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Nifedipine versus magnesium sulfate in the management of preterm labour- A randomised controlled trial

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ABSTRACT

Background: Preterm labour is the leading cause of perinatal morbidity and mortality worldwide. Preterm birth accounts for 75% of neonatal deaths and 50% of long-term morbidity including respiratory disease and neuro-developmental impairment. The use of tocolysis in women in preterm labour aims to inhibit uterine contractions and reduce perinatal morbidity and mortality associated with early delivery.
Aim: To study the effect and compare the efficacy of Nifedipine and Magnesium sulphate in management of preterm labour.
Materials and Methods: This randomized controlled trial was performed on 80 women with preterm labor between 28 and 37 weeks of gestation who were randomly assigned to receive either MgSO4 or nifedipine. All patients were checked for successful prolongation of pregnancy who had not been delivered at 48 hours [primary tocolytics effects] and more than 7 days [secondary tocolytics effects] after beginning the treatment and side effects of tocolysis.
Results: From 80 patients, 40 received nifedipine and 40 received MgSO4. There were no differences in suppression of labor pain in 24 hours, 48 hours and 7 days between the two groups. Even though there were no statistically significant differences in one-minute and five-minute Apgar scores, neonatal respiratory distress syndrome between the groups neonates of MgSO4 group had more NICU admission which is significant (p value 0.049).
Conclusion: Oral nifedipine is as effective as magnesium sulfate with regard to inhibition of preterm labor.

1. Introduction

Every year, an estimated 15 million babies are born preterm (before 37 completed weeks of gestation). Preterm birth complications are the leading cause of death among children less than 5 years of age, responsible for nearly 1 million deaths in 2015. Three-quarters of them could be saved with current, cost-effective interventions. Across 184 countries, the rate of preterm birth ranges from 5% to 18% of babies born.[1]

Preterm labour is defined by WHO as the onset of labour prior to the completion of 37 weeks of gestation, in pregnancy beyond 28 weeks of gestation with sub-categories like extremely preterm (less than 28 weeks) very preterm (28 to 32 weeks) moderate to late preterm (32 to 37 weeks). India has the highest number of preterm births 35,19,100. Preterm birth rate (per 100 live births) in 2010 is 13.[2] World Prematurity Day is observed on 17 November each year to raise awareness of preterm births since 2011. It was first created by European parent organizations in 2008. Currently, cost-effective interventions like essential hospital care during childbirth and in the postnatal period for every

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mother and baby, including antenatal steroid injections, kangaroo mother care and antibiotics to treat new-born infections.

The aetiology of preterm labour is multi-factorial and can be divided into three groups. Socio-biological variables like low maternal age,[3] marital status, race and ethnicity,[4] (more common in African-American women), cigarette smoking,[5] environmental stress,[6] short inter-pregnancy interval,[7] alcohol, coffee, and substance abuse.[8] Past obstetric history like previous preterm delivery,[9] previous abortion,[10] multiple dilatation and curettage,[11] cervical surgery like cone biopsy, large loop excision of transformation zone (LLETZ).[12] Complications of current pregnancy like elective preterm birth for a number of maternal and foetal reasons such as preeclampsia, placenta previa, abruption placenta,[4] multiple gestations due to Artificial reproductive techniques and infection.[13]

2. Materials and Methods

2.1. Source of data

The subjects for the study were selected from the patients with preterm labour between 28-37 weeks of gestation who had been admitted to the labour ward of Sri Dharmasthala Manjunatheshwara College of Medical Sciences and Hospital, Dharwad, from November 1^{st} 2016 to October 30^{th} 2017 as a time bound study.

2.2. Type of study

Simple randomised controlled trial.

2.3. Study period

November 1^{st} 2016 to October 30^{th} 2017- one year.

2.4. Sample size

A total of 80 women were included in the study from November $1^{st,}$ 2016 to October $30^{th,}$ 2017. The study was done following counseling regarding need for tocolysis and those who gave their wilful consent to be a part of the study were included. Forty patients were assigned to nifedipine (Group 1), 40 to Magnesium sulphate (Group 2) which was randomly recruited. The trial was approved by the Ethics Committee of the Medical Faculty of our Institution. All the patients gave their informed consent. (IEC.No. SDMIEC-0846:2016 dated: 28.10.2016).

2.5. Inclusion criteria

Nulliparous and multiparous women with intact membranes, showing clinical signs of preterm labour. The diagnosis is based on presence of; (1). Four uterine contractions or more over 30 minutes, each lasting for at least 30 seconds. (2). Documented cervical changes (dilatation of 0-4cm and effacement of at least 50%).

2.6. Exclusion criteria

(1) Women with clinical intrauterine infection; (2) Cervical dilatation >5cm, (3) Medical complications with tocolysis like severe preeclampsia, lethal foetal anomalies, chorioamnionitis, significant ante partum haemorrhage, maternal cardiac or liver diseases and no evidence of non-reassuring foetal status.

2.7. Data collection

In this study, eighty women between 28-37 weeks' gestations with preterm labour are randomly selected to receive oral Nifedipine or intravenous magnesium sulphate. Nifedipine tocolysis was initiated with a 30mg capsule which will be repeated every 90 minutes and Nifedipine 10mg maintenance dose every 6 hours. Tocolysis magnesium sulphate was initiated with 4gram loading dose IV for 20 minutes and 2g/hour via infusion pump. All patients received two doses of betamethasone 12mg intravenously 24 hours apart for fetal lung maturity. In all patients' fetal heart rate, blood pressure, pulse rate and uterine contractions were recorded. A statistical analysis program [SPSS version 22] was used for data analysis. All characteristics and outcome variables were evaluated with descriptive study. Descriptive statistics for continuous variables were presented as mean ±standard deviation (SD) and for categorical variables as numbers (percentages). The baseline characteristics of the two groups were compared using independent t test for continuous variables and Chi-square test for categorical variables. P-value equal or less than 0.05 was considered as significant.

2.8. Outcome variables

All patients were checked for successful prolongation of pregnancy who had not been delivered at 48 hours [primary tocolytics effects] and at more than 7 days [secondary tocolytics effects] after beginning the treatment and side effects of tocolysis. Side effects will be assessed with particular emphasis on hypotension, tachycardia, palpitations, flushing, headache, drowsiness, blurred vision and respiratory depression of the neonate related to magnesium sulphate side effects.

2.9. Sample size estimation

The sample size was calculated based on the prevalence of preterm labour at Shri Dharmasthala Manjunatheshwara College of Medical Sciences and Hospital for the past two years.

N = Sample size; n= 4pq/LXL;
P = Prevalence (which is 9.6%);
Q = 100-9.6=90.4

L = 7% (absolute error);
N = 4x9.6x90.4/7x7;
N = 70.8

In the present study, we considered a sample size of 80 with 40 in each, group 1 and group 2.

3. Results

In the present study, majority of women were in the age group 21-25 years constituting 24 (60%) in nifedipine group and 23 (57.5%) in $MgSO_4$ (Magnesium Sulfate) group. Women with age 18-20 years were 6 (15%) in group 1 and 2 (5%) in group 2. Women between 26-30 years were 7 (17.5%) in nifedipine group and 8 (20%) in MgSO4 group. Only 3 (7.5%) of nifedipine group and 7 (17.5%) of $MgSO_4$ group were aged more than 30 years. The mean maternal age was 23 years in group 1 and 25 years in group 2 as shown in the Table 1.

The majority of women belonged to socio-economic status (SES) III, i.e., 26 (65%) in group 1, 24 (60%) in group 2 whereas women belonging to SES IV comprised 9 (22.5%) in group 1 and 14 (35%) in group 2. A small group of 3 (7.5%) belonged to SES 2 in group 1 and 2 (5%) in group 2 as mentioned in the Table 1.

Majority of women completed their secondary education i.e., 27 (67.5%) in nifedipine group whereas majority of women were graduates in $MgSO_4$ group i.e., 25 (62.5%) as shown in Table 1. Majority of women were 31-33 weeks of gestational age i.e., 20 (50%) in nifedipine group and 21 (52.5%) in $MgSO_4$ group. Mean gestational age is 32 weeks in nifedipine group and 31weeks in $MgSO_4$ group as represented in Table 2.

Most of patients in Nifedipine group are multipara (22) 55% and $MgSO_4$ group are primigravida (21)52.5% using chi-square test with p-value 0.502 (not significant) as shown in Table 2. Most of the women were singleton pregnancies 37(92.5%) in both the groups and only 3 (7.5%) were multiple pregnancies as mentioned in Table 2. The interpregnancy interval among multigravida in both groups has no showed significance with p-0.540 value. Majority of multigravida women are with interpregnancy interval less than 2 years i.e., 15 (37.5%) in nifedipine group and 15 (37.5%) in $MgSO_4$ group as represented in the Table 2.

Only 2 (5%) of women in nifedipine group and 9 (22.5%) are with previous history of curettage. Majority of women i.e., 38 (95%) in nifedipine group and 31 (77.5%) in $MgSO_4$ group didn't have previous history of curettage as shown in the Table 2.

Most of the pregnant women are anaemic i.e., 31 (77.5%) in nifedipine group and 29 (72.5%) in $MgSO_4$ group (not significant at $p<0.05$) as mentioned in Table 2. Majority of women 33 (82.55%) in nifedipine group and 36 (90%) in $MgSO_4$ group didn't had previous preterm birth**.** Only 7 (17.5%) of pregnant women had previous preterm birth in nifedipine group and 4 (10%) in MgSO4 group as mentioned in Table 2.

Most of the pregnant women i.e., 39 (97.5%) in nifedipine group and 39 (97.5%) in MgSO4 group are with adequate liquor. Only 1 (2.5%) of women in both groups had polyhydramnios. Fourteen patients (35%) had urinary tract infection in nifedipine group and 9 (22.5%) in MgSO4 group. Majority of women i.e., 26 (65%) in nifedipine group and 31 (77.55%) in MgSO4 group didn't have urinary tract infection as shown in Table 2.

Only 8(20%) of nifedipine group and 11 (27.5%) in MgSO4 group had growth in urine culture. Majority of pregnant women had no growth in urine culture i.e., 32 (80%) in nifedipine group and 29 (77.5%) in MgSO4 group. Most of the women had no complaints of vaginal discharge i.e., 39 (97.5%) in nifedipine group and 39 (90%) in MgSO4 group as shown in Table 2. Only 5 (12.5%) in nifedipine group and 7 (17.5%) in MgSO4 group had growth in vaginal culture. Majority of pregnant women i.e., 35 (87.5%) in nifedipine group and 33 (82.5%) in MgSO4 group had no growth in vaginal culture as represented in table.2.

As mentioned in the Table 2, majority of women i.e., 37 (92.5%) in nifedipine group and 39 (97.5%) in MgSO4 group didn't have side effects. Only 3 (7.5%) of nifedipine group, of which 2 women had hypotension which was corrected by intravenous fluids and one women had headache and 1 (2.5%) of MgSO4 group had flushing. These side effects did not cause drug discontinuation.

Patients with cervical dilatation less than 4cm were included in this study. When change in bishops score before and after administering of nifedipine and MgSO4 was compared, there is no significant difference between the two groups with p value 0.868 as shown in Table 3.

In the present study, the Table 2, if patient delivers within 48 hours after the initiation of the treatment, then the treatment is ineffective or treatment failure. In this study, Nifedipine was successful in inhibiting preterm labour in 34 (85%) patients and MgSO4 in 32 (80%) patients and did not deliver within 48 hours (primary tocolytic effects). Six women (15%) of nifedipine group and eight (20%) of MgSO4 group delivered within 48 hours and considered as treatment failure.

Three patients (7.5%) within 24 hours, 3 patients (7.5%) between 24-48 hours, 2 patients (5%) between 48 hours-7days and 32 patients (80%) after 7 days had delivery in the nifedipine group and 6 patients (15%) within 24 hours, 2 patients (5%) within 24-48 hours, 5 patients (12.5%) between 48 hours-7 days and 27 patients (67.5%) after 7 days had delivery in the magnesium sulfate group. This characteristic was not statistically different between the two groups as shown in Table 2.

Nifedipine group didn't require alternative tocolysis within 48hours. 2(5%) required alternative type of tocolysis within 48-72hours. Thirty (75%) patients didn't require any tocolysis. 6(15%) of patients delivered before it

Table 1: Comparison of maternal age, socioeconomic status, and education in the study group

		Group-1 (n=40)		Group-2 (n=40)	
		Number	**Percentage**	**Number**	**Percentage**
Age (years)	18-20	6	15.0	2	5.0
	21-25	24	60.0	23	57.5
	26-30	7	17.5	8	20.0
	>31	3	7.5	7	17.5
Socio Economic Status	I	1	2.5	0	0
	II	3	7.5	2	5
	III	26	65	24	60
	IV	9	22.5	14	35
	V	1	2.5	0	0
Education	Primary	3	7.5	2	5
	Secondary	27	67.5	6	15
	Graduate	8	20	25	62.5
	Others	2	5	7	17.5

(Group 1– Nifedipine, Group 2- Magnesium sulfate)

required alternative tocolysis. Among MgSO4 group, 1(2.5%) required alternate tocolysis within 48hours. 4(10%) required alternate tocolysis within 48-hours, 1(2.5%) within 72hours. 26(65%) didn't require any other tocolysis. 8(20%) delivered before it required alternative tocolysis as represented in Table 4.

When risk factors of preterm labour are considered, treatment failure i.e., delivery couldn't be delayed for 48 hours in anaemic women of nifedipine and MgSO4 groups 12.9% vs 24.1%, urinary tract infection 21.4% vs 11.1%, high vaginal growth culture 20% vs 14.3%, dilatation and curettage 50% vs 33.3%, multiple pregnancy 33.3% in both the groups. Only one patient in nifedipine group and 1 out of 4 patients in MgSO4 group had vaginal discharge whose delivered within 48 hours. One patient had polyhydramnios in both groups whose delivery couldn't be delayed for 48 hours. One out of seven patients (14.3%) in nifedipine group with previous preterm birth had treatment failure as shown in Table 5.

In our study, 23 (57.5%) of nifedipine group and 28 (70%) of MgSO4 group delivered in our hospital, others lost follow up or delivered elsewhere. Out of which, when neonatal outcomes are compared, APGAR at 1 minute was more than 7 for 13 neonates (56.5%) of nifedipine group and 14 (50%) of MgSO4 group. P value not significant 0.642 as in Table 6.

When APGAR score at 5 minutes are compared among neonates, it is more than 7 for 15 (65.2%) for nifedipine group and 16 (57.1%) for MgSO4 group. P-value not significant 0.557 as shown in Table 6. Respiratory distress among neonates was more for MgSO4 group than nifedipine, 12(42.9%) vs 8(34.8%) respectively. P value-0.557 is not significant as in Table 7. Patients of MgSO4 group 16(57.1%) had more NICU admission when compared to 7(30.4%) of nifedipine group which is a significant difference (p value 0.049) as represented in Table 8.

4. Discussion

Tocolytics are an accepted component of the obstetric management of women with preterm labour and research continues to identify new tocolytic agents. In our study, maternal outcome was assessed in terms of successful prolongation of pregnancy who had not been delivered at 48 hours (primary tocolytic effects) and at more than 7 days (secondary tocolytic effects) after beginning the treatment.

Among 80 study subjects who were in preterm labour, nifedipine was more effective in inhibition of contractions for 24 hours in 92.5% of patients when compared to $MgSO_4$ (magnesium sulphate) which was effective in 85% of patients. Nifedipine was successful in prevention of labour for 48 hours (primary tocolytic effects) in 85% of patients and $MgSO_4$ in 80% patients.

Nifedipine was efficient in delaying delivery up to 7 days (secondary tocolytic effects) in 80% of patients and MgSO4 was efficient in 67.5% of patients. Although from the above, nifedipine appears to be a better tocolytic when compared to $MgSO_4$, statistically, it is not significant (p value is 0.854).Nikbakht et al. 2014 conducted a similar study and both drugs were equally effective in prevention of labour and delaying delivery >7 days, 56% vs. 64% in the nifedipine and magnesium sulphate groups, and the days gain in utero was no statistically different in two groups. [14]

Khooshideh M et al 2017 concluded that there were no differences in suppression of labour pain in 24 hours and 48 hours. [15] Tabassum S et al 2016 observed that preterm labour was prevented for 48hrs in MgSo4 group (88.80% patients) while in nifedipine group, it was prevented 74% patients with p-value of 0.003 and concluded that magnesium sulphate is associated with higher efficacy for prevention of preterm labour as compared to oral nifedipine. [16] In a study conducted by Lyell et al 2007, primary outcome

Table 2: Distribution of patients according to gestational changes

		Group 1 (n=40)		Group 2(n=40)	
		Number	**Percentage**	**Number**	**Percentage**
Gestational age (weeks)	28-30	7	17.5	10	25.0
	31-33	20	50.0	21	52.5
	34-37	13	32.5	9	22.5
Gravida	Primigravida	18	45	21	52.5
	Multigravida	22	55	19	47.5
Gestation	Multiple	3	7.5	3	7.5
	Singleton	37	92.5	37	92.5
Interpregnancy interval	<2 years	15	79	15	83.3
	>2years	4	21	3	16.7
History of Curettage	Yes	2	5	9	22.5
	No	38	95	31	77.5
Anaemia	<10	31	77.5	29	72.5
	>10	9	22.5	11	27.5
Previous Preterm Birth	Present	7	17.5	4	10
	Absent	33	82.5	36	90
Polyhydramnios	Present	1	2.5	1	2.5
	Absent	39	97.5	39	97.5
Urinary tract infection	Present	14	35	9	22.5
	Absent	26	65	31	77.5
Urine culture & sensitivity	Growth	8	20	11	27.5
	No growth	32	80	29	77.5
Vaginal discharge	Present	1	2.5	4	10
	Absent	39	97.5	39	90
High vaginal swab	Growth	5	12.5	7	17.5
	No growth	35	87.5	33	82.5
Side effects	Present	3	7.5	1	2.5
	Absent	37	92.5	39	97.5
Treatment failure	Yes	6	15	8	20
	No	34	85	32	80
Delivery	Within 24 hrs	3	7.5	6	15
	24-48hrs	3	7.5	2	5
	48hrs to 7 days	2	5	5	12.5
	After 7 days	32	80	27	67.5

(Group 1 – Nifedipine, Group 2- Magnesium sulfate)

Table 3: Comparison of change in Bishops score before and after administration of drug between the two groups

	Drug	**N**	**Mean**	**Std. Deviation**	**P value**
Bishops score change	Group 1	40	-0.45	1.584	0.868
	Group 2	40	-0.50	1.038	

(Group 1 – Nifedipine, Group 2- Magnesium sulfate)

Table 4: Distribution of patients who required alternate type of tocolysis

Required Alternate Tocolysis	**Group-1 (n=40)**		**Group-2 (n=40)**	
		%		%
Within 48hrs	0	0.0	1	2.5
Between 48hrs - 72hrs	2	5.0	4	10.0
After 72 hours	2	5.0	1	2.5
Didn't require any other tocolysis	30	75.0	26	65.0
Delivered before it required alternative tocolysis	6	15.0	8	20.0

(Group 1 – Nifedipine, Group 2- Magnesium Sulfate)

Table 5: Comparison of treatment failure among both study groups

	Group 1		Group 2		
	Number	**%**	**Number**	**%**	**P value**
Anaemia(<10g/dl)	4	12.9	7	24.1	0.215
Urinary tract infection	3	21.4	1	11.1	0.483
Urine culture	1	12.5	0	0	0.421
Vaginal discharge	1	100	1	25	0.400
High Vaginal Swab	1	20	1	14.3	0.682
History of curettage	1	50	3	33.3	0.618
Multiple pregnancy	1	33.3	1	33.3	0.8
Polyhydramnios	1	100	1	100	
Previous preterm birth	1	14.3	0		0.636

Table 6: Distribution of neonates with APGAR at 1 minute and 5 minutes among both groups

			Drug		Total
			Group 1	**Group 2**	
APGAR 1 min	<7	Number	10	14	24
		%	43.5%	50.0%	47.1%
	>7	Number	13	14	27
		%	56.5%	50.0%	52.9%
Total		Number	23	28	51
		%	100.0%	100.0%	100.0%
APGAR 5 min	<7	Number	8	12	20
		%	34.8%	42.9%	39.2%
	>7	Number	15	16	31
		%	65.2%	57.1%	60.8%
Total		Number	23	28	51
		%	100.0%	100.0%	100.0%

(Group 1 – Nifedipine, Group 2- Magnesium sulfate)

Table 7: Distribution of neonates with respiratory distress

			Drug		Total
			Group 1	**Group 2**	
Respiratory distress	Yes	Number	8	12	20
		%	34.8%	42.9%	39.2%
	No	Number	15	16	31
		%	65.2%	57.1%	60.8%
Total		Number	23	28	51
		%	100.0%	100.0%	100.0%

(Group 1 – nifedipine, Group 2- magnesium sulfate)
CHI Square = 0.345, P Value = 0.557 (Not significant)

Table 8: Distribution of neonates with NICU admission among both groups

			Drug		Total
			Nifedipine	**MGSO4**	
NICU	Yes	Number	7	16	23
		%	30.4%	57.1%	45.1%
	No	Number	16	12	28
		%	69.6%	42.9%	54.9%
Total		Number	23	28	51
		%	100.0%	100.0%	100.0%

(Group 1 – Nifedipine, Group 2- Magnesium sulfate)

was arrest of preterm labour, defined as prevention of delivery for 48 hours with uterine quiescence which was achieved by $MgSO_4$ when compared to Nifedipine (87% compared with 72%, P=.01). In our study, when change in Bishops score before and after administering of nifedipine and MgSO4 was compared (-0.45 vs. -0.5), there is no significant difference between the two groups with p value 0.868.[17]

In our study, all pregnant women with gestational age between 28-37weeks with preterm labour are treated with Nifedipine or magnesium sulphate on randomised basis. Characteristics such as age, parity, religion, socio-economic status, and gestational age were comparable between the two groups. Mean age in Nifedipine group is 23 years and MgSO4 is 25 years. In a study conducted by Tabassum S et al 2016, the mean age of women in nifedipine group was 29 years and in MgSO4 was 30 years. Sixty-five percent of women belong to socio-economic status (SES) III in nifedipine group, 60% in $MgSO_4$ group. Most of the women i.e., 67.5% completed their secondary education in nifedipine group whereas 62.5% were graduates in $MgSO_4$ group. Mean gestational age in nifedipine group was 32 weeks and $MgSO_4$ group was 31 weeks. In a study by Khooshideh M et al 2017, mean gestational age was 31weeks. Primigravida and multigravida was equally distributed in both the groups.[15,16]

Singleton and multiple pregnancies were equally distributed between the two groups. Kurdi AM et al 2004) stated that premature labour in multiple pregnancies was 7 times greater than singletons (42% versus 6.4%).[18] In our study, there were three twin pregnancies in both groups of which delivery was delayed for 48 hours in (66%) two patients. Pregnancy with polyhydramnios increased chances of preterm labour. Pri-Paz et al 2012 reported significantly higher rates of preterm (<37 weeks) and early preterm (<34 weeks) deliveries in their polyhydramnios group compared with controls.[19] In our study, multiple pregnancies and polyhydramnios were equally distributed where 1 out of 3 patients with multiple pregnancies and the one polyhydramnios pregnancy, delivered within 48 hours.

Aboushamat & Nanu 2015 observed that the lower the haemoglobin in pregnant women, the greater percentage of preterm labour. Anaemia is an important risk factor for preterm labour; most of the pregnant women in our study i.e., 77.5% in nifedipine group and 72.5% in $MgSO_4$ group were anaemic**.** Among anaemic patients, 12.9% of nifedipine group and 24.1% of $MgSO_4$ group, uterine quiescence could not be achieved and delivered within 48 hours (p value 0.215).[20]

Visintine et al. 2008, observed women with multiple prior induced abortions and a short cervix have a 3.3-fold greater chance of spontaneous preterm birth compared with those with normal cervical length (> or = 25mm).[11] But, in our study, two patients (5%) of nifedipine group, nine patients (22.5%) of $MgSO_4$ group had history of dilatation and curettage. Out of which one patient of nifedipine group and three patients of $MgSO_4$ group went into labour. Previous preterm delivery is considered as a risk factor for preterm labour in the current pregnancy.[10] Most of the patients of both nifedipine and MgSO4 group (90% vs. 82.5%) do not have a history of preterm birth. Similar to our study, Lyell et al 2007, also concluded there is no significant difference in the distribution of previous preterm birth in both the groups in his study.[17]

Most of the multigravida women in both the study groups are with inter-pregnancy interval <2years (79% vs. 83.3%). Similarly, Smith et al 2003, observed that a short inter-pregnancy interval is an independent risk factor for preterm delivery and neonatal death in the second birth.[7]

Varma et al 2014 states that recognising and treating the women having urogenital infections at a stage, when it has not become clinically evident, will decrease the percentage of women going into preterm labour and will improve the perinatal outcome. In our study, urinary tract infection lead to preterm labour in 35% of nifedipine group with 20% of positive urine culture and 22.5% of $MgSO_4$ group with 11% of positive urine culture. High vaginal swab showed growth only in 12.5% vs 17.5% of nifedipine and $MgSO_4$ groups respectively. Positive urine (p value 0.42) and vaginal culture (p value 0.68) which lead to treatment failure is not significant in our study. As per the culture report and sensitivity, antibiotics were started.[21]

Serious adverse effects like shortness of breath, pulmonary oedema which is caused by $MgSO_4$ and significant hypotension which is seen with nifedipine is not seen in our study. But 3 patients of nifedipine group had hypotension which was corrected by intravenous fluids and one had headache and one patient of $MgSO_4$ group had flushing. These side effects did not cause drug discontinuation. Khooshideh et al 2017, concluded that maternal hypotension was higher in the nifedipine group in his study, but the difference was not significant. Dyspnoea and minor maternal side effects ($P \leq 0.001$) were significantly higher in the MgSO4 group than the nifedipine group. Nikbakht et al 2014, stated that 6% of nifedipine group and 2% of magnesium sulphate group required drug discontinuation due to severe symptoms.[14,15]

Uterine quiescence was better achieved in all patients of nifedipine group for 48 hours and didn't require alternate tocolysis in 75% of patients till delivery or discharge when compared to MgSO4 group (65%). Few patients went into active labour and delivered, where other tocolytics couldn't be given (15% vs 20%).

In our study, 57.5% of nifedipine group and 70% of $MgSO_4$ group delivered in our hospital, others lost follow up or delivered elsewhere. Out of which when neonatal outcomes were compared, neonates who were exposed to $MgSO_4$ in utero had more NICU admission when compared

to nifedipine group (57.1% vs 30.4%) with p value-0.049 which is significant. Similar to our study, Lyell et al 2007, described new-borns in the magnesium sulphate group had more NICU admissions and spent longer in the neonatal intensive care unit (8.8±17.7 days compared with 4.2±8.2 days, P=.007).[17] In our study, there were no statistically significant differences in one-minute and five-minute Apgar scores in neonates although majority of neonates with reassuring Apgar score (i.e., >7) at 1 minute and 5 minute belong to nifedipine group when compared to $MgSO_4$ group (Apgar >7 at 1 minute is 56.6% vs. 50% with p value 0.642 & Apgar >7 at 5 minutes is 65.2% vs. 57.1% with p value 0.557 respectively) which is not significant. Neonates of $MgSO_4$ group had more respiratory distress when compared to nifedipine group (42.9% vs. 34.8% respectively) with p value 0.557. Similar to our study, Khooshideh et al 2017, also observed that there were no statistically significant differences in one-minute and five-minute Apgar scores in neonates. Also, there were not any statistically significant difference in neonatal respiratory distress syndrome and NICU admission between the two groups in the same study. Singh et al 2015, observed that maximum number of babies had Apgar score between 8 and 10 at 5 minutes. Mean Apgar score at 5 minute was 8.1 ± 2.20, 8.2 ± 2.00, 7.9 ± 2.39, 7.9 ± 2.39, 7.6 ± 2.34 in ritodrine, isoxuprine, nifedipine, glycerlynitrate and magnesium sulphate group respectively.[22]

Many studies reported that nifedipine is a superior drug compared to $MgSO_4$ in decreasing the rate of respiratory distress syndrome[23,24] and NICU admission in preterm and very preterm neonates.[25] Some authors reported that MgSO4 may lead to respiratory suppression in neonates.[26,27] In the present study, although neonates who were exposed to $MgSO_4$ in utero had more NICU admission when compared to nifedipine group which is significant, we have not found any significant difference in the incidence of respiratory distress syndrome and 1- and 5-minute Apgar scores between the two groups.

On the other hand, other factors which have led to the growing interest in nifedipine as a tocolytic are the availability of a wide range of immediately acting and extended-release preparations, easy availability, ease of administration and low cost. $MgSO_4$ must be used by only the infusion route and requires special monitoring and close observation. Patients taking magnesium sulphate should be monitored for toxic side effects such as respiratory depression or even cardiac arrest. Magnesium crosses the placenta and can cause respiratory and motor depression of the neonate. Moreover, Grimes and colleagues showed that the risk of total paediatric mortality was significantly higher for infants exposed to magnesium sulphate and it should not be used for tocolysis.[28] But evidence suggests that magnesium sulphate given before anticipated early preterm birth reduces the risk of cerebral palsy in surviving infants.[29] When selecting a tocolytic, patient-specific characteristics must be considered. In patients who require magnesium sulphate for neuro-protection, it may be suitable to use this therapy at tocolytic doses because it can serve both purposes.[30]

5. Conclusion

In conclusion, our data in this study showed that oral nifedipine is as effective as magnesium sulfate with regard to inhibition of preterm labour. Although, nifedipine is better than $MgSO_4$ when their primary tocolytics effects (who has not delivered till 48 hours) and secondary tocolytic effects (who has not delivered till 7 days) are compared but it is not statistically significant. Although neonates who were exposed to $MgSO_4$ in utero had more NICU admission when compared to nifedipine group which is significant, we have not found any significant difference in the incidence of respiratory distress syndrome. We conclude that as nifedipine with its easy availability, least side effects profile, low cost, ease of administration and with less intensive monitoring, can be considered as better option for management of preterm labour. No matter which tocolytic agent the clinician chooses, the evidence supports the use of short-term tocolytic drugs to prolong pregnancy for at least 48 hours to allow for administration of antenatal steroids and to allow for transport of the mother to a tertiary care facility. As this study comprised a small sample, large randomised studies are required to prove the efficacy of the tocolytics.

6. Source of Funding

None.

7. Conflict of Interest

None.

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