Comparative study between nifedipine and isoxsuprine in suppression of preterm labor

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Abstract

Background: *Preterm labor is a cause of high rates of perinatal morbidity and mortality. The use of tocolytics is one of the efforts to handle the risk of preterm labor.*

Aim :*The purpose of the study was to compare the efficacy of nifedipine against isoxsuprine in inhibiting preterm labour and also to evaluate maternal side effects and neonatal outcome.*

Materials and Methods*: This randomized prospective study comprised of 92 patients with preterm labor with a gestational age between 24 – 36 weeks, admitted to Department of Obstetrics and Gynecology ,Tishreen university Hospital , Lattakia ,Syria , during the period of November 2018 to November 2019. The Patients who fullfield the inclusion criteria for the study were divided into 2 groups; the first consisted of 58 patients, treated with Nifedipine for tocolysis, the second consisted of 34 patients, who received isoxsuprine for tocolysis. Patients were monitored throughout the course of treatment and followed until delivery.*

Results*:Baseline characteristics were well matched in both study groups. Mean prolongation of pregnancy was 31.6 days in Nifedipine and 22.9 days in Isoxsuprine group which was statistically significant. Success rate with Nifedipine was found to be 84.5% as compared to Isoxsuprine which was 70.5%. Maternal side effects like tachycardia (38.2%) and hypotension (14.7%) were common in Isoxsuprine group, while headache (51.7%) and facial flushing (56.9%) were common in Nifedipine group. The mean neonatal weight in Isoxsuprine group (2.07 kg) was lower than Nifedipine group (2.38 kg), with no differences in Apgar score between the two groups.*

Conclusion *:Nifedipine is a better tolerated, more effective and safe tocolyticagent than Isoxsuprine with few maternal complications.*

Keywords*:Preterm labor, Tocolytic, Nifedipine, Isoxsuprine*

I. INTRODUCTION

Pretem labor generally can be defined as regular and/or painful uterine contractions (≥4 every 20minutes or≥8 in60 minutes)that occur between 20 weeks and before 37weeks of gestation and are associated with changes in the cervix that involve (effacement≥80%)and(dilation≥2cm). [1]

preterm labor is the most common reason for hospitalisation of pregnant women .preterm birth affects 12%in USA and these birth represent more than 70% of all perinatal morbidity and mortality.[2]

Accurate identification of women in true pretem labor allows appropriate application of intravention that can improve neonatal outcome :antenatal corticosteroid therapy ,group B streptococcal infection prophylaxis,magnesiumsulfat for neuroprotection ,and transfer to a facillity with an appropriate level of newborn care (if necessary). [3]

the main aim of using tocolytisis is to prolong pregnancy till 37 weeks or at least delay delivery for 48 hours so as to allow the fetal lung maturity with the help of steroid .

Nifedipine and Isoxsuprine are the most commonly used tocolytic in Syria.

Isoxsuprine hydrochloride which is betasympathetomymetic act through cycic Gmp to inhibit utrrine contractios while calcium channel blockers (Nifedipine) directly inhibit calcium ion influx across the cell membrane thus decreasing the smooth muscle tone .

The objective of this study was to compare the efficacy of nifedipine against isoxsuprine in preventing preterm labor and to evaluate material side effects and neonatal outcome.

II. MATERIAL AND METHODS

This randomized prospective study was carried out in department of obstetrics and gynecology ,Tishreen hospital ,Latakia,Syria,over period of 12 months from November 2018 to November 2019.

92 antenatal cases between 24-37weeks of gestation with preterm labor .

The patients who consented for the study were divided into 2 groups ;group A conisted of 58 patients ,treated with nifedipine for tocolysis,the

group B consists of 34 patients ,who received isoxsuprine for tocolysis.

Antenatal women between 24-37 weeks of gestation with preterm labor were recruited in the study after patients demographics ,history epidemiological factors and routine inestigation were taken .Patients with the maternal factors like Diabetes mellitus ,Hypothyroidism ,Cardiac disease, Liver disease ,Severe Preeclampsia and eclampsia ,abruption placentae ,severe anemia ,multiple pregnancy, premature rupture of membrane were excluded and fetal factors such as fetal distress ,severe IUGR,and fetal anomalies incompatible with life were also considered for exclusion.

Therefore the final participarts under study were 92 patients.

Group A were given nifedipine with an initial oral dose of 10-20 mg every 20 minutes until to a maximum of 40 mg during the first hour of treatment ,followed by additional 10-20 mg orally every 4-6 hours for up to 48 hours.

Group B treated with isoxsuprine were given oral 10mg 8hourly.

Patients in both groups were given antibiotics and injection betamethasone 24mg in 2divided doses 24 hr apart .Uterine contractios ,fetal heart rate and vital signs were monitored in both the study groups .Side effects are noted from the time of adminstration of drug till the patient was discharged from the labor word.

Treatment was considered successful,if there was abolition of uterine contractions ,no progression of cervical dilation ,and also if contractions did not recur with 48 hours of cessation of therapy.

Treatment was deemed failure ,despite maximal dose mentioned for both groups ,if uterine relaxation was not achieved or patient or foetus developed some significant side effects that.

The Patients were followed up till delivery and outcome was noted with respect to weeks of gestation at the time of delivery ,prolongation of pregnancy and birth weight.

III. RESULTS

In the present study of the 92 women with signeleton pregnancies of which 58received nifedipine and 34 received isoxsuprine .

Gestational age wise distribution and clinical profile of the subjects are presented in table 1 homogenity of the two groups in age ,gestational age on admission

TABLE I:Clinical profile of the subjects

Parameters	Nifedipine N=58	Isoxsuprine N=38	T .test	P-value
Age(Mean)years	27.7±5.38	28.2±5.8	0.418	o.676
Gestationage of admission(weeks)	31.13±2.03	31.2±2.07	0.384	0.701

There is no statistically significant difference in both drugs with age or gestational age on admission [table1].

Nifedipine group has highest success rate of 84.5% .In isoxsuprine group ,success rate was noted 70.5%.

[Figure1]shows mean prolongation of pregnancy .In the present study was (31.6±17days)with nifedipine and (22.9±14.8days)with isoxsuprine .

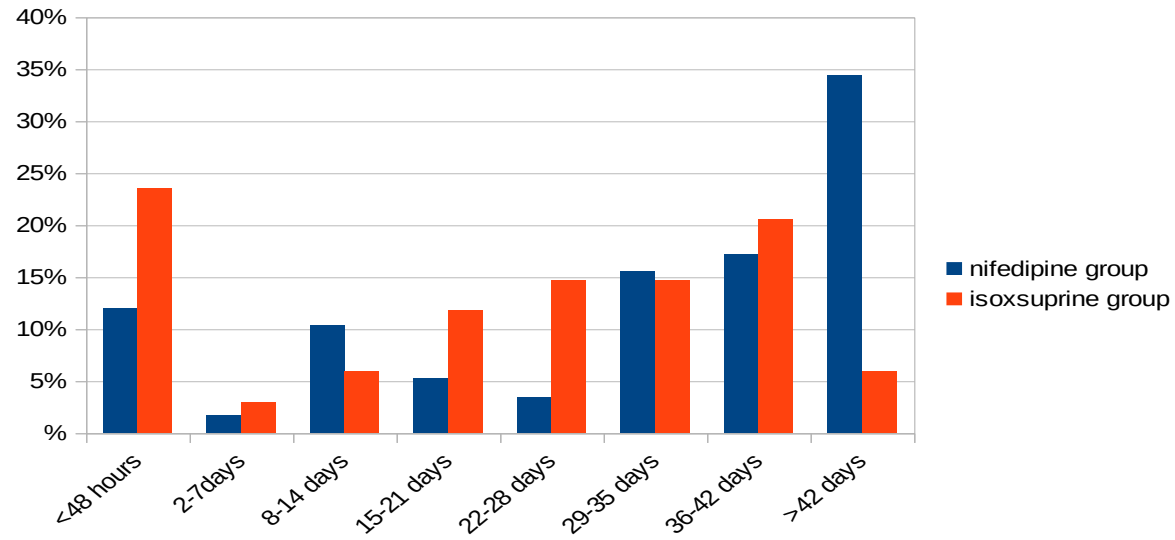

Fig 1: Distribution of the patients according to prolongation of pregnancy.

[TableII]shows the side effects of the drugs,maternal side effects like hypotension ,tachycardia were seen more in isoxsuprine group with statistically significant difference,while headache and facial flushing were seen more in nifedipine group with statistically significant difference .There is no statistically significant difference between two groups in dyspnia,dizziness,and nausea.

Table II: Maternal side effects.

Side effects	Isoxsuprine group	Nifedipine group	X^2 test	P-value
Tachycardia≥110	(38.2%)13	(17.2%)10	5.039	0.024
Headache	(29.4%)10	(51.7%)30	4.342	0.037
Nausea	(17.6%)6	(7%)4	1.48	0.22
Hypotension<90/60 mm Hg	(14.7%)5	(1.7%)1	5.925	0.014
Facial flushing	(35.3%)12	(56.9%)33	4.003	0.045
Dizzeness	(0%)0	(1.7%)1	0.593	0.44
Dyspnia	(5.9%)2	(0%)0	3.48	0.061

Table III : Gestation age at delivery in weeks

Gestational age at delivery(weeks)	Nifidipine group	Isoxsuprine group	X^2-test	P-value
<37w	(34.5%)20	(55.9%)19	0.019	0.044
≥37w	(65.5%)38	(44.1%)15		

Period of gestation at the time of delivery was ≥37weeks in 65.5% of cases in nifedipine group when compared with isoxsuprine groupn44.1%[tableIII].

Mean birth weight of infants was (2.38±0.4kg)in nifedipine group .In isoxsuprine group ,infants deliverd had maen birth weight of (2.07±0.46kg)with statistically significant difference .

Table IV :shows apgar score of the baby in the two groups .

Apgar score		Nifedipine N=58	Isoxsuprine N=34	X^2-test	P-value
1`	<7	(15.5%)9	(32.4%)11	3.571	0.058
	≥7	(84.5%)49	(67.6%)23		
5`	<7	(6.9%)4	(17.6%)6	2.557	0.109
	≥7	(93.1%)54	(82.4%)28		

There was no ststistically significant difference in distribution of patients according to apgar score in 1` or 5`(Pvalue>0.05) [tableIV]

IV. DISCUSSION

Incidence of preterm birth in USA is 12% and it is acause of high rates of perinatal morbidity and mortality [1]

Efficacy and safety of tocolytic agents in peterm labor has been a difficult task because the cause of preterm labor is generally unkommon and therapy can not be directed to a specefic cause .

Isoxsuprine was the first beta sympathomimetic drug used to inhibit preterm labor in 1961. [5]

Many studies have shown it to have limited therapeutic value in light of unpleasant side effects and efficacy

Nifidipine a calcium canal blocker was the first used clinically as a tocolytic by Ulmstan et.al in 1980. [6] since then it has emerged as a safe and effective tocolytic.

The prospective study was designed to find out the safety ,efficacy and perinatal outcome of isoxsuprine and nifedipine in women with preterm labor .

Most of the studies so far conducted have compared the efficacy and safety between nifedipine and ritodrine ,only few studies have been done between nifedipine and isoxsuprine .Kundu et al [9],Vanremmawii et al [10],Schah et al [11],Jain et al [12] have conducted studies about comparision between the efficacy and safety of nifidipine and isoxsuprine in the suppression of preterm labor .

In the present study ,nifedipine shows significantly better efficacy 84.5% as compared to isoxsuprine 70.5%.Kundu et al [9]reported a success rate of 77.1% with nifedipine and 67.1% with isoxsuprine .Shah et al [11]reported 84% success with nifedipine and 72% with isoxsuprine .Jain et al

[12] reported success rate of 90% with nifedipine and 76% with isoxsuprine.

Kundu et al [9] found nifedipine prolong pregnancy for 24.2±8 days,Vanremmawii et al [10] found it as 15.4±12 days ,Shah et al [11] found it as 32.1±20days Jain et al [12] 22.4±15.6days .In our study ,nifidipine was found to prolong pregnancy for 31±17 days .In the isoxsuprine treated group ,Kundu et al [9] found pregnancy was prolonged for 14.9±5.8days ,Vanremmawii et al[10]13.3±13days ,Shah et al [11]24.3±18days,Jain et al[12]16.5±14.5 days and in our study 22.9±14.8days.

Regarding the side effects of the drugs ,in our study.

In our study and in other studies ,Kundu et al [9],vanremmawii et al[10],Shah et al [11],Jain et al [12] all found nifedipine to be associated with significantly fewer maternal side effects as compared with isoxsuprine .

In present study hypotension ,tachycardia ,nausea,dyspnia in 14.7%,38.2%,17.6%,5.9% were more in isoxsuprine group as seen in Kundu et al [9].Headache,flashing were more in nifedipine group .In Vanremmawii et al [10] headache , tachycardia were more in isoxsuprine group .

Regarding the Apgar score of babies ,there was no statistically significant difference between the two groups as seen in Kundu et al[9] and Vanremmawii et al [10].

There was statistically significant difference in the mean birth weight of the babies between nifedipine group 2.38±0.4kg when compared with isoxsuprine group 2.07±0,46kg which has similar to other studies Kundu et al [9],Vanremmawii et al [10],Shah et al [11], Jain et al [12].

V. CONCLUSION

Prematurity continues to be the major conntributer to the perinatal mortality and morbidity .

None of the currently available tocolytic agents are ideal,the approaches which prevent and treat preterm labor will have great impact on society and long term puplic care costs .

This study shows that nifedipine is an effective tocolytic agent comparable to isoxsuprine with fewer side effects and haemodynamic compromise.

Nifedipine will play an expanded role in the suppression of preterm labor.

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