Original Research Paper Medical Science

Evaluation of Efficacy of Transdermal Nitroglycerine in the Treatment of Preterm Labour

Dr. Rizwana Taj MS OG, No 548/125, Suryanarayanan street, Royapuram, Chennai-600013

Dr. Anuradha MS OG, No 28, Munusamy Garden, 1st street , Madhavaram Milk colony, Madhavaram,Chennai 57.

ABSTRACT

Preterm labour is defined as the onset of regular, painful, frequent, uterine contractions causing progressive effacement and dilatation of cervix occurring before 37 completed weeks of gestation from the first day of last menstrual period. Because of the impact of preterm labour on the mother and the baby, various studies have been conducted on its prevention and management . In this study, 100 patients with preterm labour were randomly selected, 50 patients were recruited for nitroglycerine patch- Group A, and 50 patients for bed rest alone- Group B. The efficacy of nitroglycerine patch was compared with that of control group in prolonging pregnancy for atleast 48 hours and the maternal and fetal side effects studied. It is found on evaluation that transdermal nitroglycerine patch is absolutely safe and successful in achieving complete tocolysis and has a very good role in acute tocolysis.

KEYWORDS

INTRODUCTION:

Preterm labour is defined as the onset of regular, painful, frequent, uterine contractions causing progressive effacement and dilatation of cervix occurring before 37 completed weeks of gestation from the first day of last menstrual period(1). The symptoms of preterm labour include menstrual like cramps, low dull back ache, Abdominal cramping, Change in vaginal discharge, Uterine contractions that are 10 minutes apart or closer(2). Cunningham GH and coworkers (2001) found that preterm labour is said to be established if regular uterine contractions can be documented atleast 4 in 20 minutes or 8 in 60 minutes with progressive change in cervical score with effacement 80% or more and dilatation more than 1 cm. The social and emotional cost of perinatal mortality and morbidity associated with preterm labour is immeasurable. Ideally preterm labour should be prevented. The management involves bed rest and hydration, steroids and tocolysis. Pharmacological inhibition of preterm labour remains an effective method to delay preterm delivery and improve neonatal outcome until a most effective means of prevention is identified. The tocolytics studied for their use in preterm labour are Progestogens, Ethanol, Beta sympathomimetics, Magnesium sulphate, Prostaglandin synthetase inhibitors, Calcium channel blockers, Oxytocin antagonist, Nitric oxide donors, Potassium channel openers(3). Nitric oxide released form L- Arginine is central to inhibit uterine activity during gestation by causing myometrial smooth muscle relaxation . Organic nitrates are rapidly denitrated enzymatically in smooth muscle cell to release nitric oxide which activates Guanyl cyclase thereby increasing cGMP which causes dephosphorylation of myosin light chain kinase. This interferes with activation of myosin. It fails to interact with actin to cause contraction. Consequently relaxation occurs. In late pregnancy there is a decrease in nitric oxide level in myometrium and deciduas. Recently it has been established that nitric oxide decreases both resistance and pulsatility index in both umbilical and uterine arteries and thereby increases uteroplacental blood flow. Hence it was thought that perinatal salvage can be dramatically improved by using nitroglycerine as a tocolytic agent(5). Because of the smooth muscle relaxant property of nitroglycerine in uterine myometrium, its role in tocolysis in preterm labour has been studied. The aim of our study is to evaluate the effect and safety of transdermal nitroglycerine in acute tocolysis and its effect on maternal and neonatal outcome. Preterm fetus need glucocorticoids to enhance lung maturity. This can be achived if delivery is postponed by 24-48 hours. Inhibition of uterine contraction atleast for 2 days may therefore be regarded as optimal tocolysis.

Criteria for tocolytic therapy: Gestational age between 20 and 34 weeks from LMP, EFW less than 2kg by sonography, Membranes intact, Cervical dilatation less than 3 cm, Alive uncompromised fetus, Regular uterine contraction with progressive cervical changes.

MATERIALS AND METHODS:

It is a prospective randomized control trial, conducted at Govt. RSRM Lying-in hospital in 2015-2016. In this study, 100 patients with preterm labour were randomly selected, 50 patients were recruited for nitroglycerine patch- Group A, and 50 patients for bed rest alone- Group B. Both the groups received intramuscular corticosteroids.

Inclusion criteria: 1.Gestational age between 28 to 34 weeks as determined by menstrual dates, clinical examination, USG; 2. 2 Uterine contractions in 10 minute period , each contraction lasting for 20 seconds ; 3. Progressive cervical effacement upto 75%; 4. Cervical dilatation upto 3cm; 5. Intact membranes. Patients with multiple gestation,cardiac diseases, PIH, previous caeserian section, renal disease and pulmonary disorders and fetuses with fetal distress, IUGR, congenital anomalies, polyhydramnios/ oligohydramnios, erythroblastosis were excluded.

Transdermal (TTS) containing 25 mg(TTS 5), 50 mg(TTS 10) and 75 g(TTS 15) were available. TTS is a flat ,multi layered patch designed to deliver nitroglycerine continuously through release membrane. TTS -10 denotes normal amount of nitroglycerine in mg delivered by system/24 hours.

GROUP A:

5 mg of Nitroglycerine patch applied to the skin of the abdomen. Even after 1 hour, if there was no decrease in the frequency and strength of contractions, additional patches were applied for a maximum of 20mg in 24 hours. Patches were removed after 24 hours and the same number of fresh patches were applied for 24 hours. Treatment discontinued if BP < 90/60, PR>100, PROM, persistent uterine contractions even after maximum dosage of drug.

GROUP B: Observed with bed rest.

Treatment is considered successful if uterine contractions sub-

sided and tocolysis achieved for > 48 hours and a failure if the patient delivered within 48 hours of initiation of therapy. 2 doses of betamethasone 12 mg im 24 hours apart were given. Maternal pulse rate, blood pressure, uterine contractions and fetal heart rate, rhythm, tone were monitored for every 30 minutes for first 2 hours then every 2 hours for 12 hours, then 4th hourly for 48 hours.

RESULTS AND ANALYSIS:

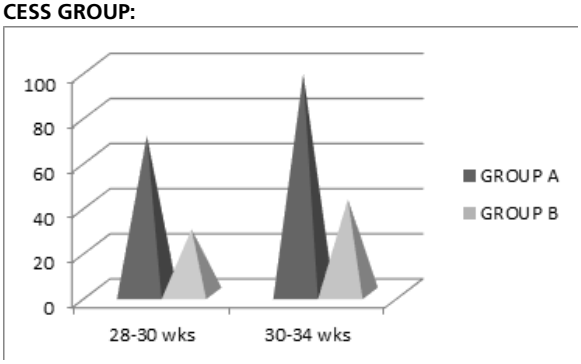
After inspection of pooled outcome data, the following results were obtained.

In 30-34 weeks of gestation, pregnancy was prolonged in 97.5% and 41.8% in case and control study respectively. In 28-30 weeks of gestation, pregnancy was prolonged in 70% and 28.5% in Group A and B respectively. P value is 0.031 which is statistically significant.

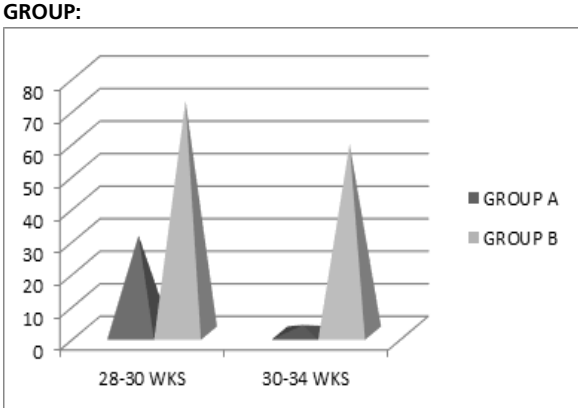
TABLE NO:1

SNO	Gestational age(weeks)	GROUP A		GROUP B	
		Success	Failure	Success	Failure
1	28-30	7(70%)	3(30%)	2(28.5%)	5(71.5%)
2	30-34	39(97.5%)	1(2.5%)	18(41.8%)	25(58.1%)

RESPONSE ACCORDING TO GESTATIONAL AGE IN SUCCESS GROUP:



RESPONSE ACCORDING TO GESTATIONAL AGE IN FAILURE GROUP:



CONCLUSION:

On analysis of data, tocolysis with transdermal nitroglycerine is considered safe with good therapeutic efficacy. In this study, it has been observed that, the success of nitroglycerine patch as indicated by prolongation of pregnancy beyond 48 hours was observed in 92% of cases compared with 40% in controls. Nitroglycerine patch 10 mg was required in 60% of patients, 20 mg was required in 4% of patients to subside the uterine contractions. In 30-34 weeks of gestation, success was observed in 97.5% in Group A and 41.8% in Group B. In 28-30 weeks of gestation, success rate was 70% and 28.5% in Group A and B respectively. When the cervix was 25% effaced, successful tocolysis was observed in 93.75% of cases in Group A and 60% in Group B. When cervix was 50% effaced, prolongation of pregnancy beyond 48 hours was seen in 95% of the patients in Group A and 37.5% in Group B. With 75% of effacement, successful tocolytic effect was seen in 85.7% Group A and 14.2% in Group B. When the cervix was <2 cm dilated, prolongation of pregnancy beyond 48 hours was observed in 94.4% of cases in Group A and 56.2% in Group B. When the cervix was 2-3cm dilated, successful tocolysis was observed in 85.7% and 11.1% of cases in Group A and Group B respectively. Mean duration of prolongation of pregnancy in Group A was 6.6 days. Neonatal mortality was due to complications of prematurity. It is 2.1% in study group compared to 15% in control group among babies born after 48 hours of tocolysis. The incidence of RDS in Group A was 8% and in Group B it was 18 %. APGAR of >7 was observed in 90.2% of babies in Group A and only 33.3% in Group B. Hence, transdermal nitroglycerine is considered to be a safer drug for its ease of use, easy metabolism with no side effects besides headache. While efficacy was studied, Transdermal nitroglycerine acts as a good acute tocolytic for effective action of steroid and to provide time for the patient to get transferred to tertiary care unit. Both cost and consequence of treatment was evaluated as a secondary analysis, though it is little costlier, compared to patient care in neonatal unit and hospital stay , it is cost effective. To conclude, because of its safety and simplicity, transdermal nitroglycerine has a very good role to play as acute tocolytic and in the management of preterm labour. It is not only safe but also has minimal side effects on mother like headache . It has no untoward side effects on neonate. Neonatal outcome is good in all aspects like APGAR score, less neonatal admission in nitroglycerine therapy.

REFERENCES:

1. American college of obstetricians and gynaecologists: preterm labour bulletin no 206, June 1995.
2. Iams J.D. Johnson FF, Parker M. A prospective Evaluation of signs and symptoms of preterm labour.
3. Tocolytic drugs for women in preterm labour, RCOG clinical guideline Oct 2002.
4. Williams obstetrics 24th edition, preterm birth
5. Kumar A Bhardwaj B Pawar N. Glyceryl trinitrate patch in the management of preterm labour, J Obstet and Gynaec India 2001.