ORIGINAL ARTICLE

COMPARISON OF SALBUTAMOL AND NIFEDIPINE IN TREATMENT OF PRETERM LABOUR

Sadia Dilawer, Javed Iqbal Khan*, Tahir Angez Khan, Rubina Bakhtzada***, Tahir Iqbal Khan†, Mehwish Naz††**

Department of Gynaecology and Obstetrics, *Surgery, **Medicine, Abbottabad International Medical Institute, Abbottabad, ***Department of Gynaecology and Obstetrics, †Radiology, ††Surgery, DHQ Teaching Hospital, Haripur, Pakistan

Background: Preterm labour can cause many foetal complications. Oral nifedipine, subcutaneous terbutaline and intravenous salbutamol are effective agents for patients with pre-term labour. The objective of this study was to compare efficacy of salbutamol and nifedipine in the treatment of preterm labour. **Methods:** This randomized controlled study was conducted at Department of Obstetrics & Gynaecology, DHQ Teaching Hospital, Haripur over 6 months. A total of 178 patients were included using consecutive (non-probability) sampling technique and divided into two groups of 89 each. Women in group A were subjected to nifedipine (20 mg stat, followed by 10 mg three times a day) and women in group B were given salbutamol (50 micrograms per minute, i.e., 8 ampules of salbutamol injection (4 mg) per 500 ml of 0.9% normal saline infusion at 8 drops per minute (0.5 ml/min). Treatment in either group was considered successful if the labour is deferred till 48 hours after initiation of therapy. Data was analysed using SPSS-17. **Results:** Nifedipine and salbutamol were effective in 80% and 84% patients respectively. Maternal and foetal undesirable effects were significantly less in nifedipine group. Nifedipine was safe in 94% patients and salbutamol was safe in 88% patients. **Conclusion:** Salbutamol and nifedipine are equally effective regarding delay of delivery but the latter is more effective in view of easy intake, less active maternal and foetal monitoring and very few adverse effects as compared to salbutamol which requires strict monitoring of both mother and foetus.

Keywords: Preterm labour, salbutamol, nifedipine

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INTRODUCTION

Preterm labour (PTL) can cause many foetal complications. The primary aim of preventing PTL is to delay foetal birth to allow the administration of ante partum corticosteroids to reduce the incidence of idiopathic respiratory distress syndrome (IRDS) in an attempt to improve perinatal outcome. Researchers have shown that oral nifedipine, subcutaneous terbutaline and intravenous salbutamol are effective agents for patients with PTL. Preterm births are most commonly classified as long term, moderate and very premature depending on their period of gestation.[1]

PTL and delivery are common phenomena in modern obstetrics and are defined as labour or birth before 37 weeks gestation. Recent studies, using better methods of gestational dating, however, revealed that many of these babies were actually delivered at term but were small because of decreased foetal growth (intrauterine growth restriction —IUGR).[2–4]

Known causes of PTL include: poor nutrition, alcoholism, smoking, infection, premature rupture of membranes, multiple gestation, coagulation disorders, and placental abruption. A common component to many of these conditions, however, is inflammation at the maternal-foetal interface, mediated by pro-inflammatory cytokines.[5,6]

Infection is the most frequent cause of PPROM and PTL and is clearly identifiable in over 30% of cases. The organisms most commonly associated with PTL include haemophilus influenza and para-influenza, streptococcus pneumonia, trichomonas and chlamydia etc. Clinical studies have also demonstrated that intra-amniotic infection is associated with PTL and other adverse pregnancy outcomes. Infection may cause PTL by causing a premature activation of cytokine cascades that in turn, activate the parturition.[6]

Administration of IL-1β was able to mimic the effects of bacteria by causing PTL, suggesting a causal role for this cytokine in infection-induced PTL. TNF-α did not cause preterm birth but did cause intrauterine foetal death.[7]

Due to the correlative role of inflammation in PTL, some of the newer strategies being investigated are focused on the anti-inflammatory effects of IL-10 and progesterone.[8,9] Different studies have led to a flurry of research that is now underway to determine if progestin supplementation is effective in women with multiple gestations, and whether other routes of administration and other types of synthetic progestins are effective.[10] Hopefully these new treatments either, alone or combined with other therapies, will reduce the huge burden of infant morbidity and mortality caused by PTL and PPROM that is placed on families and society.

If detected early, PTL can be prolonged by administering medication in time, providing good care and informing the patients of their likelihood in

experiencing preterm labour. The current study was designed to compare the efficacy and safety of salbutamol and nifedipine in the treatment of preterm labour.

MATERIAL AND METHODS

This randomized controlled study was conducted in Department of Obstetrics & Gynaecology, DHQ Teaching Hospital, Haripur over 6 months from 1st April 2019 to 30th September 2019. Sample size was calculated as 89 in each group using 65% efficacy of nifedipine and 84% efficacy of salbutamol in the treatment of PTL, 95% confidence interval and 90% power of the test using WHO sample size calculator.

Consecutive (non-probability) sampling technique was used. All patients with preterm labour with age range 15–45 years with any gravidity were included in the study. Patients with intrauterine deaths, detected through ultrasonography, premature rupture of membranes detected through per speculum examination, nifedipine allergy from past history, with eclampsia, pre-eclampsia, gestational diabetes, placenta previa, placental abruption (diagnosed on specific investigation) and having foetus with umbilical cord around neck on ultrasound were excluded from study.

All women meeting inclusion and exclusion criteria, presenting with uterine contractions at least every 10 minutes associated with cervical effacement of 80% and dilatation of more than 2 Cm before 36 weeks and 6 days of gestational period were included in the study. Procedures were explained to all women and a written informed consent was obtained.

Maternal tachycardia was defined as heart rate >90 per minute. Hypotension was taken as 70 to 80% reduction in baseline systolic blood pressure or systolic blood pressure <90 mmHg.

Patients were randomly divided into two groups by lottery method. Women in group A were subjected to nifedipine (20 mg stat, followed by 10 mg three times a day) and women in group B were subjected to salbutamol (50 micrograms per minute, i.e., 8 ampules of salbutamol injection (4 mg) per 500 ml of 0.9% normal saline infusion at 8 drops per minute (0.5 ml/min). Treatment in either group was considered successful if the labour is deferred till 48 hours after initiation of therapy. Intravenous dosage has advantage that it ensures exact dosage required for individual patient and exact titration is possible. Patients were followed up further for detection of maternal and foetal complications, if any.

Data was analysed using SPSS-17. Descriptive statistics like mean standard deviation was calculated for quantitative variables. Frequencies and percentages were calculated for categorical variables. Chi-square test was used to compare the efficacy and safety of both the groups while keeping $p<0.05$ as significant.

RESULTS

Maternal age distribution among 178 patients was analysed as mean age 27±5.82 years. In nifedipine group, 27 (30%) patients were in age range <20 years, 53 (60%) patients were in age range 20–40 years, 9 (10%) patients were in age range >41 years. Mean age was 27±6.14. In salbutamol group 31 (35%) patients were in age range <20 years, 49 (55%) patients were in age range 20–40 years, 9 (10%) patients were in age range >41 years.

In nifedipine group 36 (40%) patients were primigravida, and 53 (60%) patients were multi gravida. In salbutamol group 40 (45%) patients were primigravida, and 49 (55%) patients were multi gravida.

In nifedipine group 36 (40%) patients were primipara, and 53 (60%) patients were multi para. In salbutamol group 40 (45%) patients were primipara, and 49 (55%) patients were multi para.

In nifedipine group 42 (47%) patients had POG 30–33 weeks, and 47 (53%) patients had POG ranged 34–37 weeks. In salbutamol group 40 (45%) patients had POG 30–33 weeks, and 49 (55%) patients had POG ranged 34–36 weeks.

Nifedipine was effective in 71 (80%) patients, and it was not effective in 18 (20%) patients. Salbutamol was effective in 75 (84%) patients and was not effective in 14 (16%) patients (p=0.721).

In nifedipine group 2 (2%) patients had headache, 2 (2%) patients had tachycardia (heart rate >90 per minute) and 2 (2%) patients had hypotension (systolic blood pressure dropped to 70–80% of baseline value). In salbutamol group 7 (8%) patients had headache, and 4 (4%) patients had tachycardia (p=0.042).

In nifedipine group, 7 (8%) neonates had neonatal death and 12 (14%) neonates had prolonged stay in nursery. In salbutamol group 14 (16%) neonates had neonatal death while 14 (16%) neonates had prolonged stay in nursery (p=0.611).

Nifedipine was safe in 84 (94%) patients and had side effects in 5 (6%) patients. Salbutamol was safe in 78 (88%) patients and had side effects in 11 (12%) patients (p=0.583). Stratification of efficacy and safety with age and gravidity are given in Table-1, 2, 3, and 4.

Table-1: Stratification of efficacy with age distribution (n=178)

Age (Yrs)	Efficacy	Nifedipine	Salbutamol	Total	*p*
<20	**Yes**	18	24	42	0.51
	No	9	7	16	
	Total	27	31	58	
21–40	**Yes**	47	43	90	0.75
	No	6	6	12	
	Total	53	49	102	
>41	**Yes**	6	8	14	0.44
	No	3	1	4	
	Total	9	9	18	

Table-2: Stratification of efficacy with gravidity (n=178)

Gravidity	Efficacy	Nifedipine	Salbutamol	Total	*p*
Primi-gravida	Yes	26	32	58	0.35
	No	10	8	18	
	Total	36	40	76	
Multi-gravida	Yes	45	43	88	0.31
	No	8	6	14	
	Total	53	49	102	

Table-3: Stratification of safety with age distribution (n=178)

Age (Yrs)	Efficacy	Nifedipine	Salbutamol	Total	*p*
<20	Yes	26	28	54	0.43
	No	1	3	4	
	Total	27	31	58	
21–40	Yes	50	43	93	0.38
	No	3	6	9	
	Total	53	49	102	
>41	Yes	8	7	15	0.35
	No	1	2	3	
	Total	9	9	18	

Table-4: Stratification of safety with gravida (n=178)

Gravidity	Efficacy	Nifedipine	Salbutamol	Total	*p*
Primi-gravida	Yes	33	36	69	0.34
	No	3	4	7	
	Total	36	40	76	
Multi-gravida	Yes	51	42	93	0.38
	No	2	7	9	
	Total	53	49	102	

DISCUSSION

Preterm births are mainly caused by rupture of membranes (25%), spontaneous PTL with intact membranes (50%) and complications of pregnancy which make foetal and maternal life at risk (25%). About 75% of neonatal deaths occur in preterm births before 34 weeks of gestation and mortality rate after 32 weeks gestation are comparable to foetuses delivered at term.[11] Various drugs have been used in inhibiting preterm labour with the aim of tocolytic therapy to prolong gestation long enough till maturation of foetus is completed. This is done to delay delivery for at least 48 hours so that corticosteroid administration is effective or for transfer of patient to tertiary care centre with neonatal intensive care facility. In this study, highest number of patients (53%) was in 25–30 years and lowest number (21%) among 20–25 years which is comparable to another study.[12] Similarity of results in both studies may be due to similar population groups in Pakistan and they have similar socioeconomic backgrounds. Our study was in contrast to the study by Lockwood CJ, *et al*, who found the increased risk of preterm delivery in women <20 years and over 35 years of age.[13] This may be due to the lack of knowledge about the exact age in female and increased incidence of pelvic infections in Pakistan.

In this study, most of the patients were of low parity which is contradictory to the results found in study of Copper L, *et al*, where incidence of preterm labour was high in multipara.[14] This may be due to fact that more multipara delivered at home and did not come to the hospital in our set up as no age is immune to preterm labour. In this study, mean gestational age in both groups is comparable to another study and this finding further strengthen the validity of present study.[15] In our study 86% patients with salbutamol delivered after 24 hours showing it to be an effective drug and this is comparable to other studies, whose results were 85% and 86% respectively and this adds to authenticity of present study and can be generalized for welfare of patients.[14,15]

Delivery with nifedipine was found comparable to salbutamol in this study, and this is also proved in many different studies and this finding authenticates the efficacy of both drugs in our set up.[12,15] In this study, 18% patients in group A as compared to only 4% in group B had side effects, thus as compared to salbutamol, nifedipine had no serious maternal side effects which is similar to another study.[16] This further strengthens the opinion that nifedipine is a better choice as compared to nifedipine in terms of patient safety. Regarding neonatal outcome in terms of stay in nursery was similar in both groups. This shows no significant difference in the birth related outcomes between groups. Similar results were found in different control trials. This study shows that nifedipine is a better choice for tocolysis as compared to salbutamol in view of less maternal side effects and comparable results regarding prolongation of pregnancy and neonatal outcome are also evident from international studies.[17]

CONCLUSION

Salbutamol and nifedipine are equally effective regarding delay of delivery, prolongation of gestation and neonatal outcome but nifedipine is more effective in view of easy intake, less active maternal and foetal monitoring and very few side effects as compared to salbutamol which requires strict monitoring of both mother and the foetus. Salbutamol has further disadvantage of an intravenous route.

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Address for Correspondence:

Dr. Javed Iqbal Khan, Assistant Professor, Department of Surgery, Abbottabad International Medical Institute, Abbottabad, Pakistan. **Cell:** +92-300-5612071
Email: drjavedikhan@gmail.com

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Contribution of Authors:

SD: Original conception of idea, set data collection proforma and involved in patients monitoring.
JIK: Involved in setting proforma, statistical analysis and literature review
TAK: managing cardiovascular and medical problems of patients
RB: patients monitoring and data collection.
TIK: involved in repeated ultrasound scan for foetal monitoring.
MN: data collection and patient monitoring

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