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A COMPARITIVE STUDY "NIFEDIPINE VS ISOXSUPRINE IN PRETERM LABOR"

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ABSTRACT

Background:- Preterm delivery is a major reason behind perinatal morbidity and mortality. Numerous tocolytic agent are accustomed inhibit preterm labour among which calcium channel antagonist Nifedipine and beta mimetic Isoxsuprine is employed. The effectiveness of Nifedipine and Isoxsuprine is assessed during this prospective study.

Materials and method: - A comparative, prospective and randomised distributed in 100patient within the department of obstetrics and gynaecology, MGM MEDICAL COLLEGE AND HOSPITAL, NAVI MUMBAI. The subjects were randomised into 2 group, first group receiving oral Nifedipine whereas second group receiving injectable Isoxsuprine followed by oral tablets.

Results: - During this study, 50 women received oral nifedipine and 50 women received injectable isoxsuprine followed by oral tablets, successful tocolysis was achieved in 96% with Nifedipine group and 76% with isoxsuprine group.

Conclusion: - Nifedipine as compared to isoxsuprine in management of preterm labour is significantly related to longer postponement of delivery with fewer maternal side effects.

KEYWORDS : Preterm labour, Nifedipine, Isoxsuprine hydrochloride, tocolytic

I.INTRODUCTION

Preterm labour is a challenge for obstetric care despite improvements in obstetric care over the past three decades, the incidence of preterm birth remains unchanged. There is no accurate worldwide data but estimates of preterm birth range from a relative stable 5-10% [1] in developed countries to as high as 25% in some worst hit developing countries. Preterm labour and delivery is one of the largest challenges for obstetricians and so are the preterm babies for the paediatricians [2]. Increasing rates of preterm labour might be due to artificial reproductive techniques, psychosocial stress or medically induced prematurity. [2]. Preterm affects 11% in US [3] or greater in developing countries (23.3%) in India [4].Thesebirthrepresent over 70% of all perinatal morbidity and mortality. Thus, prevention or early treatment of preterm labour could potentially be of tremendous importance.The mainstay of hospital treatment has been the ustilisation of tocolytic agents. Tocolytic use is justified in woman with preterm labour as they will stop contractions and preterm delivery in 75-80% of patients for 48 hours for steroid action which decreases respiratory distress in neonate ultimately improving the neonatal outcome. [4]. Nifedipine, a dihydropyridine calcium channel blocker, is an efficient smooth muscle relaxant with low toxicity. Although nifedipine is an antihypertensive drug, the drop in blood pressure in normotensive women after starting tocolytic therapy is significantly more with intravenous salbutamol as compared to nifedipine. Nifedipine carries the potential for fetal hypoxia associated with maternal hypotension. [5]Isoxsuprine hydrochloride being a beta-adrenergic agonist and a potent vasodilator, and was actually the primary drug to be published as a tocolytic agent. Variety of huge clinical trials have shown the therapeutic efficacy of isoxsuprine in patients in danger of preterm labour and risk of abortion, including evidence of good tolerability when used for acute (intravenous) and maintenance (oral or intramuscular administration) therapy [5]. Additionally , a recent study examining the pharmacokinetics of standard and high doses of isoxsuprine in healthy female subjectsdemonstrated good tolerability with low bioavailability and small change in heart rate [6].

II. AIMS AND OBJECTIVE: -

To compare the efficacy of nifedipine and isoxsuprine hydrochloride in preterm labor in terms of:-

1. Increasing the time of labor
2. Fetal morbidity/ mortality
3. Maternal complications (if any)

III. MATERIALS AND METHODS

A sample size of patients was selected using purposive randomized sample technique. A total of 100 patients satisfying inclusion and exclusion criteria were randomly divided into 2 groups 50 each supported type of management: -

Group A: tocolysis with nifedipine
Group B: tocolysis with isoxsuprine hydrochloride

INCLUSION CRITERIA:-

i. Antenatal women with 28-36 weeks of gestation.
ii. Patient should have uterine contraction of 1 in 10 minutes.
iii. Minimum cervical changes in the form of effacement and dilatation less than 3cms.

EXCLUSION CRITERIA: -

i. Patient with PPROM
ii. Maternal factors
a) Preeclampsia
b) Eclampsia
c) Antepartum haemorrhage

d) Oligohydroaminos
e) Chorioamnionitis
f) Cardiac disease
g) Thyroid disorders
h) Advanced labour

iii. Patients with IUGR, IUFD and other fetal anomaly incompatible with life.

IV. METHODOLOGY

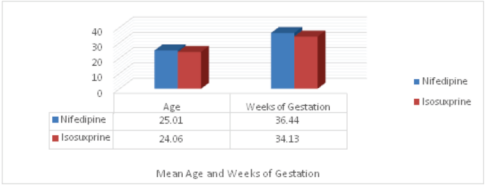
After informed consent is taken, the patient is assigned to either group A or group B.Group A subjects were given 20 mg oral nifedipine initially followed up by 10 mg at 4hourly interval for 48hours, drug dose was gradually tapered every 24 hours and then stopped. If contraction persist at 90minute, the first 10 mg dose was started at the identical time.Group B subjects were given injection isoxsuprine 10 mg intramuscularly and repeated at 6 hours interval for 48hour. Patients who responded were changed over to 20 mg oral retard tablet given 12hourly as maintenance therapy for 1 week.In both the groups, subjects were strictly monitored for uterine contractions, maternal pulse rate, palpitations, and fetal heart rate. In case of any serious side effects or progression of labour the respective drug should be stopped.In both the groups, subjects were strictly monitored for uterine contractions, maternal pulse rate, palpitations, and fetal heart rate. In case of any serious side effects or progression of labour the respective drug should be stopped.

V. RESULTS

1. Mean age and weeks of gestation of study subjects

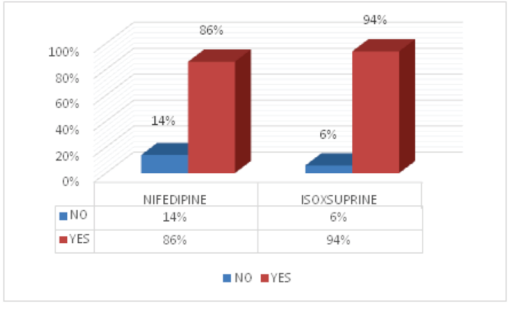
VARIABLES	Group	N	Mean	SD	p-value
Age (yrs)	Nifedipine	50	25.01	5.61	0.41
	Isoxsuprine	50	24.06	5.04	
Weeks of gestation	Nifedipine	50	36.44	3.07	<0.05
	Isoxsuprine	50	34.13	2.87	

Mean age of mother was comparable among both groups (25.01 vs 24.06 years; p-0.15) while weeks of gestation was more in Nifedipine groups as compared to isoxsuprine (36.44 vs 34.13 weeks; p<0.05).



2. Distribution of subjects based on requirement of steroids

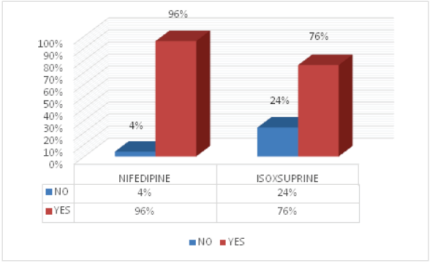
STEROIDS GIVEN	NIFEDIPINE	ISOXSUPRINE	TOTAL
NO	7	3	10
	14.0%	6%	10%
YES	43	47	90
	86.0%	94%	90%
TOTAL	50	50	100
	100%	100%	100%
p- value – 0.32			



Steroids were given in 86% and 94% females to prevent the risks of complications of prematurity in nifedipine and isoxsuprine group respectively (p-0.32)

3. Distribution of subjects based on treatment success

TREATMENT GIVEN	NIFEDIPINE	ISOXSUPRINE	TOTAL
NO	2	12	14
	4%	24%	14%
YES	48	38	86
	96%	76%	86%
TOTAL	50	50	100
	100%	100%	100%

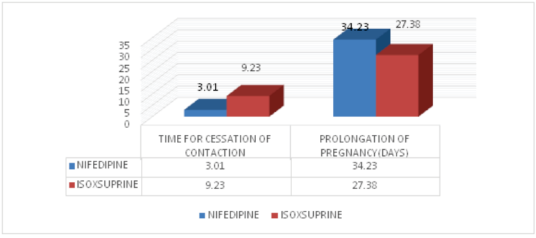


Successful delay in delivery at least for 48 hours(primary success) was achieved in 96% and 76% females of nifedipine and isoxsuprine group respectively (p<0.05)

4. Mean time of cessation of contraction and prolongation of pregnancy

VARIABLES	GROUP	N	MEAN	SD	p-value
TIME FOR CESSATION OF UTERINE CONTRACTION(HRS)	NIFEDIPINE	50	3.01	1.01	<0.05
	ISOXSUPRINE	50	9.23	7.66	
PROLONGATION OF PREGNANCY(DAYS)	NIFEDIPINE	50	34.23	5.32	<0.05
	ISOXSUPRINE	50	27.38	4.89	

Mean time for cessation of uterine contractions was significantly lower in nifedipine as compared to isoxsuprine (3.01hrs vs 9.23hrs; p<0.01) while prolongation of pregnancy was also significantly more with nifedipine group (34.23 vs 27.38; p<0.01)



5. Distribution of the subjects based on mean birth weight and APGAR score

VARIABLES	GROUP	N	MEAN	SD	p-value
BIRTH WEIGHT	Nifedipine	50	2.42	0.34	<0.05
	Isoxsuprine	50	2.17	0.62	
APGAR AT 1 MIN.	Nifedipine	50	7.21	0.53	0.56
	Isoxsuprine	50	6.86	0.38	
APGAR AT 5 MIN.	Nifedipine	50	9.23	0.53	0.3
	Isoxsuprine	50	8.81	0.49	

Mean Birth weight was significantly more in nifedipine group as compared to isoxsuprine (2.42 vs 2.17Kg; p<0.5) while mean apgar score at 1 and 5 min was less in isoxsuprine group (6.86 and 8.81 vs 7.21 and 9.23; p>0.05) but the difference was not significant.

VI. DISCUSSION

Efficacy and safety of tocolytic agents in preterm labour has been a difficult task because the cause of preterm labour is generally unknown and therapy cannot be directed to specific cause. Isoxsuprine hydrochloride is a potent vasodilator, and was actually the first drug to be published as tocolytic agent while Nifedipine, a calcium channel blocker, is an effective smooth muscle relaxant. Few studies have been conducted about the comparison between the efficacy and safety of Nifedipine and Isoxsuprine in preterm labour. The mean prolongation of pregnancy in the present study was 34.23 days with Nifedipine and 27.38 days with Isoxsuprine while cessation of uterine contractions was significantly lower in

nifedipine group as compared to isoxsuprine group (3.01hrs vs 9.23hrs; $p<0.01$). these results were similar to those reported by Kalita D et al.[4] that is prolongation of pregnancy as 31.16days with Nifedipine and 23.06 days with Isoxsuprine hydrochloride. Kedar et al.[2] reported mean prolongation of pregnancy as 22.4±15.6days with nifedipine and 16.5 ± 14.5 days with isoxsuprine. Rayamajhi et al.[3] reported mean prolongation time of pregnancy as 39.26 ±25.5 days with nifedipine and 245.5 ± 15.75 days with isoxsuprine.

MEAN PROLONGATION (DAYS)		
STUDIES	**NIFEDIPINE**	**ISOXSUPRINE**
Kedar et al.2	22.4	16.5
Rayamajhi et al.3	25.7	19.18
Kalita D et al.4	31.16	23.6
Present study	34.23	27.38

In present study, successful tocolysis was achieved in 96% with Nifedipine group and 76% with Isoxsuprine group. Mean birth weight was significantly more in Nifedipine group as compared to Isoxsuprine (2.42 vs 2.17 kg; $p<0.05$) while mean APGAR score at 1 and 5 min was less in Isoxsuprine group (6.86 and 8.81 vs 7.21 and 9.23; $p>0.05$), nut the difference was not significant.

The comparision of successful tocolysis and mean birth weight across various studies was:-

SUCCESSFUL TOCOLYSIS		
STUDIES	**NIFEDIPINE**	**ISOXSUPRINE**
Kedar et al.2	81.25%	70%
Rayamajhi et al.3	88%	76%
Present study	96%	76%

MEAN BIRTH WEIGHT		
STUDIES	**NIFEDIPINE**	**ISOXSUPRINE**
Rayamajhi et al.[3]	2.38	1.94
Zahir Fet al.[1]	2.06	1.94
Present study	2.42	2.17

VII. CONCLUSION

From the present study, we infer that

1. successful tocolysis was achieved in 96% with Nifedipine group and 76% with Isoxsuprine group.
2. Mean birth weight was significantly more in Nifedipine as compared to isoxsuprine, (2.42 vs 2.17 kg; $p<0.05$) while mean APGAR score at 1 and 5 min was less in isoxsuprine (6.86 and 8.81 vs 7.21 and 9.23; $p<0.05$) but difference was not significant.
3. Steroids were given in 86% and 94% females to prevent the risk of complication of prematurity in nifedipine and isoxsuprine group respectively.
4. Successful delay in delivery for atleast 48 hours was achieved in 96% and 76% females of nifedipine and isoxsuprine group respectively.

Prematurity continues to be the major contributor to perinatal morbidity and mortality. None of the currently available tocolytic agents are ideal. Our study found a favorable outcome with Nifedipine (96% vs 76%), safer and more effective than Isoxsuprine. In view of increasing evidence of efficacy, safety and its ease of administration, Nifedipine will play an expanded role in the suppression of preterm labor.

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