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 fullfilled 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 tocolytic agent than Isoxsuprine with few maternal complications.

Keywords: Preterm labor, Tocolytic, Nifedipine, Isoxsuprine

I. INTRODUCTION

Preterm labor generally can be defined as regular and/or painful uterine contractions (≥4 every 20 minutes or ≥8 in 60 minutes) that occur between 20 weeks and before 37 weeks of gestation and are associated with changes in the cervix that involve (effacement ≥ 80%) and (dilation ≥ 2 cm). [1]

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

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

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 steroid.

Nifedipine and Isoxsuprine are the most commonly used tocolytic in Syria. Isoxsuprine hydrochloride which is betasympathothemymetic act through cyclic Gmp to inhibit utreric contractistics 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 conducted in the Department of Obstetrics and Gynecology, Tishreen Hospital, Lattakia, Syria, over a period of 12 months from November 2018 to November 2019.

92 antenatal cases between 24-37 weeks of gestation and preterm labor were included. The patients who consented for the study were divided into 2 groups; group A consisted 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 investigation were taken. Patients with the maternal factors like Diabetes mellitus, Hypothyroidism, Cardiac disease, Liver disease, Severe Preeclampsia and eclampsia, Abortion placenta, 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 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 8-hourly.

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

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 singleton pregnancies of which 58 received nifedipine and 34 received isoxsuprine.

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

**TABLE 1: Clinical profile of the subjects**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Nifedipine N=58</th>
<th>Isoxsuprine N=38</th>
<th>T-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean years)</td>
<td>27.7±5.38</td>
<td>28.2±5.8</td>
<td>0.418</td>
<td>0.676</td>
</tr>
<tr>
<td>Gestational age of admission (weeks)</td>
<td>31.13±2.03</td>
<td>31.2±2.07</td>
<td>0.384</td>
<td>0.701</td>
</tr>
</tbody>
</table>

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±17 days) with nifedipine and (22.9±14.8 days) with isoxsuprine.

![Fig 1: Distribution of the patients according to prolongation of pregnancy.](image-url)
[Table II] 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 dyspnea, dizziness, and nausea.

Table II: Maternal side effects.

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Nifedipine group</th>
<th>Isoxsuprine group</th>
<th>X² test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachycardia ≥110</td>
<td>(38.2%)13</td>
<td>(17.2%)10</td>
<td>5.039</td>
<td>0.024</td>
</tr>
<tr>
<td>Headache</td>
<td>(29.4%)10</td>
<td>(51.7%)30</td>
<td>4.342</td>
<td>0.037</td>
</tr>
<tr>
<td>Nausea</td>
<td>(17.6%)6</td>
<td>(7%)4</td>
<td>1.48</td>
<td>0.22</td>
</tr>
<tr>
<td>Hypotension &lt;90/60 mm Hg</td>
<td>(14.7%)5</td>
<td>(1.7%)1</td>
<td>5.925</td>
<td>0.014</td>
</tr>
<tr>
<td>Facial flushing</td>
<td>(35.3%)12</td>
<td>(56.9%)33</td>
<td>4.003</td>
<td>0.045</td>
</tr>
<tr>
<td>Dizziness</td>
<td>(0%)0</td>
<td>(1.7%)1</td>
<td>0.593</td>
<td>0.44</td>
</tr>
<tr>
<td>Dyspnia</td>
<td>(5.9%)2</td>
<td>(0%)0</td>
<td>3.48</td>
<td>0.061</td>
</tr>
</tbody>
</table>

Table III: Gestation age at delivery in weeks

<table>
<thead>
<tr>
<th>Gestational age at delivery (weeks)</th>
<th>Nifedipine group</th>
<th>Isoxsuprine group</th>
<th>X²-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;37w</td>
<td>(34.5%)20</td>
<td>(55.9%)19</td>
<td>0.019</td>
<td>0.044</td>
</tr>
<tr>
<td>≥37w</td>
<td>(65.5%)38</td>
<td>(44.1%)15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There was no statistically significant difference in distribution of patients according to apgar score in 1' or 5' (P-value>0.05) [Table IV]

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

<table>
<thead>
<tr>
<th>Apgar score</th>
<th>Nifedipine N=58</th>
<th>Isoxsuprine N=34</th>
<th>X²-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1' &lt;7</td>
<td>(15.5%)9</td>
<td>(32.4%)11</td>
<td>3.571</td>
<td>0.058</td>
</tr>
<tr>
<td>≥7</td>
<td>(84.5%)49</td>
<td>(67.6%)23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5' &lt;7</td>
<td>(6.9%)4</td>
<td>(17.6%)6</td>
<td>2.557</td>
<td>0.109</td>
</tr>
<tr>
<td>≥7</td>
<td>(93.1%)54</td>
<td>(82.4%)28</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IV. DISCUSSION

Incidence of preterm birth in USA is 12% and it is a cause of high rates of perinatal morbidity and mortality [1]. Efficacy and safety of tocolytic agents in preterm labor has been a difficult task because the cause of preterm labor is generally uncommon and therapy cannot be directed to a specific 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. Nifedipine a calcium channel 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], Shah et al [11], Jain et al [12] have conducted studies about comparison between the efficacy and safety of nifedipine 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
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.

ACKNOWLEDGMENT

The authors are grateful to the members of, Department of Gynecology and Obstetrics, Tishreen University Hospital in Lattakia, Syria for supplying medical samples.

REFERENCES


V. CONCLUSION

Prematurity continues to be the major contributor 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 pupile care costs.