To Determine the Safety and Efficacy of Transdermal Nitroglycerine Patch as Shortterm Tocolytic in Preterm Labor

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Abstract

Background and Objectives: Preterm labour complicates 5-10% of pregnancies and is a leading cause of neonatal morbidity and mortality worldwide. It is a major public health problem in terms of loss of life, long-term disability (cerebral palsy, blindness, deafness, chronic lung disease) and health care costs both in the developing and the developed world.

There is need for tocolytic therapy to reduce perinatal mortality and morbidity by delaying delivery at least for 48 hours to allow time for therapeutic effects of corticosteroids

Methodology : This study was undertaken at Sri Siddhartha medical college and hospital research centre tumakuru between October 2017 to October 2019.

76 Antenatal cases with gestational age 28weeks-37weeks as per the inclusion and exclusion criteria's who were admitted and clinically diagnosed as preterm labour were selected . The selected patients were treated with Nitro-glycerine patch

Results : Success rate for acute tocolysis was 88.2%.Mean prolongation of pregnancy was 14.46 days and mean birth weight of babies was 2.19 kilograms. Most common side effect with Nitroglycerine patch was headache (5.3%).

Conclusion: Nitroglycerine patch is effective in suppression of preterm labor as short term tocolytic in prolongation of pregnancy. Nitroglycerine is well tolerated and safe for the mother and fetus with minor side effects

Keywords: *Preterm labor, nitroglycerine patch, prolongation of pregnancy, side effects.*

Introduction

Preterm birth, the leading cause of neonatal morbidity and mortality worldwide, is a major public health problem in terms of loss of life, long term disability and health-care costs. The magnitude of the problem is evident from the fact that after exclusion of genetic and anatomic defects, it accounts for 75-80% of perinatal mortality and morbidity.[1]

The outcome of preterm infants is directly related to the gestational age at delivery .With the advent of new born special care units ,there have been dramatic improvement in neonatal survival rates of preterm infants but neonatal intensive care is very expensive .so preterm labour is not only a medical and social problem ,but also an economic one.

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Each day that delivery is delayed between 28 and 34 weeks of gestation survival increases by 3%. There is ample evidence that tocolysis delays delivery for long enough to permit administration of a complete course of antepartum glucocorticoids and to facilitate in utero transfer to a tertiary care unit where neonatal care will be optimal .[2]

In many instances preterm labour represents the desperate needs of the growing foetus to escape from the unfavourable intrauterine environment. Many modalities of treatment are presently being recommended to halt preterm labour. Although many drugs are now routinely available, and no single drug has clear therapeutic advantage.[1]

Nitro-glycerine, a nitric oxide donor is a recently used drug as a transdermal patch, a direct smooth muscle relaxant without any reported cardiovascular side effects. It is a vasodilator that is essential for maintenance of normal smooth muscle tone of uterus.[3]

Pregnancy is prolonged by its direct effect on uterine blood flow. This drug was studied in U.K during December 1994 –august 1996 and proved to be a safer alternative compared to other tocolytics with fewer maternal side effect profile and treatment discontinuation rates.

Methodology

This study was undertaken at Sri Siddhartha medical college and hospital research centre tumakuru between October 2017 to October 2019.

76 Antenatal cases with gestational age 28weeks-37weeks as per the inclusion and exclusion criteria's who were admitted and clinically diagnosed as preterm labour were selected. The selected patients were treated with Nitro-glycerine patch.

Inclusion Criteria:

- Gestational age between 28-37weeks.
- Painful uterine contractions of 4 in 20 minutes or 8 in 60 minutes each contraction lasting for 30 seconds.
- Intact membranes.
- Cervical effacement of >80%.
- Cervical dilatation >1cm and <3cms.

Exclusion Criteria:

- Antepartum haemorrhage.
- Eclampsia and severe preeclampsia.
- Heart disease causing moderate to severe functional impairment.
- Severe anaemia.
- Foetal demise.
- Foetal congenital malformations.
- Documented ruptured membranes.
- Cervical dilatation >3cms.
- Chorioamnionitis
- Sensitivity or contraindication to Nitro-glycerine.
- Hypotension (systolic bp<90mm of hg).

When a case of preterm labour meeting the inclusion, criteria was admitted detailed history was taken regarding age, occupation, socioeconomic status and any history of infections, obstetric history and history of previous preterm deliveries, abortions, history of diabetes mellitus, heart disease, chronic renal failure, hypertension and asthma.

Patient's general physical examination should be done. Vitals should be recorded Cardiovascular system and respiratory system to be examined.

Period of gestation to be calculated from naegles rule in patients with known last menstrual period, otherwise assessed by clinical examination and ultrasound.

Abdominal examination –uterine heights, presentation, position, lie of the foetus, liquor volume, foetal heart rate to be recorded. Uterine contractions to be evaluated with respect to frequency and duration.

Per speculum examination-speculum to be introduced into the vagina and high vaginal swab to be taken for culture and sensitivity. Any discharge /leak / bleed to be noted. presence or absence of herniation of membranes noted.

Per vaginal examination to be done-consistency, position, effacement, dilatation of cervix, status of membranes, and station of presenting part to be noted.

Routine investigations like Hb%, total count, differential count, ESR, Urine for albumin, sugar and microscopy, blood grouping and Rh typing, HIV, HBsAg, Ultrasound examination, non-stress test, cervical swab or high vaginal swab for culture and sensitivity, urine for culture and sensitivity. Must be sent.

After informed consent Transdermal nitro-glycerine patch releasing 10mg/24 hours in a drug release area of 20cm2 to be applied to a clean, dry area of intact skin on the fundus of uterus. Uterine contractions should be reassessed after 2 hours of application of the patch, and if relaxation of uterus occurred the patch should be continued for 24 hours or till the full dose of steroid administration .In instances where Uterine contractions did not subside after 2hours of application of the patch ,a second patch should be applied. With the application of second patch, if uterine contractions subsided it was continued for 24hours.on the second day another patch should be applied for completion of steroid course. In spite of second patch on the first day, if the uterine contractions did not subside then patch should be discarded and another rescue tocolytic should be used.

Monietring:

1.Half an hourly abdominal palpation to note frequency and strength of contractions for 2 hours and then 6th hourly.

2.Pulse, BP, foetal heart rate monitoring every ½ hourly for 2 hours and then 6th hourly.

3.Close monitoring for any side effects.

Treatment should be discontinued, if there will be any maternal tachycardia greater than 120 beats/ min, drop of blood pressure 15mm of Hg or more from baseline diastolic pressure, fever more than 100degree F or premature rupture of membranes. If the contractions subside, patients will be discharged and assessed antenatally every week until delivery.

Treatment will be considered successful if uterine contractions subsides and tocolysis to be achieved for more than 48 hours.

All patients received injection Betamethasone 12mg 1M 24 hours apart 2doses.

Patients received antibiotics if indicated.

Gestational age at delivery, mode of delivery, birth weight, APGAR at 1

minute and 5 minutes were recorded in followed up cases.

The Following data was collected from each case:

1) Gestational age at tocolysis
2) Gestational age at delivery
3) Prolongation of pregnancy
4) Maternal side effects
5) Birth weight of the baby
6) APGAR Score at 1 and 5 minutes.
7) NICU admissions.

Results

During the study period of 24 months, Total numbers of threatened and established preterm labour cases were 93, out of which 85 patients needed tocolysis. Of the 85, 09 patients were lost to follow up and were excluded from further analysis.

Total cases in the study- 76.

Majority of cases were between 18 and 24 years of age. Mean age of mothers was 22.7 years. Out of 76 subject's majority were Unbooked cases. Primigravidas are of 37 subjects and multigravidas were 39 in number.

Gestational age at tocolysis are more in between 33-36 weeks and mean gestational age was 32.73 at presentation.

Majority of patients delivered between 33-36 weeks and mean gestational age was 34.9 weeks

Prolongation of pregnancy in maximum cases is between 3-7 days, mean prolongation of pregnancy was 14.46 days.

Table 1: Baseline characteristics of subjects

Parameter	value	
Age	mean age-22.7 years	
Distribution	Booked	26
	Unbooked	50
Parity	Primi	37
	Multi	39
Gestational age Tocolysis (weeks±SD)	32.73 weeks	

The outcome is assessed by gestational age at delivery and prolongation of pregnancy and is shown in table 2.

Table 2. outcome assessment

Parameter	value
Gestational age at delivery (weeks±SD)	34.9 weeks
Prolongation Of pregnancy (mean)	14.46 days
Mode of delivery	Lscs 26
	Vaginal delivery 50

This shows majority of subjects delivered at mean age of 34.9 weeks and mean prolongation was 14.46 days and majority of the subjects delivered by vaginal delivery.

Table 3. Maternal side effects

None	69(90.8%)
Yes	7(9.2%)
• Headache	4(5.3%)
• Hypotension	1(1.3%)
• Tachycardia	2(2.6%)
• Skin rash	0

The various side effects noted were headache, hypotension, tachycardia among the subjects is shown in table 3.

Table 4: Neonatal outcomes

Birth weight in kgs (mean)	2.19 kg
APGAR (Majority)	1min- score 4-6(56.6%)
	5min- score 7-10(92.1%)
NICU admission	12(15.8%)
RDS	10(13.2%)

Majority of Apgar is in range of 5min 7-10 score which shows a good prognosis of 92.1%.

Discussion

Preterm labour remains one of the unconquered frontiers in the present era Obstetrics. Throughout the years a variety of drugs with different pharmacologic principles are used to suppress preterm labour. The choice is limited by their efficacy, safety and side effects.

Despite the availability of tocolytic agents the rate of prematurity has not declined over the past few years for several reasons.

Firstly, the aetiology is usually not known. So, it is difficult to devise a method that will predict which group of patients go into labour and delivery.

Second, the signs and symptoms of threatened preterm labour are frequently subtle. Thus, very often patients present themselves for care too late to the obstetricians to attempt to inhibit preterm labour and prevent a premature delivery.

Third, although most cases fall into the category of idiopathic preterm labour certain clinical entities like PIH, APH etc, may require immediate termination regardless of maturity of foetus.[4]

Recently used drug is Nitro-glycerine, a transdermal patch, a nitric oxide donor, a direct smooth muscle relaxant without any reported cardiovascular side effects.[5]

The incidence of preterm labour in Sri Siddhartha Medical College, Hospital and Research centre between October 2017 to September 2019 is 5.84%. Present study incidence is comparable to chythra R rao study 5.8%

In the present study Majority of cases were between 18 and 24 years of age. Mean age was 22.7 years. Thus its comparable with Peter wagura et.al, chythra R rao et.al, Mohammed Zolad et.al

In the present study distribution according to parity it is seen more in multigravidas comparable to Goffinet F study.

Mean gestationl age at tocolysis is 32.73 weeks comparable with kumar aruna, smith GN[6] studies.

Success rate with present study is 88.2% comparable with Rowland study[7]

Most common side effect in the present study was headache which is compared with the study conducted by Kumar Aruna et al.

In another study conducted by Smith GN[6] et al, side effects were seen in 69.7% and in this also commonest side effect was headache.

In the present study mean birth weight after tocolysis was 2.19 kilograms. Comparable with Krishna et.al.

Conclusion

Nitroglycerine patch is effective in suppression of preterm labor as short term tocolytic in prolongation of pregnancy. Nitroglycerine is well tolerated and safe for the mother and fetus with minor side effects hence improves perinatal outcome.

Ethical Approval:Taken from institutional ethical committee

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