Original Article

Comparative Study of Tocolytic Efficacy of Nifedipine and Nitroglycerine

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Abstract

Objectives: To compare the efficacy of nifedipine and nitroglycerine in preterm labour for prolongation of pregnancy for at least 48 hours.

Study Design: A Randomized control trail.

Methodology: This study was conducted in Gynae unit 2 of Services Institute of Medical Sciences Lahore. Total 100 patients were selected and randomly divided into two equal groups and treated with Nifedipine and Nitro glycerin. Sample size of 100 (50 in each group) is calculated with 80% power of test, 5% level of significance and taking expected percentage of efficacy (in terms of successful tocolysis of 48 hours or more) in both groups 64% in nitroglycerine group versus 88% in nifedipine group in patients with preterm labour.

Result: The age range of patients was 15-40 years. The mean gestational age was 33.38±1.79 in group A and 32.19±1.24 in group B. There were 37 (74%) patients had an efficacy of drug in group A and 26 (52%) patients were in group B with a p value (0.023) which is statistically significant.

Conclusion: Nifedipine is a safe and effective drug for prolongation of gestational age and tocolytic efficacy as compared to nitroglycerine.

Key Words: Preterm birth, Gestational age, Nifedipine, Nitroglycerine, Tocolysis efficacy.

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Introduction

Preterm birth is the birth of a baby before 37 weeks of gestation (as confirmed by the first day of last menstrual period or by first ultrasonography for fetal gestational age).[1] Regular palpable painful uterine contraction may precede preterm delivery.[2] By gestational age 5% of preterm birth occurs at less than 20 weeks (extreme prematurity) 15% at 28-31 weeks (late prematurity).[3] Exact cause of preterm labour is still unknown, but a number of risk factor include demographic factors such as maternal age (<18 years of >35 years), low socioeconomic or educational status, single motherhood, low pre-pregnancy weight and aspects of obstetric history such as previous preterm deliveries.[4]

There is no recent accurate worldwide data but estimates show the preterm birth rate ranges from 5% in developed countries to 25% in developing countries.[5] In Europe, preterm birth rate is 5-9% and in the USA it even rose to 12-13% in last decades[3] preterm birth is the major contributor to perinatal

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morbidity and mortality. Newborn born at 34 weeks of gestation has 20 times more risk of morbidity compared to infants born at term.[6] Approximately 65% non-anomalous fetal and neonatal deaths are attributed to complications of prematurely.[7] Preterm infants have increased risk for RDS[8,] long term neural developmental problem such as cerebral palsy, mental retardation, disabilities of vision and hearing.[9]

Pharmacological therapy for acute preterm labour is tocolytic, corticosteroids, antibiotics though controversial.[10] Progesterone is used as maintenance tocolytic agent in women with recurrent preterm labour.[7,8] Tocolytic drugs are given to prolong pregnancy for at least 48 hours to allow parenteral maternal corticosteroids administration for fetal lung maturity and in utero transfer to tertiary care hospital, a single course of corticosteroids administered to women with preterm labour reduces the risk of respiratory distress syndrome, perinatal morbidity, and mortality.[11]

The rationale of the study is to compare the efficacy of nifedipine and nitroglycerine in preterm labour, as no randomized controlled trial is available in the local literature. Based on study result the drug with better tocolytic efficacy can use in our patients with preterm labour.

Methodology

This study was carried out in the Department of Obstetrics and Gynaecology, Unit-II, SIMS/Services Hospital, Lahore. Study period was six months from March, 2012 to September 2012. Sample size of 100 (50 in each group) is calculated with 80% power of test, 5% level of significance and taking expected percentage of efficacy (in terms of successful tocolysis of 48 hours or more) in both groups 64% in nitroglycerine group versus 88% in nifedipine group in patients with preterm labour.

After proper permission from ethical committee patients were consecutively selected from the Gynae Unit II. Patients consent was taken for therapy and research. Patients randomly divided into two groups. One group was given nifedipine 10mg orally at an interval of 15 minutes maximum up-to 10 doses and after the 10th dose and afterward observed for 4 hours for stoppage of palpable uterine contraction and then followed by 20mg orally nifedipine 8 hourly for 48 hours. The second group was applied nitroderm patch (nitroglycerine) 10mg per 24 hours and observed for stoppage of palpable uterine contraction.

All the data was analyzed using SPSS 16 and chi square test used for comparison of efficacy.

Results

Total one hundred patients were included in the study, 50 patients were in group A (Nifedipine) and the remaining 50 patients were in group B (Nitroglcerine) treated respectively.

The age range of patients was 15-40 years. The mean & standard deviation were 25.82±3.42 in group A and 26.18±4.18 in group B. A major proportion of the patients were between 26-34 years of age out of that there were 27 (54%) in group A and 28 patients (56%) in group B. while 23 patients (46%) in group A were between 15-24 years of age and 28 (56%) patients in group B. No patient in both groups >35 years of age. (Table I)

Table I: Proportion of the patients between the two groups (n=50)

Age (years)	Group A (Nifidipine) (n=50)		Group B (Nitroglycerine) (n=50)	
	No. of Pts.	%age	No. of Pts.	%age
15 – 25	23	46	28	56
26 – 35	27	54	22	44
>35	0	0	0	0
Total	**50**	**100**	**50**	**100**
Mean ±SD	**25.82±3.42**		**26.18±4.18**	

Out of total 100 patients, 16 (32%) were gestational age in group A and 18 (18%) patients in group B between 29-32 weeks of gestation. There were 34 (68%) in group A between 33-36 weeks of gestational age in group B. The mean gestational age was 33.38±1.79 in group A and 32.19±1.24 in group B. (Table II)

Table III shows the prolongation of pregnancy for 48 hours in both groups. There were 37 (74%) patients had prolongation of pregnancy for 48 hours in group A while 26 (52%) patients in group B. Statistically there was a significant difference of prolongation of

pregnancy for 48 hours in both groups with a p value (0.023) which shows group A is better than group B.

Table II: %age of Gestational age in each group

Gest. age (weeks)	Group A (n=50)		Group B (n=50)	
	No. of Pts.	%age	No. of Pts.	%age
29 –32	16	32	18	12
33 – 36	34	68	32	88
Total	**50**	**100**	**50**	**100**
Mean ± SD	**33.38±1.79**		**33.19±1.24**	

Table III: Prolongation of pregnancy in both groups

Pregnancy for 48 Hours	Group A (n=50)		Group B (n=50)	
	No. of Pts.	%age	No. of Pts.	%age
Yes	37	74	26	52
No	13	26	24	48

There were 37 (74%) patients had an efficacy of the drug in group A and 26 (52%) patients were in group B with a p value (0.023) which is statistically significant. Group A shows much difference of efficacy of drug than group B. (Table IV)

Table IV: Difference in Drug Efficacy in both groups

Efficacy of drug	Group A (n=50)		Group B (n=50)	
	No. of Pts.	%age	No. of Pts.	%age
Yes	37	74	26	52
No	13	26	24	48

Discussion

Preterm birth (PTB) is a major determinant of neonatal mortality, morbidity and childhood disability and remains one of the most serious problems in obstetrics. The incidence of preterm birth is generally around 6–7% of all births. By gestational age, 5% of preterm births occur at less than 28 weeks (extreme prematurity), 15% at 28–31 weeks (severe prematurity), 20% at 32–33 weeks (moderate prematurity), and 60–70% at 34–36 weeks (late preterm). It is estimated that one-third of these low birth weight deliveries are due to preterm delivery. Despite numerous management protocols proposed, the incidence of preterm birth has changed little over the past 40 years.[11, 12, 13, 14]

Preterm birth is a significant cost factor in healthcare, not even considering the expenses of long-term care for individuals with disabilities due to preterm birth. The costs increase exponentially with decreasing gestational age and weight.[15]

The most effective intervention to improve newborn outcomes for women in preterm labour is the administration of corticosteroids. Pharmacological treatment of preterm labour should aim at preventing preterm delivery for at least 48 hours.[16]

Approximately 2/3rd of all preterm births occur spontaneously after premature labour or premature rupture of the membrane.[17]

It is important to identify the risk factors associated with preterm delivery which includes

It has multifactorial etiology. Patients of extreme ages, Low maternal pre-pregnancy weight, cigarette smoking, Malnutrition and malabsorption leading to anemia.[19, 20, 21]

There is strong correlation between infection and preterm labour. Dr. Hosny and colleagues have found the four groups of potential microorganisms. However role of antibiotic is controversial and it varies with gestational age. Maternal stress significantly is an independent risk factor for preterm birth.[22, 23, 24]

The tocolysis is to delay preterm birth to allow time for maternal administration of corticosteroids and in-utero transfer to a tertiary perinatal center.

A wide variety of tocolytic drugs available including beta mimetic, atosiban, Nitric oxide Donor, (GTN Glyceryl trinitrate. Patch) and calcium channel Blocker.[25, 26]

Nifedipine widely used calcium channel blocker, and Glyceryl Trinitrate are both relatively cost effective, readily available in our set up so we will try to sort out which will be more effective regarding tocolytic therapy.[25]

In our study, we have included 100 patients with preterm labour which was defined as palpable

uterine contraction leading to cervical dilatation up to 4 cm. They were divided into 2 groups 50 of each and treated with 2 drugs namely nifedipine and GTN glyceryl nitrate respectively. They were aged from 15-40 years. The drug efficacy of both drugs was tested in terms of delaying pregnancy for 48 hours. Our study results showed drug efficacy for Nifedipine 74% as compared to Glyceryl Trinitrate which had 52% drug Efficacy.

One of the Comparative study of Nifedipine and nitroglycerine by Ammorium et al also showed efficacy of Nifedipine was 87.5% greater than of nitroglycerine 64%.[25]

The currently available evidence supports calcium-channel blockers appear to have a good maternal and fetal safety profile[26]. Nifedipine and Glyceryl Trinitrate are both relatively cost effective, and readily available in our set up so the comparative study was performed. In one of systemic review of 12 randomized, controlled trails Nifedipine appeared to reduce the frequency of neonatal respiratory distress syndrome, necrotizing enterocolitis, intraventricular hemorrhage & neonatal jaundice Nifedipine is effective for fetus.[27, 28] Tocolytics like betamimetics have proven efficacy, but potentially serious side effects like cardiac arrhythmia's & hypokalemia, effect on fetal heart rate as it crosses the placenta. Prostaglandin synthesis inhibitor (indomethacin) is also effective tocolytic but with fetal side effects like premature closure of ductus arteriosus after 32 weeks of pregnancy.[29]

Calcium channel blockers have the highest probability of delaying delivery and improving neonatal outcomes. Nifedipine is a safe and effective drug for prolongation of gestational age for more than 48 hours and tocolytic efficacy as compared to nitroglycerine with a p value of 0.023 which is statistically significant. The currently available evidence supports the view that it is safe for both mother and baby, and suggests that when used for tocolysis it may be associated with improved neonatal outcomes when compared with other tocolytic drugs.[30]

Conclusion

Based on the comparison with other studies and results of our study it suggests that the Nifedipine as a better tocolytic agent with good maternal and fetal safety profile as compared to another drug like Glyceryl Trinitrate. It can be used in prolongation of pregnancy. This study was conducted in one unit. It is recommended for further research.

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