ABSTRACT

OBJECTIVE: To compare the effectiveness of nitroglycerine transdermal patch verses oral nifedipine in suppression of preterm labor.

STUDY DESIGN: Cross sectional study.

PLACE AND DURATION: An interventional study was conducted in Gynecology and Obstetrics Department of Cantonment General Hospital, Rawalpindi from June 1, 2013 to May 31, 2015.

METHODOLOGY: 72 patients were included in the study after exclusion criteria i.e medical and obstetrical problems and congenital anomalies. All the patients were divided into two groups i.e 36 patients were randomized in each group with gestational age of 26-35 weeks. Suppression of labor up to 7 or more than 7 days, adverse effects and neonatal outcome in both the groups were compared.

RESULT: In nitroglycerine group tocolysis was achieved in 80.6% of patients as compare to nifedipine group in which 86.2% patients attained successful tocolysis and the mean prolongation of gestation age in group 1 was 28% as compare to group 2 which was 23% beyond 48 hours. Headache was observed in 28.5% whereas no complaints of headache was noted in group 2. Tachycardia was observed in 16.6% in group 2 but it wasn’t observed in group 1. There was no marked difference in the neonatal outcome of both groups.

CONCLUSION: Nitroglycerine transdermal patch is as effective as oral nifedipine in inhibition of preterm labor but oral nifedipine has better side effects profile.

KEY WORDS: Nitroglycerone, Nifedipine, Transdermal patch, Tocolysis, Preterm labour.

INTRODUCTION

‘Preterm labor’ is defined as regular contraction of uterus and cervical changes before 37 weeks of gestation1. Preterm birth is the second most common cause of death in children younger than 5 years after pneumonia. World health organization has estimated 12.9 million births worldwide were preterm in 2005. Rate of preterm labor ranges between 5% to 18% across 184 countries. The prevalence of preterm birth has also raised in United States in last two decades i.e 17% where as in Pakistan rate of preterm delivery is 15.8% according to WHO. Total number of preterm birth is 748100 in Pakistan. Almost 1 million babies die each year due to complication of preterm delivery, those who survive may face physical or mental disability.

Management of preterm labor and prevention of preterm delivery have always been a serious concern for obstetrician in nearly every decade. Despite in advancement in obstetrics incidence of preterm babies is still high which leads to long term physical and mental complication. About 40-45% of preterm births occur after spontaneous preterm labor. The main focus of treatment of preterm labor is to inhibit uterine contraction with tocolytic agents to prolong pregnancy. The best tocolytic agent should be effective in averting preterm delivery, easy in administration and able to improve neonatal outcome with fewer adverse effects.

Nifedipine is considered as a first line tocolytic agent suggested by some researcher and authors, who reduces the risk of preterm delivery and prolong gestation age for up to 7 days more. Nitroglycerine is another tocolytic agent which is used from last few decades for inhibition of labor. It has high first pass metabolism by liver so to avoid this complication transdermal route is used so that sufficient level of drug reaches plasma level. It delays the delivery by relaxing the smooth muscles of uterus and also improve blood flow to the uterus and placenta.

Besides these drugs several other agents are used for tocolysis but unfortunately there is no clear evidence that which agent should be used as an 1st line agent for tocolysis.

In our study comparison between nitroglycerine transdermal patch and oral nifedipine is compared for the tocolysis in preterm labor. Safety, efficacy, fetal outcome and adverse effects of both the drugs are compared. The objective of our study is to compare the effectiveness of nitroglycerine transdermal patch versus oral nifedipine in suppression of preterm labor.
METHODOLOGY

This study design was interventional done in Cantonment General Hospital, Rawalpindi during the period of 1st June 2013 to 31st May 2015. It was a cross sectional observational study in which those patients with preterm labor were included whose gestational age was between 26-35 weeks, painful contraction of 2-3 in 10 minutes, intact membranes, effacement of 2cms or less, cervical dilatation of 3 or less than 3 cm. Those patients with ruptured membranes, antepartum hemorrhage, preeclampsia or eclampsia, fetal demise, congenital anomalies, history of chorio amnitis, cervical dilatation more than 3cm or and patients allergic to nifedipine or nitroglycerine and with medical problems were not included.

During two years 72 patients were included in the study. All the patients were randomized in two groups, each group containing 36 patients (n=36) after exclusion criteria. In Group-1 10mg nitroglycerine transdermal patch was applied to women anterior abdominal wall for 24 hours to inhibit preterm labor. If the contraction persisted beyond two hours another nitroglycerine patch of same dosage was applied. Patches were replaced by new patches 24 hours after initiation of treatment.

In Group 2 all patients (n = 36) with preterm labor were given loading dose of 20mg oral nifedipine, if there were persistent contraction after 1 hour then similar dose was repeated if labor was suppressed with initial dose then maintenance dose of 20mg 6 hourly given for 48 hours. Treatment was labeled as failed when both the drugs were not successful in suppression of preterm labor or prolongation of gestation beyond 48 hrs. In such cases therapy was stopped and patients were managed accordingly. The study outcome was measured in terms of prolongation of duration of labor (tocolysis), gestational age at the time of delivery, adverse effects of drugs and fetal outcome. The statistical data was analyzed on SPSS 17. Test and chi square are used to analyses both the groups.

RESULT

The study included 72 women with preterm labor and were divided into two groups. Each group had 36 patients i.e. Group 1 (NTG gp) n=36 and Group 2 (nifedipine gp) n=36. Patients age range was between 20yrs to 35 yrs with mean of 26.52+_4 in both groups. In group 1 there was history of preterm labor and delivery in 6 patients (n=6) 13.8% where as in Group 2 only 11.1% i.e. 4 patients (n=4) had previous history of preterm labor and delivery (Table-I). In Group 1 80.60% women had successful tocolysis as compare to Group 2 in which tocolysis was achieved 86.2% so there is no marked difference both the groups.

All the preterm babies were shifted to NICU. In Group 1 n=3 babies (8.3%) expired on 2nd day of delivery whereas 2 babies expired (5.5%) in Group 2.

10 patients who used nitroglycerine 28.5% had headache and which was successfully treated with use of acetaminophen PO whereas there was no headache in patients who used nifedipine. In Group 2, 6 patients had tachycardia (16.6%) but no such adverse effects seen in Group - 1. (Table -II)

DISCUSSION

Our study showed that there is no significant difference between nifedipine and nitroglycerine in preventing preterm labor. Treatment with nitroglycerine patch showed reduction in risk of neonatal morbidity and mortality. Most common side effect noted with nitroglycerine was headache and local irritation. There was no significant difference between fetus exposed in utero to nitroglycerine and calcium channel blocker. Transdermal nitroglycerine has the attraction of its simplicity of administration and potential effectiveness. Corticosteroids were used in both groups in prenatal period to reduce fetal mortality and morbidity. Currently there is no notable evidence to rationalise the routine use of nifedipine for maintenance therapy of preterm labor. Further studies are required for the optimal dosage efficacy and safety of nifedipine in premature rupture of membrane and prolongation of gestational age and long term fetal effects.

Weni found that nitroglycerine delayed delivery beyond 7-14 days in 86 % and 85 % of patients compared to 72 % - 68 % in ritodrine group, whereas Lees et al found the same to 76% and 73% for nitroglycerine versus 80% and 78% for ritodrine. Graeme et al didn’t find any significant reduction in delivery within 48 hours use of nitroglycerin but current study has marked reduction in preterm labour and delivery. Study conducted by Gill et al has no significant difference in neonatal mortality and morbidity same as current study. The RNOTT trail found that nitroglycerine prolongs pregnancy for more than 7 days in 53 % of patients and 59 % in ritodrine group, where as in our study nifedipine delayed delivery from 7-
13 days in 69.2% and 60 % which was not a marked difference\textsuperscript{15,16}. The mean pregnancy prolongation duration was 28 days in nitroglycerine group as compare to 32.2days in nifedipine group which was similar to Papatsonis et al study. (34days for nifedipine verses 22 days with ritodrine). Numerous studies have showed that nifedipine reduces the incidence of respiratory distress syndrome. Smith et al reported that only few neonates had RDS in nitroglycerine group as compared to placebo our study has little bit high rate i.e. 19 % in nitroglycerine group as compare to nifedipine group 10.6 %.\textsuperscript{17,18} Kashnian et al found that nifedipine user had hypotension in 27.7% patients whereas current study showed that 38% patients in nitroglycerine group had headache as compare to nifedipine group i.e. 2%. There was no significant in the incidence of hypotension and tachycardia in both groups. In summary there is no significant clinical difference between nitroglycerine and nifedipine in preventing preterm labor and delivery.

CONCLUSION

Nitroglycerine transdermal patch is as effective as oral nifedipine in inhibition of preterm labor but oral nifedipine has better side effects profile.

CONTRIBUTION OF AUTHORS:
Kanwal M: Conceived idea, Designed Study, Final proof reading.
Iftikhar PM: Data Collection, Data Analysis, interpretation of data,

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