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ORIGINAL ARTICLE

Effectiveness of Nifedipine in Preterm Labour Suppression

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ABSTRACT

Objective: To understand the safety and effectiveness of nifedipine as a tocolytic agent in preterm labor.
Study Design: A Quasi-experimental study.
Place and Duration: The study was held in the Obstetrics and Gynecology Department of Riphah International Hospital Rawalpindi for one-year duration from January 2021 to December 2021.
Methodology: 90 singleton pregnancies with cervical dilatation less than 3 cm and intact membranes with preterm labour occurred between 28-34 weeks of pregnancy were included and nifedipine was given as a tocolytic agent.
Results: This study was performed on 90 patients, 55(61.1%) of whom were primigravida and 35(38.9%) were multiparty. 27.1 + 5.2 years was the mean age of patients (range 20 to 45 years), 74.4% were unbooked patients compared to 25.6% were booked patients. The tocolysis was obtained successfully in 76.7% of patients. The number of days obtained in delayed delivery was analyzed (Table 1B). Overall achievement in postponing delivery over 2 and 3 days is 76.7% (69/90). 21 patients (23.3%) were considered treatment failures. Of the patients who failed treatment (21/90), 18 patients gave birth in one day and 3 patients in two-days. The mean delay in delivery <2 days was 1.0 + 0.3 days, while the delay >2 days was 4.31 + 9.0, which is statistically important at> p 0.008. The mean heart rate prior to treatment was 83.0 + 5.0, afterwards to treatment with nifedipine it was 92.0 + 5.0, indicating a difference of 9 bpm: statistically insignificant in heart rate.
Conclusion: Nifedipine was effective in suppressing preterm delivery and delaying delivery long enough to achieve therapeutic effect and transfer the mother to the 3rd degree care unit.
Keywords: Tocolysis, Premature labour, Nifedipine (calcium channel blocker).

INTRODUCTION

Premature births are the foremost sources of infant mortality and disability, leading to long-term health care costs and disability in developed and developing countries[1-2]. Delivery up to 37 weeks affects 5 to 10% of patients and 1-2% of gestations before 32 weeks[3]. In the Pakistan, the incidence of preterm births augmented from 9.8 percent in 1992 to 11.9 percent in 2003[4]. Treatment and prevention of preterm delivery is a key matter in care of pregnancy aimed at reducing complications and perinatal mortality[5]. It is widely accepted that effective prevention and treatment will progress neonatal outcomes and have long-term and profound impact on environmental and public health costs. In case of impending preterm delivery, tocolysis is involved[6]. The goals of therapy with tocolytics are to decrease neonatal mortality and morbidity by postponing delivery, allowing corticosteroids to be administered, and transferring the mother to a tertiary care facility. There are several measures to prevent premature birth including B-2 agonists currently in use, prostaglandin synthetase inhibitor, calcium channel blocker, oxytocin receptor antagonist (Atosiban), nitric oxide donor and MgSO4. Atosiban is the 1st line tocolytic treatment for preterm delivery spontaneously, but presently not accessible in Pakistan[7-8]. The utmost frequently castoff group is the Beta-2 agonist, but the high risk of side effects associated with the beta agonists use in the management of spontaneous preterm labor requires close monitoring in the HDU. MgSO4 is unproductive in postponing labor or averting premature labor, and its usage is related with amplified neonatal mortality[9]. Indomethacin can not prolong pregnancy and premature babies are born with a Patent ductus arteriosus. To prevent the negative effects of immaturity, effective tocolysis is needed with a drug that is cheaper, has fewer side effects, is easier to prescribe, and requires less active monitoring[10-11]. Recent research shows that calcium channel blockers, especially nifedipine, are comparatively harmless for usage during pregnancy. They are effective tocolytic agents and help improve some important clinical outcomes in infants, including intraventricular hemorrhage, mild respiratory distress syndrome, jaundice, necrotizing enterocolitis and ICU risk[12]. They have low teratogenic or fetal potential and the incidence of maternal side effects is significantly reduced. A current meta-analysis shows that calcium channel blockers are much operative and more tolerable than beta-agonists. The reason for this analysis is to understand the safety and efficacy of nifedipine as a tocolytic agent in preterm labor.

METHODOLOGY

This was a quasi-experimental study held in the Obstetrics and Gynecology Department of Riphah International Hospital Rawalpindi for one-year duration from January 2021 to December 2021.A total of 90 patients with a single pregnancy between weeks 28 and 34, with regular painful uterine contractions lasting more than 1 hour and 1 or more contractions in 10 minutes, with indications of effacement and healthy membranes, cervical dilation <3 cm were included. Patients with fetal malformations, prenatal fetal death, fetal anxiety, severe heart disease or hypotension, cervical dilatation of more than 3 cm, and multiple pregnancies were excluded. All patients who met the criteria of study were admitted to the delivery room or clinic and were informed about the risks and benefits. To prevent possible hypotension secondary to nifedipine, all women were injected with 0.9% saline intravenously or Ringer's lactated solution up to 500 ml at a rate of 200 ml per hour. Physical inspection was done, blood samples were drawn for blood glucose, blood count, and urine and cervical culture were done for accurate reporting. All patients underwent abdominal ultrasound to confirm survival and estimate gestational age. Oral tocolysis was initiated with long-acting nifedipine tablets (Adalat retard 20 mg). Uterine contractions were monitored abdominally. If uterine contractions continued, the same dose was administered again after 30-minute of time: If the contractions did not stop afterwards the 2nd dose, 20 mg nifedipine as the 3rd dose was given after 30-minutes of time to the maximum dose of 60 mg for 1 hour of treatment. Afterward the third dose, Adalat retard (20 mg) in tablet form given every 8 hours for 48-72 hours with 160 mg / day maximum dose. Heart rate, Maternal blood pressure, FHR and uterine contractions were monitored before and after treatment. For the 1st hour, every half hour, up to four-hours and then every hour after 4 hours, observation was recorded for twenty-four hours. All subjects were given steroids to support maturation of fetal lungs and were hospitalized for 72 hours. After this period, women whose uterus remained stable were discharged and instructed to continue to rest in bed. When uterine contractions stopped during more than 48 hours of pregnancy, tocolysis was considered effective. Data were analyzed using SPSS software 22.0. Mean

descriptive statistics were calculated by standard deviation of age, number of deliveries, uterine contractions, blood pressure, FHR, gestational age and number of days. Paired t-test was used to compare these variables formerly and afterward of treatment. Statistical significance was considered at P <0.05.

RESULTS

This study was performed on 90 patients, 55(61.1%) of whom were primigravida and 35(38.9%) were multiparty. 27.1 + 5.2 years was the mean age of patients (range 20 to 45 years), 74.4% were unbooked patients compared to 25.6% were booked patients. Uterine contractions were compared before and after treatment with nifedipine (Table 1A).

Table 1:

Frequency of uterine contraction	Before treatment	Mean + SD	After treatment Up to 24-hours
0 / 10 minutes		1.0 + 0.3	60 (66.7%)
1 / 10 minutes	15 (16.7%)	4.31 + 9.0	
2 / 10 minutes	49 (54.4%)		16 (17.8%)
3 /10 minutes	26 (28.9%)		14 (15.5%)
B. Gain in days after treatment with nifedipine. (n = 69).			
Time in days	No		P - value
> 2	29		0.008
> 3	39		
	%		
	32.2%		
	43.3%		

The tocolysis was obtained successfully in 76.7% of patients. The number of days obtained in delayed delivery was analyzed (Table 1B). Overall achievement in postponing delivery over 2 and 3 days is 76.7% (69/90). 21 patients (23.3%) were considered treatment failures. Of the patients who failed treatment (21/90), 18 patients gave birth in one day and 3 patients in two-days. The mean delay in delivery <2 days was 1.0 + 0.3 days, while the delay >2 days was 4.31 + 9.0, which is statistically important at> p 0.008. Therefore, the average increase in the days afterwards treatment with nifedipine was 5.1 + 9 days.

Table 2:

Base line	Pre treatment After treatment	Vitals	Mean ± SD	P – value
Systolic B.P mmHg	119.3 ±6.4	105.2 ± 4.2	< 0.01	
Diastolic B.P mmHg	73.6 ± 6.2		65.8 ± 5.1	< 0.01
Pulse	83.0 ± 5.0		92.0 ± 5.0	< 0.80
Respiratory rate	15.9 ± 2.0		15.9 ± 2.0	< 0.01
B. Perinatal Outcome.				
Perinatal outcome		No	%Age	
FHR Prior to treatment Afterwards of treatment		142.9 ± 3.9 140.7 ± 20.1	P – value < 0.01	
APGAR SCORE > 7 < 7		 69 21	 76.7% 23.3%	
NICU admission		9	10%	

The mean heart rate prior to treatment was 83.0 + 5.0, afterwards to treatment with nifedipine it was 92.0 + 5.0, indicating a difference of 9 bpm: statistically insignificant in heart rate. While prior to treatment the mean systolic blood pressure was 119.3 + 6.4, afterward to the treatment it was 105.2 + 4.2, indicating a statistically significant reduction in systolic blood pressure of 14 mm Hg, whereas the mean diastolic blood pressure formerly and after treatment with Nifedipine was 73.6 ± 6.2 and 65.8 ± 5.1 mm Hg which was significant, hypotension was significant, but without any clinical signs of hypotension (Table 2A). There were no statistically significant changes in the FHR, respiratory rate, before and after nifedipine treatment. (Table 2B).

DISCUSSION

Premature birth is clinically a challenge for pregnant mothers and doctors. It happens in 7 to 9% of altogether births and has uniformly augmented newly. On the other hand, a condition that is often associated with infant mortality and morbidity, in addition to birth defects, is preterm labor[13]. The rate of neurological and sensory disorders is high, especially in infants less than 31-32 weeks. Although early prevention is ideal, there is a prerequisite to recognise females at danger for preterm delivery and initiate interventions[14]. Nifedipine, a calcium channel blocker is potentially better and safe tolerable tocolytic mediator. In this analysis, it was reported that treatment with nifedipine was effective in suppressing uterine contractions without side effects, and delivery was deferred by more than 48 hours and more than 72 hours[15]. Failure of tocolysis was observed in 21 patients (23.3%). N. maitra study comparing nifedipine with retrodine showed that these observations were statistically significant in 91.5% of women taking nifedipine with a delayed delivery of more than two weeks compared with retrodine (62.9%)[16]. Different nifedipine treatment regimens were used in dissimilar groups. In the present study, nifedipine was given 20 mg, shadowed by 20 mg orally as needed, a maximum of 60 mg in the first hour, and then 20 mg orally every eight-hours for three days[17]. Ferguson et al in 1984, after oral administration of 30 mg of nifedipine, the mean reduction in systolic and diastolic blood pressure was observed from 135.80 mm Hg to 120.70 mm Hg and noted a decrease in diastolic blood pressure and significant upsurge in maternal heart rate and moderate rise in arterial pressure after oral or sublingual nifedipine administration, but believe that these variations are not of physiological significance[18]. Our results are reliable with previous studies. A multicenter randomized controlled trial by Paptsonis DN et al showed that nifedipine was associated with longer delivery delays and fewer ICUs for nefidipine than retrodine. In the present study, no perinatal death was reported and neonates born after 48 hours of tocolytic therapy and steroid therapy[19-20]. Hospitalization to the ICU was only required for infants born within 24 hours. N maitra stated that 2 neonates in the group of nifedipine and 13 neonates in the retrograde group at 1 min: had Apgar score> 7[21-22]. Olmsten did not report perinatal mortality and institute suitable neonates' birth weight[23]. Wellby also reported a comparable Apgar score without perinatal mortality in the nifedipine and retrograde groups, and therefore nifedipine appears to be one of the most effective and safest tocolytic agents available for use when needed[24-25].

CONCLUSION

Nifedipine (a calcium channel blocker) supposed to be safe and an effective tocolytic agent, in suppressing uterine contractions and is related with rarer side effects. Delayed delivery is more than 2 days which is useful for prescribing corticosteroids and the mother is transferred to the tertiary care center and therefore is useful in reducing perinatal complications and mortality.

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