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Comparative Study of Isoxsuprine and Nifedipine in the Management of Preterm Labour.

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ABSTRACT

Background: The purpose of the study was to compare the efficacy of Isoxsuprine and Nifedipine as tocolytic agent on preterm labour and to compare the Obstetrical outcome following Isoxsuprine and Nifedipine therapy as a tycolytic agent. **Methods:** The study which was randomized prospective study, comprised of 100 patients with preterm labor, admitted in antenatal ward of State Referral Hospital, Falkawn, Mizoram during the period of January 2015 to December 2017. The Patients who fullfield the inclusion criteria for the study were divided into 2 groups; group-A consisted of 48 patients, treated with Nifedipine for tocolysis, the group-B consisted of 52 patients, who received isoxsuprine for tocolysis, and were monitored throughout the course of treatment. **Result:** Successful tocolysis was achieved by Nifedipine in 77.1% of the case as compared to 67% with the isoxsuprine treated cases. And Nifedipine prolonged pregnancy for 15.427±12.875 days while Isoxsuprine prolonged pregnancy for 13.356±13.612 days. Apgar score of babies less than 7 was 33.3% in Group-A and 32.6% in Group-B. The incidence of perinatal death (16%) in group-A is lower as compared to (19.6%) group-B. **Conclusion:** Nifedipine is more effective tocolytic agent, as compared to Isoxsuprine. The neonatal outcome with respect to birth weight, Apgar score and perinatal death were better in the cases treated with nifedipine as compared to Isoxsuprine.

Keywords: Isoxsuprine, Nifedipine, Preterm Labour.

INTRODUCTION

Preterm Labour is defined as initiation of regular uterine contraction with increase in frequency and magnitude with progressive cervical dilation and effacement (unless inhibited by tocolysis) culminating in delivery of the preterm infant.

Prematurity is the leading cause of perinatal morbidity and mortality. If has been reported to cause 75% - 85% of early neonatal deaths. Prematurity also contributes significantly to mental retardation, visual and hearing impairment and cerebral palsy.[1] Even though there has been a lot of research and attempt to diagnose and predict women at risk of developing preterm labour, But the definitive causative factor is still elusive, and the obstetrician has to manage preterm labour. The main aim of using tocolysis 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 a steroid. Isoxsuprine and nifedipine are the most commonly used tocolytic in India, Isoxsuprine hydrochloride which is betasympathetomymetic act through cyclic Gmp to inhibit uterine contraction while Calcium channel blockers (Nifedipine) directly inhibit calcium ion influx across the cell membrane thus decreasing the smooth muscle tone. This study was conducted to compare their efficacy and analyze the overall outcome.

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MATERIALS AND METHODS

The study which was randomized prospective study, comprised of 100 patients with preterm labor, admitted in antenatal ward of State Referral Hospital, Falkawn, Mizoram during the period of January 2015 to December 2017.

The Patients who consented for the study were divided into 2 groups; group A consisted of 48 patients, treated with Nifedipine for tocolysis, the group B consisted of 52 patients, who recieved isoxsuprine for tocolysis. Antenatal women between 28 – 37 weeks of gestation with preterm labour as per the ACOG criteria ie. 4 uterine contraction in 20 minutes with or without cervical dilatation more than 1 cm or effacement 80% or greater were recruited in the study after Patients demographics, history, epidemiological factors and routine investigations were taken. Patients with the maternal factors like Diabetes mellitus, hypothyroidism, cardiac desease,

severe pre-eclampsia, and eclampsia, abruption placentae, chorioamnionitis, hydramnios, premature rapture 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 participants under study were 100 patients.

Group A were given Nifedipine 30 mg orally at diagnosis. If uterine contraction persist after 90 minutes another 20 mg Nifedipine was given orally. If contraction was suppressed after the first or second dose, a maintenance dose of 20 mg was given 8 hourly till 37 weeks of gestation, however if uterine contraction persist for 60 minutes after the second dose the treatment was considered a failure.

Group B treated with Isoxsuprine were given a loading dose of 10 mg i.m and repeated 6 hourly for 48 hours. Patient who responded were switched over to 20 mg retard orally every 12 hours as maintenance dose for 1 week.

In both the groups subjects were monitored for uterine contraction, palpitation, maternal pulse rate and fetal heart rate. If there is any unacceptable side effects like severe palpitation, chest pain and tachycardia more than 120/min or progress of labour the respective drugs were stopped.

The patients were followed up till delivery and outcome was noted with respect to weeks of gestation at the time of delivery, mode of delivery, time interval between beginning of treatment and time of delivery.

RESULTS

Gestational age wise distribution and clinical profile of the subjects are presented in table 1. Homogeneity of the two groups in Age, Parity, Gestational age, Socio economic status and obstetrical history was found significant.

Table 1: Clinical profile of the subjects

Parameters	Nifedipine (N=48)	Isoxsuprine (N=52)	P-value
1. Age (Mean) Years	24.92±4.37	25.37±5.18	P = 0.57
2. Parity P0 P1 P2 P3	 25 (52%) 15 (31.2%) 6 (12.5%) 2 (4.16%)	 23 (44.2%) 14 (26.9%) 10 (19.2%) 5 (9.6%)	 P = 0.57
3. Socio Economic Status Low Middle	 30 (62.5%) 18 (37.5%)	 34 (65.3%) 18 (55.8%)	P = 0.35
4. Previous abortion History	8 (17.9%)	9 (17.3%)	P = 0.15
5. Previous Preterm Delivery	6 (12.5%)	11 (!&.3%)	P = 1.0
6. Gestational age on Admission (Weeks)	32.59±1.83	32.51±2.1	P = 0.50

[Table 2] shows the tocolysis in the two groups, Nefidipine tocolysis was successful at 77.1% and delivery was delayed for 7 days at 18.7% and upto 28 days at 37.5%. The mean prolongation of pregnancy was 15.427±12.875 days while Isoxsuprine tocolysis was successful at 67.3% and delivery delayed for 7 days at 17.3% and upto 28 days at 23%. The mean prolongation of pregnancy was 13.356±13.612 days in Isoxsuprine group.

Table 2: Comparison of Tocolysis in Group A and B

Admission Delivery Interval	Nifedipine (N=48)	Isoxsuprine (N=52)	X2= 3.2
< 48 hours	11 (22.9%)	16 (30.7%)	
48 hrs – 7 days	09 (18.7%)	09 (17.3%)	
7 days – 14 days	05 (10.4%)	09 (17.3%)	P = 0.52
14 days – 28 days	18 (37.5%)	12 (23%)	
> 28 days	05 (10.4%)	06 (11.53%)	

[Table 3] shows the side effects of the drugs; maternal side effects like Hypotension, Tachycardia, Headache, Nausea, Vomiting and Hot flashes were seen more in Isoxsuprine group.

Table 3: Side effects of the drugs

Side Effects	Nifedipine (N=48)	Isoxsuprine (N=52)	P - Value
Hypotension	8 (16.6%)	12 (23%)	P = 0.93
Tachycardia	15 (31.25%)	40 (77%)	P = 0.04
Headache	10 (21%)	3 (5.7%)	P = 0.004
Nausea	3 (6.25%)	8 (15.4%)	
Vomiting	1 (2.1%)	6 (11.5%)	
Hot flashes	5 (10.41%)	Nil	

[Table 4] shows the Birth weight and Apgar score of the baby in the two groups. The mean birth weight among the nifedipine group and the Isoxsuprine group were 1989.58±518.69 gms and 1892.31±527.24 gms respectively.

Variables	Distribution	Nifedipine N=48	Isoxsuprine N=52
Birth Weight (kg)	>2.5	07 (14.58%)	08 (15.38%)
	2 – 2.5	21 (47.75%)	11 (21.15%)
	1.6 – 2	06 (12.50%)	16 (30.76%)
	1.1 – 1.5	12 (25%)	14 (26.90%)
	≤ 1	02 (4.16%)	03 (5.76%)
Apgar Score	0	3 (6.25%)	4 (7.69%)
	< 4	4 (8.30%)	4 (7.69%)
	4 - 6	9 (18.70%)	9 (17.30%)
	> 7	32 (66.60%)	35 (67.30%)

DISCUSSION

Preterm labour resulting in prematurity and neonatal complications is still a major obstetrical problem, no definite cause or preventive measure have been found, over the last 2 decades a number of drugs have been used to suppress uterine activity. Gulati A et al found Nifedipine prolong pregnancy for 21.1±17.4 days,[2] Kalita D et al found it as 31.68±10.02 days,[3] Sachan A et al 39.26±15.5 days.[4] In our study, Nifedipine was found to

prolong pregnancy for 15.50±12.79 days. In the isoxsuprine treated group. Gulati A et al found pregnancy was prolonged for 13.10±18.40 days,[2] Kalita D et al 23.08±9.30 days,[3] Sachan A et al 39.26±25.5 days,[4] and 13.44±13.53 days in our study.

In Nifedipine treated group, Smith CS et al found Successful tocolysis in 75% of the patients,[5] Gulati A et al 80% of the patients,[2] Kalita D et al 84% of the patients,[3] and Nagpal P et al 85.3% of the patients.[6] Nisha S et al reported successful tocolysis in 80% of the patient.[7] Bankatlal JP et al reported 90% with nifedipine.[8] In the present study, successful tocolysis was seen in 77.1% of the patients with preterm labour treated with nifedipine.

Gulati A et al found successful tocolysis in 52% of the patients treated with isoxsuprine,[2] Kalita D et al 64% of the cases,[3] Sachan A et al 50%.[4] And in the present study successful tocolysis was achieved in 67.3% of the patient treated with isoxsuprine. Nisha S et al reported successful tocolysis with isoxsuprine in 68% of the patient.[7] Bankatlal JP et al found 68.3% with ritodrine.[8] Our findings are comparable to Smith CS et al (1993) and Gulati A et al (1993).

The mean birth weight of the babies in the nifedipine treated group was 1989.58±598.69 gm in this study which was similar to the mean birth weight of the babies found in the studies of Patki A et al (1993), Gulati A et al (1993), and Kalita D et al (1996) In the Isoxsuprine treated group the mean birth weight of the babies was 1892.31±527.24 gm in the present study which was comparable to Gulati A et al (1993) and Patki A et al (1993).

Regarding the Apgar score of babies, there was no significant difference between the two groups. 73% of the babies in Nifedipine group and 71.2% of the babies in Isoxsuprine treated group had Apgar score score of >7 at 5 min after delivery, which is comparible to the findings of Gulati A et al (1993) and Kalita D et al (1996) in their studies.

Regarding the side effects of the drugs, Ganla KM et al observed tachycardia in 46% of the Nifedipine group as compared to 56% of Isoxsuprine treated group. Hypotension was seen 36% and 20% of the patients on Isoxsuprine and Nifedipine treated groups respectively. Nausea and vomiting was seen in Isoxsuprine 34% and Nifedipine 10%. Hot flashes and headache were seen in 40%, 30%. 17% and 12% of the patients on Isoxsuprine and Nifedipine respectively.[10] Palenik SR et al observed flushing in 96%, headache in 38% in the patients treated with nifedipine. He reported a transient fall of blood pressure following second dose of nifedipine which was not significant. He also reported that isoxsuprine caused nausea in 22 – 30% of the patients and palpitation and tachycardia in 50% of the patients.[11] In this studies, transient hypotension was seen in 17% of the patients treated with nifedipine as compared to 23% of the patients treated with isoxsuprine. Tachycardia was seen in 32% and 77% of the patients on nifedipine and isoxsuprine respectively. Headache was seen more commonly with nifedipine (21%) as compared to isoxsuprine (5.7%). 32% of the patients on isoxsuprine had more than one side effects while only 10% of the patients on nifedipine had more than one side effects.

CONCLUSION

Lowering the incidence of preterm delivery is obviously a better way of reducing neonatal morbidity and mortality especially in India, where sophisticated neonatal intensive care units are not available everywhere. Thus various drugs have been tried for tocolysis, in an effort to prolong intrauterine existence.

This study shows that Nifedipine, a dihydropyridine derivative calcium channel blocker is an effective tocolytic agent, comparable to Isoxsuprine in efficacy, with fewer side effects and lesser haemodynamic compromise. The neonatal outcome with respect to birth weight, Apgar score and perinatal death were better in the cases treated with nifedipine though the difference was not significant statistically. The mortality of the infant was not related to nifedipine or isoxsuprine, but due to prematurity and respiratory distress syndrome.

Limitations of the study:

Keeping in view the relatively small number of patients and short period of study in the present study, further controlled study involving a large number of patients, preferably coordinated multicenter trial with special attention to haemodynamic changes due to the drugs will be necessary to throw more lights on the subject.

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