prolongation.

Author Contributions:

Conception and design : Mustafa Awais

Collection and assembly of data: Momina Awais

Analysis and interpretation of the data: Mustafa Awais

Drafting of the article: Momina Awais

Final approval and guarantor of the article: Mustafa Awais

Conflict of Interest: None declared

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