

Role of Nifedipine in Comparison to Salbutamol in the Management of Preterm Labour

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ABSTRACT

Preterm labour refers to the onset of labour after the gestation of viability (24-28wks) and before 37 completed weeks of pregnancy. Different Tocolytics are now being used to reduce the uterine contractibility and prolonging the pregnancy for better fetal outcome.

Objective: Objective of this study is to compare oral nifedipine and intravenous salbutamol as better and effective Tocolytics.

Study setting: Obstetrics and Gynaecology department of Sheikh Zayed Hospital, Rahim Yar Khan during 01-01-2010 to 30-06-2010.

Study design: Quasi – Experimental study.

Material and methods: Total 60 patients were included and divided into two groups. One group of patients were given nifedipine and other group was given salbutamol.

Results: Total 60 patients were included in the study divided into two groups side effects observed were palpitation, nausea/vomiting, Headache, Chest Pain, Hypotension out of which chest pain and hypotension were statistically non-significant (P-value 0-15 & 0-71 respectively). Effect of both drugs on uterine contraction & prolongation of pregnancy were also studied, both were statistically non-significant (P-value 0.09, 0.02 respectively).

Conclusion: This study concludes that nifedipine is a useful Tocolytics agent compare able in efficacy to β -agonist with fewer fetomaternal side effects.

Key word: Preterm labour, Nifedipine, Salbutamol.

INTRODUCTION

Preterm labor refers to the onset of labor after the gestation of viability (24 – 28 weeks, depending on definition) and before 37 completed weeks or 259 days of pregnancy¹. Preterm labor and preterm delivery has a very serious impact on increase in perinatal mortality and morbidity not even in developing countries but also in developed countries². Perinatal mortality falls with increasing gestational age at the time of delivery³.

Tocolytics are drugs to reduce uterine contractility, i.e. stop uterine contraction and these include beta agonists (Ritodrine, salbutamol, and terbutaline), calcium channel blockers (nifedipine) and glyceryl trinitrate (GTN)⁴.

Nifedipine is more effective than the beta agonists in delaying delivery at least 48 hours⁵. Nifedipine significantly reduced perinatal morbidity and that the number of maternal side effects as compared with beta 2 agonists and also has the benefit of oral administration in contrast to beta 2 agonists which are administered intravenously (I/V)

and therefore, nifedipine is the first choice in the management of threatening preterm labor⁶.

Nifedipine is an anti-hypertensive agent; it inhibits voltage dependent calcium channels that lead to vascular (and other) smooth muscle relaxation and negative inotropic and chronotropic effects on heart⁷. Salbutamol, a beta agonist, is also another effective drug that inhibits the preterm labor and consequently prolongs the pregnancy⁸. The purpose of this study was to compare the efficacy of Nifedipine and salbutamol in the management of preterm labor in terms of the prolonging the pregnancy and their maternal and fetal side effects.

MATERIAL AND METHODS

This study was carried out in the Department of Obstetrics and Gynaecology, Sheikh Zayed Hospital, Rahim Yar Khan from 01-01-2010 – 30-06-2010. Total 60 patients were included in the study divided into two groups. One group of patients were given nifedipine and other group was given salbutamol. Sampling techniques was non-probability and convenience sampling. It was Quasi experimental study. All those patients with 28 To 36 weeks of gestation, regular painful uterine contractions, having cervical length from 1 – 1.5cm or cervix dilated from 1 – 3cm were included in the study. The patients

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having contraindications to tocolysis i.e. cervix more 3cm dilated, preterm rupture of membranes, fetal distress, IUGR, congenital fetal malformations, antepartum haemorrhage, pre-eclampsia, Chorioamnionitis, IUD, multiple pregnancy, contraindication to nifedipine i.e. allergy to nifedipine, maternal cardiac disease, hypotension < 90/50mmHg, hepatic dysfunction, concurrent use of I/V salbutamol, MgSO₄, transdermal nitrates and contraindications to salbutamol i.e., cardiac disease, hypertension, hyperthyroidism were excluded from the study.

RESULTS

Interventional Quasi experimental study was carried out at the department of Obstetrics and Gynaecology, Sheikh Zayed Hospital, Rahim Yar Khan. Total 60 patients were taken in this study. Further, they were divided into two groups. Group-A (30 patients) received nifedipine and Group-B (30 patients) received salbutamol.

In group-A majority of the patients 10 (33.3%) were between 26-30 years, in Group-B there were 11 (36.7%) between 26-30 years. Minimum 3 patients (10.0%) were ≤ 19 years in Group-A and 4 patients (13.3%) in Group-B. Mean age was observed 25.4±4.4 in Group-A and Group-B, respectively (Table-1).

Table-1: Distribution of cases by age

| age | Group A(Nifedipine) (n=30) | | Group-B (Salbutamol) (n=30) | |
|-------|----------------------------|------|-----------------------------|------|
| | n= | %age | n= | %age |
| ≤ 19 | 03 | 10.0 | 04 | 13.3 |
| 20-25 | 13 | 43.4 | 11 | 36.7 |
| 26-30 | 10 | 33.3 | 11 | 36.7 |
| 31-35 | 04 | 13.3 | 04 | 13.3 |

Table-2: Side Effects Observed (Total No. of cases in each group = 30)

| Side effect observed | Group A | Group B | Chi-square value | P value |
|----------------------|-----------|------------|------------------|------------------------|
| Palpitation | 5 (16.7%) | 24 (80%) | 24.09 | < 0.001 (significant) |
| Nausea / vomiting | 8 (26.7%) | 16 (53.3%) | 4.44 | 0.03 (significant) |
| Headache | 9 (30%) | 0 (0%) | 10.59 | <0.001 (significant) |
| Chest pain | 0 (0%) | 2 (6.7%) | 2.07 | 0.15 (Non-significant) |
| Hypotension | 5 (16.6%) | 4 (13.3%) | 0.13 | 0.71 (Non-significant) |

Table-3: Effect on Uterine Contraction & Prolongation of Pregnancy

| | Group A | Group B | Chi-square value | P value |
|-----------------------------------|-----------|------------|------------------|------------------------|
| Uterine contraction stopped | 24 (80%) | 18 (60%) | 2.86 | 0.09 (Non-significant) |
| Prolongation of pregnancy > 4.8hr | 8 (26.7%) | 16 (53.3%) | 2.96 | 0.22 (Non-significant) |

All patients in both group were evaluated for maternal complication. Regarding palpitation 5 patients (16.7%) in Group-A and 24 patients (80.0%) in Group-B suffered from palpitation. There was significant difference between two groups ($P > 0.001$) table - 2 depicts that 8 patients (26.7%) in Group-A and 16 patients (53.3%) in Group-B suffered from nausea vomiting. Statistically significant difference was found ($P = 0.03$).

In Group-A, 9 patients (30.0%) developed headache while none of the Group-B patient had headache ($P = < 0.001$). In Group-A no patient made complaint of chest pain, while in group-B only 2 patients (6.7%) had chest pain ($P = 0.15$). Regarding blood pressure, 5 patients (16.6%) in Group-A and only 4 patients (13.3%) in Group-B developed hypotension ($P = 0.71$).

Regarding effectiveness of drug in stopping uterine contraction in Group-A, 24 patients (80.0%) tocolysis was effective and in 6 patients (20.0%) tocolysis was failed, and in Group-B. 19 patients (60.0%) tocolysis was effective and failed in 12 patients (40.0%). ($P=0.09$) (Table-3).

All patients in each group were evaluated for prolongation of gestation for 48 hours. In Group-A, 4 patients (13.3%), 2 patients (6.7%), 24 patients (80.0%) and in Group-B, 7 patients (23.3%), 5 patients (16.7%) and 18 patients (60.0%) gestation was prolonged for 12, 24 and 48 hours, respectively (Table-4).

DISCUSSION

Preterm labour and delivery accounts for major proportion of neonatal deaths. Its incidence is 4-10% of all births⁹. The cause of preterm labour is usually not known but in more instances maintaining the fetus in utero appears to be preferred than to allow the preterm delivery.

Numerous pharmacological agents have been utilized to inhibit preterm labour but none has proven to be ideal. Currently β -adrenoreceptor stimulants such as salbutamol ritodrine, terbutaline isoxsuprine and fenoterol have the good efficacy and are commonest form of tocolytic therapy to prevent preterm labour. However, because of their potential side effects adequate maternal and fetal surveillance needs to be maintained throughout their administration.

Other drugs such as the prostaglandin synthetase inhibitor (indomethacin), calcium channel blocker (nifedipine) are also potent labour inhibitor. Calcium channel blockers have the ability to inhibit contractility in smooth muscle cells consequently. Nifedipine has emerged an effective and rather safe alternative tocolytic agent for management of preterm labour after several studies have shown that the use of nifedipine in comparison with other tocolytic is associated with a more frequent successful prolongation of pregnancy, resulting in significantly fewer admissions of newborns to the neonatal intensive care unit^{10,11}.

This study aimed to compare the efficacy of calcium channel blocker (Nifedipine) an prolonging gestation for 48 hours in preterm labour. A study carried out by Tsatsaris in 2001 showed that calcium channel blockers (Nifedipine) was more effective than the beta agonist in delaying delivery at least 48 hours⁵.

It was also desired to compare maternal adverse effects like headache, tachycardia, hypotension, or pulmonary oedema and fetal side effects (variation in fetal heart rate) of nifedipine and salbutamol. The goal of therapy of preterm labour is the drug which is effective and with minimum adverse effects. This study showed that nifedipine which is calcium channel blocker is an effective tocolytic agent comparable to salbutamol which is β -agonist it causes fewer fetomaternal side effects.

Success of tocolysis was defined as prolongation of labour for at least 48 hours to allow enhancement of fetal lung maturity with glucocorticoids. Using these criteria successful tocolysis was achieved in 80.0% of the patients treated with nifedipine. In similar study by Smith and Woodland showed 68% success rate in women with preterm labour¹².

Papatsonis et al in their study in 2002⁶ concluded that calcium antagonist's significantly reduced perinatal morbidity and that the number of maternal side effects was statistically lower compared with B_2 sympathomimetics and nifedipine also has benefit of oral administration.

A study carried out in Jinnah Hospital, in 2007 by Korejo et al¹³ showed that 6% patients suffered from side effects with nifedipine as compared to 28% patients with salbutamol. In present study 30% patients suffered from side effects with nifedipine i.e headache and 80.0% patients suffered from side effects with salbutamol i.e palpitation, so that results are comparable. Another study carried out in 2007 by Hayes showed that side effect with nifedipine was 27% and for B_2 sympathomimetic was 57.9%, results are close to our study¹⁴.

In present study no adverse effect observe on fetal heart rate in patients with calcium channel blocker for preterm labour as compared to salbutamol which is associated with significant increase in fetal heart rate. A study carried out in 2001 by Tsatsaris showed similar results⁵.

Present study has shown that common maternal side effects with salbutamol were tachycardia palpitation and nausea. These were compared to study conducted by Jannet et al¹⁵ concluded that maternal pulse rate was significantly increased in salbutamol group as compare to calcium antagonist. Our study also agreed with these results. The most common maternal side effects in nifedipine group were headache i.e. 30.0%.

Current study clearly showed that salbutamol has pronounced effect on maternal and fetal cardiovascular system than nifedipine. So nifedipine has an excellent safety record and it might be an alternative to beta agonist for preterm labour.

Preterm labour and delivery are major cause of perinatal morbidity and mortality especially in developing countries. Preventable and treatable cause of preterm labour should be identified and dealt with for the better maternal and fetal outcome.

CONCLUSION

The study concludes that nifedipine is a useful, tocolytic agent comparable in efficacy to β -agonist drug but with fewer fetomaternal side effects.

On the basis of this study nifedipine appears to be safe and well tolerated, non-invasive and effective method of suppressing uterine contractions in preterm labour as compared to salbutamol.

As sample size in my study was small so, large randomized controlled trails are required to be conducted to determine the significance of this breakthrough in management of preterm labour.

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