ORIGINAL ARTICLE

To Compare Efficacy of Nifedipine and Nitroglycerine as Tocolytic Agent in Preterm Labor patients

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ABSTRACT

Aim: To compare Nifedipine and Nitroglycerine to find out the better tocolytic agent in terms of pregnancy prolongation and safety.
Study Design: A randomized controlled trial.
Methods: This study was conducted in the Department of Gynecology and Obstetrics in Saira Miraj Memorial Hospital, Lahore. In this study 200 women were randomly divided into two groups in preterm labour receiving Nifedipine and Nitroglycerin.
Results: Tocolytic effect of Nifedipine and Nitroglycerin was directly compared. Total two hundred patients were included in this study, 100 patients were in group A (Nifedipine) and 100 patients were in group B (Nitroglcerine) and we measured the prolongation of pregnancy for 48 hours in both groups. There were 74 patients had prolongation of pregnancy for 48 hours in group A and 52 patients in group B. SPSS computer base software was used for statistical analysis. Statistically there was a significant difference of prolongation of pregnancy for 48 hour in both groups with a p value (0.023).
Conclusion: Nifedipine is a better tocolytic agent than Nitrogycerin for the preterm patients.
Keywords: Preterm labour, Nifedipine, Nitroglycerin, Tocolysis.

INTRODUCTION

Preterm delivery is defined by a birth occurring before 37 weeks of gestation or before 259 days from the last menstrual period. Prematurity is multifactorial and its incidence has increased during the last decade in most developing countries[1-2]. The leading cause of infant morbidity and mortality in developed countries, accounting for 75% of perinatal deaths[3]. The mechanisms for preterm labour are still unclear. It could be associated either with a premature activation of the physiological contracting process or with a pathological factor responsible for uterine contractions, leading to preterm delivery. Regular palpable painful uterine contraction may precede preterm delivery[4]. By gestational age 5% of preterm birth occurs at less than 20 weeks 15% at 28-31 weeks[5]. Pharmacological therapy for acute preterm labour is tocolytic, corticosteroids, antibiotics though controversial[6] Progesterone is used as maintenance tocolytic agent in women with recurrent preterm labour[7] allow parenteral maternal corticosteroids administration for fetal lung maturity and in utero-transfer to tertiary care hospital, single course of corticosteroids administered to women with preterm labour reduces the risk of respiratory distress syndrome, perinatal morbidity and mortality[8].

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The side effects as well as the limited success have stimulated the investigators to search for new drugs such as oxytocin antagonists, calcium channel openers and calcium channel blockers.[9] Nifedipine, type II calcium channel antagonist inhibits calcium influx into myometrial and other cells thereby reduces muscle contractility. It reaches peak plasma level within 45-60 minutes after being taken orally and has plasma half life of 2-3 hour[10]. Tocolytic drugs are given to prolong pregnancy for at least 48 hours to both nitroglycerin and Nifedipine[11].

Drugs safety and side effect profile is a major concern not only for the pregnant women but also for the fetus. Nifedipine and nitroglycerine showed tocolytic efficacy of Nifedipine was 87.5% and of nitroglycerine 87.5%[12]. An experimental study carried out at tocolytic. Previously one study of efficacy and safety profile of transdermal nitroglycerine showed that 64% had successful tocolysis of 48 hours[13].

In one of systemic review of 12 randomized, controlled trails Nifedipine appeared to reduce frequency of neonatal respiratory distress syndrome, necrotizing enterocolitis, intraventricular hemorrhage & neonatal jaundice Nifedipine is effective for fetus[15].

MATERIAL AND METHODS

In this study 200 women were randomly divided into two groups in preterm labour receiving Nifedipine and Nitroglycerin. Patients with age from 15 to 40 years which was confirmed by date of birth. Parity up to gravida 5 known by previous history. Patients with

gestation of (>24 weeks and <37 weeks of gestation) (determined by first day of last menstrual period). Patients with singleton pregnancy (confirmed on ultrasonography). Patients with preterm labour contraction and cervical softening or effacement upto 4cm of dilatation (determined by per abdominal examination and pelvic examination). Following patients were excluded: Patients with premature rupture of membrane (confirmed on per speculum examination).

Vaginal bleeding due to placenta previa or placental abruption (determined by per speculum examination). Known fetal anomalies (confirmed on USG). Patients with intrauterine death (confirmed on USG). Patients with hypertension (BP >130/90mmHg at least 2 readings taken 6 hours apart). Permission was taken from Hospital Committee and patients were selected from the labour room of Saira Meraj Memorial Hospital, Gynecology Ward. Informed consent was taken from the patients after discussing the risks and benefits of the therapy and use of data for the research work. The patients were divided randomly by using lottery method in two groups.

One group was given Nifedipine 10mg orally at interval of 15 minutes maximum upto 10 doses and after 10^{th} and then followed by 20mg orally Nifedipine 8 hourly for 48 hours. Second group was applied nitroderm patch 10mg and observed for stoppage of palpable contraction. Tocolysis was considered successful in terms of prolongation of pregnancy for more than 48 hours at least.

The quantitative variable like gestation age was expressed as mean and standard deviation. Frequency and percentages were calculated for qualitative variables like efficacy of the Nifedipine and nitroglycerin. Chi-square test was used to compare efficacy in both groups. P value <0.05 was considered as statistically significant dose observed for 4 hrs for stoppage of palpable uterine contraction

RESULTS

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. There were 54 patients (54%) in group A and 56 patients (56%) in group B while 46 patients (46%) in group A between 15-24 years of age and 56 (56%) patients in group B. No patient in both groups >35 years of age (Table 1). Out of total 200 patients, 32 (32%) were gestational age in group A and 36 (18%) patients in group B between 29-32 weeks. There were 68 (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 2). Table 3 shows the prolongation of pregnancy for 48 hours in both groups. There were 74 (74%) patients had prolongation of pregnancy for 48 hours in group A while 52 (52%) patients in group B. Statistically there was a significant difference of prolongation of pregnancy for 48 hour in both groups with a p value (0.022) which shows group A is better than group B. There were 74 (74%) patients had efficacy of drug in group A and 52 (52%) patients were in group B with a p value (0.032) which is statistically significant. Group A shows much difference of efficacy of drug than group B (Table 4).

Table 1: Age distribution of patients

Age (yrs)	Group A	Group B
15 – 25	46(46%)	56(56%)
26 – 35	54(54%)	56(56%)
>35	0	0
Mean±SD	23.25±3.36	24.26±4.16

Table 2: Frequency of gestational Age (weeks)

Gestational age	Group A	Group B
29 –32 weeks	32(32%)	36(36%)
33 – 36 weeks	68(68%)	64(64%)
Mean±SD	33.38±1.79	33.19±1.24

Table 3: Frequency of prolongation of pregnancy for 48 hrs

Pregnancy for 48 Hours	Group A	Group B
Yes	74(74%)	52(52%)
No	26(26%)	48(48%)

Table 4: Frequency of efficacy of drug

Efficacy of drug	Group A	Group B
Yes	74(74%)	52(52%)
No	26(26%)	48(48%)

DISCUSSION

Preterm birth incidence is generally around 6–7% of all births. In the USA the incidence is 12%. Despite numerous management protocols proposed, the incidence of preterm birth has changed little over the past 40 years. Preterm birth is the leading cause of neonatal mortality both in developed and developing countries. Preterm labour is the most common cause for antenatal hospitalization in developed countries. In our study the mean age of patients were 25.82±3.42 in group A and 26.18±4.18 in group B. The age range of patients was 15-40 years of age. A major portion of patients was in 15-25 years of age. In this age there were 46 (46%) patients in group A and 56(56%) were in group B. In age between 26-35 there were 54(54%) in group A and 56(56%) patients in group B. There was no patient in both groups >35 years of age. Studies reported by different authors, in premature neonates, antenatal corticosteroids reduce morbidity and mortality. Tocolytic therapy may therefore have an important role in improving outcomes from preterm delivery. Preterm births in the

United States alone 12.3% of all births in 2008 and 29% of these being less than 34 weeks' gestation, preterm delivery is an important public health issue[16] drugs have been used for tocolytic therapy. These include beta agonist, magnesium sulfate; prostaglandin inhibitors, calcium channel blockers such as Nifedipine; and others with unique side effects and mechanism of action .In this study the mean and standard deviation of gestational age were 33.38±1.79 weeks in group A and 34.10±1.24 weeks in group B.

Tocolytics like betamimetics have proven efficacy, but potential serious side effects like cardiac arrhythmia's & hypokalemia ,effect on fetal heart rate as it crosses 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[17].

Calcium channel blockers like Nifedipine is safe & effective but hazardeous in women with evidence of cardiovascular disease or unstable hemodynamically sulphate is ineffective tocolytic agent with adverse outcome[18] as the first-line tocolytic was safe. However, severe maternal hypotension can occur and close monitoring of vital signs is warranted[19]. Oxytocin receptor antagonist atosiban is effective but expensive agent, complicated intravenous route of administration & not easy availibility[20].

Nifedipine appears to be at least as effective as other tocolytic agents is more effective with the advantage of less maternal side effects. 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[21].

Nifedipine appears to be superior to ß2-adrenergic-receptor agonists and magnesium sulfate and should be considered as the first-line tocolytic agent for the management of preterm labor. In our study 74(74%) patients had prolongation of pregnancy for 48 hours in group A while 52(52%) in group B and the same also in efficacy of drug in both groups. In comparison of Nifedipine and nitroglycerine both drugs were used to see the tocolytic efficacy of drugs. In is concluded that our study shows the tocolytic efficacy of Nifedipine is a safe and effective for prolongation of pregnancy for 48 hours as compare to nitroglycerine with a p value (0.032) which is statistically significant.

CONCLUSION

Nifedipine is a safe and effective drug as a tocolytic agent compared to nitroglycerine.

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