IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 1 Ser.11 (January. 2021), PP 01-05
www.iosrjournals.org

Observational Study of Role of Nifedepine as Tocolytic in Preterm Labour and Maternal and Fetal Outcome

*Dr.Sangeeta Shah, Lawdya Sravanthi[1], L.Rani Kumari[2], Aparna Sarwade[3]
**Professor , Department of Obstetrics and Gynaecology, Gandhi Medical College, Secunderabad, Telangana.*
1.Postgraduate, Department of Obstetrics and Gynaecology, Gandhi Medical College, Secunderabad, Telangana.
2.Assistant Professor, Department of Obstetrics and Gynaecology, Gandhi Medical College, Secunderabad, Telangana.
3.Postgraduate, Department of Obstetrics and Gynaecology, Gandhi Medical College, Secunderabad, Telangana.
**Corresponding Author:- Dr.Sangeeta Shah, M.D. (OBG) Professor & HOD of Obstetrics & Gynaecology, Gandhi Medical College/Hospital, Secunderabad, Telangana State*

Date of Submission: 05-01-2021 Date of Acceptance: 20-01-2021

I. Introduction

Prematurity often results in significant short and long term morbidity and mortality related to birth asphyxia, sepsis, intraventricular haemorrhage, respiratory distress syndrome, PDA, jaundice, retinopathy of prematurity, cerebral palsy, neurodevelopment and pulmonary disorders. Therefore, Preterm labour before 34 weeks of gestation needs to be arrested for at least 48 hours with the tocolytic agents so that fetal pulmonary maturity is attained by using betamethasone.

Tocolytic agents are intended to arrest uterine contractions during an episode of PTL or maintain uterine quiescence after an acute episode. The use of tocolytics in management of patients with PTL will reduce both neonatal morbidity, mortality and also the cost of neonatal intensive care

Nifedepine, a dihydropyridine is a calcium channel blocker. It acts by relaxing smooth muscle thereby inhibiting uterine contractions and prolonging the time to delivery

This study was undertaken to evaluate the efficacy of oral nifedipine to reduce labour pains in PTL, to complete doses of steroids in lung maturity, in utero transfer to NICU, evaluate adverse maternal side effects with nifedipine and focuses on morbidities that could be prevented by ANC.

II. Aims And Objectives Of The Study

1. To determine efficacy of oral nifedipine as tocolytic agent to prevent PTL with intact membranes.
2. To assess adverse effects of nifedipine on mother.
3. Comparison of neonatal outcome born to mothers with complete steroid coverage i.e. after 48hrs of tocolysis and incomplete steroid coverage i.e. with in 48hrs of tocolysis.

III. Materials And Methods

An observational study was undertaken in the Department of Obstetrics and Gynaecology of Gandhi Medical College , during the period November 2017 to october 2019. All the cases with inclusion and exclusion criteria were selected during the study period. They were randomized into two groups using simple randomization technique. A total of 100 cases were included in the study.

Inclusion criteria

1.Singleton pregnancy with gestational age between 28-34 weeks 2.Four uterine contractions occuring in 20 min /Eight contractions in 1hr with cervical changes. (confirmed by CTG) 3.Cervical dilatation ≤ 3 cm 4. Intact membranes. 5. No previous administration of Tocolytics. 6. No signs of fetal distress.

Exclusion criteria

1. Pregnancy with any obstetric complications like suspected chorio-amnionitis, Antepartum haemorrhage , intrauterine growth retardation, Congenital anomalies, Multiple pregnancy,Advanced labour.•

2. Pregnancy with any medical disorders like Chronic Medical diseases, Serious maternal illness, Cardiovascular diseases, Diabetes mellitus, Bronchial asthma, Pregnancy induced hypertension, Severe anaemia•

Complete history was taken. Patient's general physical examination was done. Vitals were recorded. Cardiovascular system and respiratory system examined. Abdominal examination was done to note Uterine height, presentation, position, lie of the fetus, liquor volume, fetal heart rate were recorded. Uterine contractions were clinically evaluated with respect to frequency ,intensity and duration, and then confirmed by CTG. In CTG intra uterine pressure were calculated in mmHg over 20minutes. A minimum pressure of above 15mmhg was taken as criteria for tocolytics therapy.

Per speculum examination was done and high vaginal swab was taken for culture and sensitivity. Any discharge /leak /bleed noted. Presence or absence of herniation of membranes noted. Per vaginal examination was done to note the consistency, position, effacement, dilatation of cervix, status of membranes, and station of presenting part noted.

Routine investigations like Hb%, total count, differential count, E.S.R, Urine for albumin, sugar and microscopy, blood grouping & Rh typing, HIV, HBsAg, ultrasound examination, non stress test, cervical swab or high vaginal swab for culture and sensitivity, urine for culture and sensitivity were sent after satisfying the above mentioned criteria and after excluding the contraindications.

Informed consent was taken. 100 patients received oral Nifedipine. Loading dose of 30 mg followed by 10 mg at 6 hourly intervals for 48 hours for acute tocolysis. . If contractions persist at 90 minutes, the first 10 mg dose started at the same time. All subjects were strictly monitored for uterine contractions, maternal pulse rate, palpitations and fetal heart rate. In any case of any serious side effects or progression of labor, drug was stopped.

All the patients were stratified into two subgroups for comparing the efficacy in early or late onset tocolysis.
Subgroup-A:- cervical dilatation<1cm
Subgroup-B:- cervical dilatation 1 to 3cm
All the patients received Injection Betamethasone 12 mg intramuscularly 2 doses ,24 hours apart
The end point of successful tocolysis was considered at the end of 48 hours after the onset of tocolysis .
Tocolysis was considered as failed if uterine quiscence was not achieved despite maximum dose and delivery occurred with in 48hours .
Patients in whom delivery was delayed for at least 48 hours ,were taken as cases of primary success.
Patients were followed for till 1 week and was recorded about side effects that patients developed during the treatment and time interval between admission and delivery. Patients who had prolonged pregnancy by 7 days were discharged. 2 doses of betamethasone 12mg IM, 24hrs apart given to women at risk of PTL between 28 to 34weeks gestational age.
Statistical analysis of 100 cases was done using mean values, standard deviations, P values,Chi- Square test .

IV. Observations And Results

Total number of deliveries in Gandhi hospital were 10,870 during 2017 to 2019 .Out of that 2170 are preterm deliveries.The incidence of preterm labour was 20%.

Age wise distribution:- Majority of cases were between 21-25 years. Mean age was 23+3.3 years

Paritywise distribution :- Out of 100 patients , 68 were multigravida and 32 were primigravida

Gestational Agewise distribution:- More number of patients were between gestational age of 32- 34 weeks , being 54 per cent. The mean gestational age at tocolysis was 32.4 + 1.55 weeks .

TABLE- 1 :- Pregnancy outcome according to the parity

Gravida	Successful tocolysis	Failed tocolysis
Primigravida(32)	26	6
Multigravida(68)	52	16

Lower success rate in multigravidas than primigravida.

TABLE-2:- :Pregnancy outcome according to the gestational age :

Gestational Age (weeks)	Successful tocolysis	Failed tocolysis
28-30	9	4
30-32	26	7
32-34	43	11

Tocolysis failure was slightiy more among earlier gestational age (28-30 weeks) but there was no significant difference with p value<0.711 , chi-square 0.68.

All the patients were stratified into two subgroups for comparing the efficacy in early or late onset tocolysis.

TABLE-3:- Comparison of efficacy in early and late onset tocolysis

	Sub group A(N=42)	Sub group B (N=58)
Success	40	36
Failure	2	22

Analysis of the tocolytic effect in the two subgroups showed that subgroup A(95%) has better success rate as compared to subgroup B(62%), showing statistically highly significant (p value < 0.0001, chi square value =15.41).

TABLE-4:- Prolongation of pregnancy upto 1 week

No of Days	N=100
48 hours	76
Upto 1 week	57

The prolongation of pregnancy up to 48 hours was seen in 76%.. The prolongation of pregnancy upto 1 week was seen in 57%. This shows that Nifedipine was more successful in delaying delivery for 48 hours.

Side Effects
The side effects noted due to Nifedipine group were predominantly headache (8%) and hot flushes (4%).

TABLE-5:- Neonatal Outcomes

Gestational Age	28-30 Weeks(N=13)	30-32 Weeks(N=33)	32-34 Weeks(N=54)
	Success (N=9)	Success (N=26)	Success (N=43)
Mean Birth weight (grams)	1488	1711	2117
Low Apgar	3(33.3%)	6(23%)	3(7.3%)
NICU admissions	2(22.2%)	5(19.3%)	2(4.8%)
Perinatal death	1(11.1%)	2(7.6%)	0
Respiratorydistress syndrome	2(22.2%)	7(26%)	5(12%)
NEC	0	2(7.6%)	0

Interpretations:-

Apgar score in betnesol covered group is good.

Neonates with low apgar score (<7 at 1min, <8 at 5min) are at increased risk of RDS.

Risk of RDS increased with decreasing birth weight, low apgar scores.

Neonatal death in betnesol covered group(4%) is less than incompletely covered group (27%) between 28-34 weeks GA.

Incidence of RDS between 28-34 weeks GA is 54.5% in betamethasone uncovered group and 18.5% in betamethasone covered group.

NEC seen in betamethasone covered group is 7% and in uncovered group is 3%.

V. Discussion

This prospective study was designed to find out the efficacy and safety of Nifedipine in woman with preterm labour and noenatal outcome with betamethasone coverage.

Most of the studies so far conducted have compared the efficacy and safety between Nifedipine and other tocolytics.
Only few studies have been done between Nifedipine and placebo, Rayamajhi R et al[1] and Singh Nisha et al[2] have
conducted studies about comparison between efficacy and safety of Nifedipine and Isoxsuprine in suppression of preterm labour. Kashanian et al[3] conducted study on nifidepine and atosiban.

The incidence of preterm labour in the present study population was 20% is similar to the Singh Nisha et al[2] study group.

The efficacy of Nifedipine in the present study population was comparable with other study groups

The number of patients who remain undelivered for 7 days in our study (57%) was comparable to Rayamahji et al[1] study(56.26%). Prolongation of delivery for 48hrs in our study was 76% which was comparable to Kashanian et al[3] study(75%).

The side effects in our study were headache (8%), nausea, vomiting, flushing, tachycardia and palpitation. Dhawle et al[4] observed headache in 4.7%cases, tachycardia was observed in 11.6% cases. Gasper et al[5] noted such side effects in 10%. No significant change in BP was observed with Nifedipine in our study that necessitated discontinuation of therapy, as Nifedipine exhibits greater selectivity for inhibition of uterine activity relative to cardiovascular effects.

In this study nifedipine as a tocolytic with good efficacy and safety could be demonstrated.

The survival analysis shows that at 48 hours, 76 per cent of

Nifedipine patients remain undelivered. This is relevant because it permits use of steroids to promote fetal lung maturation.

Crowley[6] showed that most marked benefit in neonatal outcome when delivery occurred after 24hrs after initiation of corticosteroid treatment. In present study it found to be after 48hrs.

In our study we found that if the interval between administration of betnesol to birth was less than 48hrs it was associated with increased risk of perinatal morbidity and mortality. The results are in line with other studies.

In the present study it was seen that 70% of newborns with 1 minute apgar <7 and 15% of newborns with 1 minute Apgar more than 7 developed RDS .Study done by M.Lureti et al[7]has shown that a low apgar score at 1st and 5th min <7 was associated with increased risk of RDS .

In our study the incidence of RDS with incomplete betnesol coverage was 54.5% as compared to 43%, 17.6%, 16% in studies by Amorium et al[8], Cochrane Syst. Rev. [9]and Balci et al[10].With complete betnesol coverage the incidence of RDS was 18.5% as compared to 23%, 11.3%, 4% for the studies by Amorium et al[8] , Cochrane Syst. Rev. [9] and Balci et al[10]respectively.

The incidence of neonatal morbidity like RDS; NEC, sepsis , NICU admissions and neonatal mortality are significantly less in betnasol treated group which are similar to following studies liggins[11] , De lemos et al[12] , Kotas and arey[13].

Incidence of NEC in our study are in line with other studies. In the incomplete betamethasone covered group the incidence of NEC is 4%,3%,7% and in complete betamethasone covered group it was 2%,3%,3% in the studies by Amorium et al(75), Kari et al[14] and present study respectively.

Perinatal deaths in present study was 23% and 4% in betnesol covered and incompletely covered groups respectively which was comparable to Liggins[11] study with 19% and 17% respectively.

VI. Conclusion

Prematurity continues to be the major contributor to the perinatal morbidity and mortality. The approaches which prevent and treat preterm labour have greater impact on society and long term public health care costs. There is a high incidence of pre term labour in India. None of the currently available tocolytic agents are ideal. In the present study the Nifedipine drug was proved to be a better tocolytic especially when started with earliest signs of preterm labour.

Nifedipine has the ease of oral administration and there is lack of relative sideeffects on maternal cardiac and carbohydrate metabolism.

In this study , Nifedipine has emerged as a better tocolytic drug in preventing delivery within 48hrs and thus helped in improving perinatal outcomes in patients between 31 and 34 weeks gestational age , more so when administered in earliest signs of preterm labour.

Administration of complete dose of betamethasone has a clear positive effect on morbidity and survival in preterm neonates.

References

[1]. **Rayamajhi R, pratap K.** A Comparative study between nifedipine and isoxsuprine inthe suppression of preterm labor, Kathamandu University Medical Journal (2003) voll (2), 85-90.

[2]. **Singh Nisha, Singh Uma, Seth shikha.** Comparative study of nifedipine and isoxsuprine as tocolytics for preterm. The Journal of obstetrics and Gynecology of India (September October 2011) 61 (5): 512 -515.

[3]. **Kashanian M, A R Akbarian, M Soltanzadeh**, Atosiban and Nifedipine for treatment of preterm labour. International Journal of Gynaecology and Obstetrics (2005), 91, 10-14.

[4]. **Dhawle A, Kalra J, Bagga R, Aggarwal N. Nifedipine** versus nitroglycerin for acute tocolysis in preterm labor: a randomised controlled trial. Int J Reprod Contracept Obstet Gynecol. 2013;2(1):61-6.

[5]. **Gasper R, Toth JH. Calcium Channel Blockers as Tocolytics:** Principles of their actions, adverse effects and therapeutic combinations. Pharmaceuticals (Basel). 2013;6(6):689-99.

[6]. **Crowley P, Chalmers I, Keirse MJNC.** The effects of corticosteroid administration before preterm delivery: an overview of the evidence from controlled trials. British Journal of Obstetrics and Gynaecology 1990;97: 1125.
[7]. **M lureti:** Risk factors for respiratory distress syndrome in the newborn: A multicenter Italian survey.Acta Obstetricia et Gynecologica Scandinavica 1993; Vol. 72, No. 5: 359-364.
[8]. **Amorim MM, Santos LC, Faundes A. Corticosteroid therapy** for prevention of respiratory distress syndrome in severe
[9]. preeclampsia. American Journal of Obstetrics and Gynecology 1999; 180 (5):1283 8.**76.**
[10]. **Cochrane Database Syst Rev.** 2017 Mar; 2017(3): CD004454
[11]. **Balci O, Ozdemir S, Mahmoud AS, Acar A, Colakoglu MC**. The effect of antenatal steroids on fetal lung maturation between the 34th and 36th week of pregnancy. Gynecologic and Obstetric Investigation 2010;70(2):95 9.
[12]. **Liggins GC, Howie RN.** A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants. Pediatrics 1972;50(4):515 25.
[13]. **De Lemos, R. A., Shermata, D. W., Knelson, J. H.,Kotas, R., and Avery, M. E. (1970):** American Review of Respiratory Disease, 102, 459.
[14]. **Kotas, R. V., and Avery, M. E. (1971): Journal** of Applied physiology, 30358.
[15]. **Kari MA, Akino T, Hallman M.** Prenatal dexamethasone (DEX) treatment before preterm delivery and rescue therapy of exogenous surfactantsurfactant components and surface activity in airway specimens (AS). Proceedings of the 14th European Congress of Perinatal Medicine; 1994 June 5-8; Helsinki, Finland. 1994:Abstract no: 486.

Sangeeta Shah, et. al. "Observational Study of Role of Nifedepine as Tocolytic in Preterm Labour and Maternal and Fetal Outcome." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(01), 2021, pp. 01-05.