ORIGINAL ARTICLE

# Efficacy of Nifedipine in suppression of Preterm Labour

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**Abstract**

**Objectives: To find out the efficacy and safety of Nifedipine as a tocolytic agent in preterm labour.**

**Design: Quasi experimental study.**

**Setting & Duration: The study was conducted at Gynaecology / Obstetrics Department, Unit–I, Sheikh Zaid Women Hospital Chandka Medical College Larkana from 1stDec 2007 to 30th Nov 2009.**

**Methodology: 85 singleton pregnancies with preterm labour occurring between 28 and 34 weeks of gestation having cervical dilatation < 3c.m with intact membranes were included in this study and nifedipine was used as tocolytic agent.**

**Results: Successful tocolysis was achieved in 74.1% (63/85 patients). The number of uterine contractions before the treatment were 3/10 minutes in 30.58% , 2/10 minutes in 52.94% and 1/10 minutes in 14.11% of patients while after the nifedipine treatment , uterine contractions were 0/10 in 74.1%, 2/10 minutes in 11.76% while 3/10 in 14.11% of patients. The use of nifedipine delayed for 2 days in 26 patients and 3 days in 37 cases. The combined success in delaying delivery for 2 and 3 days was74.1% (63/85).**

**Conclusion: Nifedipine effectively suppressed preterm labour and delayed delivery for a period which is sufficient for the effect of therapy and maternal transfer to tertiary care unit.**

**Keywords: Preterm labour, Tocolysis, Nifedipine (Calcium channel blocker)**

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**Introduction:**

Preterm birth, a leading cause of neonatal morbidity and mortality is a major contributor to loss of life, long term disability and health care cost both in developing and developed countries.1 Birth before 37 weeks complicates 5-10% of all pregnancies[1,2] and 1-2% of pregnancies before 32 weeks. The frequency of preterm birth in States increased from 10.7 % in 1992 to 12.3% in 2003.[3] In Pakistan the perinatal mortality rate is 96 / 1000 live births[4] and the percentage of perinatal death due to prematurity is 8.81%[5]. The prevention and treatment of preterm labour is a central issue in pregnancy care to reduce the perinatal morbidity and mortality.[5]

It has been widely recognized that its prevention and effective management will improve neonatal outcome and have a profound effect on society and long term public health care cost.[6] The management of threatened preterm labour includes tocolysis.[5] The goal of tocolytic therapy is to reduce neonatal morbidity and mortality by delaying birth, allowing for corticosteroid administration and maternal transfer to tertiary care center.[1] A variety of agents are used for inhibition of preterm labour, those in current use includes B-2 agonist , Calcium channel blocker , prostaglandin synthetase inhibitor , nitric oxide donor , oxytocin receptor antagonist (Atosiban) and magnesium sulphate.[7]

Atosiban is considered a first line tocolytic for the management of spontaneous preterm labour but it is not currently available in Pakistan.[7] Most commonly used group is B-2 agonist

but the risk of adverse events associated with B-agonist in management of spontaneous preterm labour requires close monitoring in high dependency unit.[7] Magnesium sulphate is ineffective at delaying the birth or preventing spontaneous preterm labour and its use is associated with increased infant mortality.[7] Indomethacin fails to prolongs gestation and infants are delivered prematurely with patent ductus arteriosus.[7] There is a need to achieve effective tocolysis to avoid adverse effects of premaurity, a drug which is less expensive, has lesser side effects is easy to administer and which will need less active monitoring should be used.[6] Recent studies have suggested that the calcium channel blokers specifically nifedipine is considered relatively safe for use in pregnancy. They act as more effective tocolytic and helpful in improvement in some clinically important neonatal outcome including less respiratory distress syndrome, intraventricular haemorrhage, necrotizing enterocolitis, jaundice and risk of admission to NICU. They are little teratogenic or fetotoxic potential and with marked reduction in the frequency of adverse maternal side effects.[8] Recent meta analysis suggests that calcium channel blockers are more effective and much better tolerated than B- Agonist.[9] The rationale of this study is to demonstrate the efficacy and safety of nifedipine as a tocolytic agent in preterm labour.

**Methodology:**

This was quasi experimental study conducted in the Department of Obstetrics & Gynaecology, Unit – I, Sheikh Zaid Women Hospital & CMC Larkana from 1st Dec 2007 to 30th June 2009. Total eighty five patients were included in this study having singleton pregnancy of gestational age between 28 to 34 weeks, having regular painful uterine contractions at frequency of 1 or more in 10 minutes for more than 1 hour with signs of effacement and dilatation of cervix < 3c.m with intact membranes. The patients excluded from the study were with fetal malpresentation, fetal death in utero, fetal distress warranting delivery, significant maternal cardiac disease or hypotension, cervical dilatation > 3c.m & multiple gestation. All patients fulfilling the study criteria were admitted in the labour room via emergency or via out patient department and were informed regarding risk & benefits. All women received intravenous infusion of 0.9% saline or lactated ringer's solution at a rate of 200ml/hour given up to 500ml to prevent the possible development of hypotension secondary to nifedipine.

Physical examination was carried out, blood samples were taken for complete blood count, blood sugar, urine for detailed report and cervical culture were also obtained. All patients had an ultrasound per abdomen for the confirmation of viability and estimation of gestational age. Tocolysis started with long acting nifedipine in tablet form (Tab: Adalat retard 20mg) given orally. Uterine contractions were monitored abdominally, if uterine contraction persisted a similar dose was repeated at interval of 30 min: if contractions were not suppressed after the second dose a third dose of 20 mg was repeated at interval of 30 min: up to maximum total dose of 60mg during the 1st hour of treatment. After the 3rd dose patient was put on Tab: Adalat retard (20mg) 8 hourly for 48 to 72 hours as indicated, the maximum dose given during the study was 160mg /day. Maternal blood pressure, pulse, uterine contractions & FHR were checked before treatment and after the initiation of treatment. Charting was done half hourly for the 1st hour, then hourly up to 4 hours and there after 4 hours observation for 24 hours. All patients received steroids to promote fetal lung maturation and they remained in hospital for 72 hours. Women in whom uterine quiescence was maintained after this period were discharged and instructed to continue with bed rest. Tocolysis was considered successful when uterus stopped to contract with prolongation of duration of pregnancy > 48 hrs.

Data were analyzed by using SPSS (recent version) Descriptive statistics mean with standard deviation were calculated for age, parity, uterine contraction, B.P, FHR, gestational age and days gained. Pair sample t – test was applied to compare these variable before and after the treatment. Statistical significance was taken at $P< 0.05$.

**Results:**

Study was conducted in eighty five patients, among them 60% were primigravida while 40% were multiparous. The mean age was 26.8 + 5.6 years (range is 18 -40 years), un booked patients were 58.8% (50/85) while 41.17% (35/85) were booked. Uterine contractions were compared before & after nifedipine treatment(table 1A). Successful tocolysis was achieved in 74.1%. The number of days gains in delaying the labour were analyzed (table 1B). The combined success in delaying delivery for both more than 2 days and 3 days is 74.1% (63/85). Twenty two patients (25.88%) were considered as a treatment failure.

In treatment failure patients (22/85) 20 were delivered in one day and two patients were delivered in two days. The mean delaying in delivery for less than two days was 1.0 + 0.2 days while delay for more than two days was 4.90 + 10.0 which is statistically significant at > p 0.009. Thus the mean gain in days after nifedipine treatment is 4.9 + 10 days.

The mean pulse rate before the nifedipine treatment was 82.0 + 4.0 while after the treatment was 94.0+ 4.0 which shows a difference of 12 b/min: in pulse rate, that is statistically insignificant. The mean systolic blood pressure before treatment was 118.4 + 5.3 while after treatment was 104.1+ 3.6 which shows a decrease in systolic B.P of 14mm Hg that is statistically significant, while the mean diastolic blood pressure before the treatment with nifedipine is 74.5 + 5.4 and after treatment was 66.4 + 4.9mm Hg, this decrease in blood pressure was significant but was not accompanied with any clinical symptoms of hypotension (Table 2 A). There was no statistically significant change in respiratory rate, FHR before & after the treatment with nifedipine. (Table 2 B).

Table 1: *Efficacy of Nifedipine.*

*A. Frequency of uterine contraction before and after treatment. (n = 85).*

| Frequency of uterine contraction | Before treatment | After treatment Up to 24 hours |
|---|---|---|
| 0 / 10 minutes | -- | 63 (74.1%) |
| 1 / 10 minutes | 12 (14.11%) | -- |
| 2 / 10 minutes | 47 (52.94%) | 10 (11.76%) |
| 3 /10 minutes | 26 (30.85%) | 12 (14.11%) |

*B. Gain in days after nifedipine treatment. (n = 63).*

| Duration in days | No | % | Mean + SD | P - value |
|---|---|---|---|---|
| > 2 | 26 | 30.5% | 1.0 + 0.2 | 0.009 |
| > 3 | 37 | 43.5% | 4.90 + 10.0 | |

*Value is statisticallysignificant.*

**Discussion:**

Preterm labour is a clinical challenge for both expectant mothers and clinicion.[10] It occurs in 7 -9% of all births and has even increased recently. Moreover, the most frequently associated condition with neonatal mortality and morbidity excluding congenital malformation is the preterm delivery. Neurological and sensorial deficiency rates are especially high in new born of less than 31- 32 weeks. Although primary prevention would be ideal[11] there fore there is a need to identify the women at risk of preterm labour & institute intervention. Nifedipine a calcium channel blocker has emerged as a potentially safe and better tolerated tocolytic agent.[12,13] In our study successful treatment with nifedipine has been reported, it effectively suppressed uterine contractions without causing any side effects and delivery was delayed for > 48 hours and > 72 hours in 26 and 37 patients respectively. Failure of tocolysis occurs in 22 cases (25.88%). A study conducted by N.maitra[14] comparing nifedipine with ritrodine, they found 91.5% of subjects on nifedipine in which labour was delayed > two weeks as compared to ritrodine (62.9%), this observation was statically significant. Different regimes of nifedipine has been used in different study groups. In current study nifedipine was administered as a single course of 20mg followed by 20mg orally if needed, maximum of 60mg in 1st hour, followed by 20mg orally at 8 hours interval for 3 days. Read and wellby[15] gave an initial loading dose of 30mg of nifedipine and a maximum maintence dose of 20mg every 8 hour for 3 days.

Ulmsten et al 1984[16] found a decrease in both systolic and diastolic B.P from a mean of 135/80mmHg to 120/70 mmHg after oral ad-

Table 2: *Safety of Nifedipine*

*A. On Mother.*

| Vitals | Base line pre – treatment Mean ± SD | After treatment Mean ± SD | P –value |
|---|---|---|---|
| Systolic B.P mmHg | 118.4 ± 5.3 | 104.1 ± 3.6 | < 0.01 |
| Diastolic B.P mmHg | 74.5 ± 5.4 | 66.4 ± 4.9 | < 0.01 |
| Pulse | 82.0 ± 4.0 | 94.0 ± 4.0 | < 0.79 |
| Respiratory rate | 16.8 ± 1.0 | 16.8 ± 1.0 | < 0.01 |

*B. Perinatal Outcome.*

| Perinatal outcome | No | Percentage |
|---|---|---|
| FHR | | |
| Before treatment | 145.4 ± 2.6 | |
| After treatment | 1413 ± 23.2 | P – value < 0.01 |
| APGAR SCORE | | |
| More then 7 | 63 | 74.1% |
| Less then 7 | 22 | 25.88% |
| NICU admission | 10 | 11.76% |

ministration of 30mg of nifedipine.

Ferguson et al reported a statistically significant increase in maternal heart rate and decrease in both diastolic B.P and mean arterial pressure after sublingual and oral administration of nifedipine, but they consider these changes unlikely to be of physiological importance.[17]

Our findings are consistent with above studies, the decrease in blood pressure which we observed after oral administration of nifedipine, although statistically significant, was unlikely to be of clinical importance. In our study, increase in maternal heart rate was found following each dose, but this was transient and less pronounced. No significant changes were noted in the fetal heart rate.

Vicenc Cararach et al compare ritrodine with nifedipine & they found that ritrodine was associated with 76.9% of maternal side effects and lower rate of side effects in nifedipine group, treatment was discontinue in 4 patients in ritrodine group because of serious side effects but no case in nifedipine group.[11] In one randomized multi center trial by paptsonis DN and coworkers, nifedipine was found to be associated with a longer postponement of delivery, fewer administration to NICU in infedipine as compared to ritrodine.[18] In current study, there were no perinatal deaths reported and those babies who delivered after 48 hours of tocolytic treatment and who received steroid cover born with apgar score > 7 in 63 cases and < 7 in 22 cases. NICU admission were required only in those babies who born within 24 hours. N maitra reported 2 neonates in nifedipine and 12 in ritrodine group had 1 min: apgar score > 7.14 ulmsten reported no perinatal death and found appropriate birth weight in the neonates. Read & Wellby also reported similar apgar score in the nifedipine and ritrodine group and no perinatal death so nifedipine would appear to be among the more efficacious and safe tocolytic available to use when properly indicated.

**Conclusion:**

Nifedipine (calcium channel blocker) seems to be effective and safe tocolytic agent, it effectively suppressed uterine contraction and is associated with less side effects. It delayed delivery for > 2 days that is helpful for corticosteroid administration and maternal transfer to tertiary care centers thus helpful in reducing the perinatal morbidity and mortality.

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