ABSTRACT

Objective: To compare the efficacy and safety of oral Labetalol and Nifedipine in preeclampsia patients and to aid professionals in making appropriate therapeutic decisions in the management of preeclampsia.

Methods: A Prospective observational study with the total of 152 pregnant women with preeclampsia is conducted in a Tertiary Care Hospital in India. Pregnant women with preeclampsia prescribed with either oral labetalol or oral nifedipine were selected. Main outcome measures include monitoring of adverse effects of labetalol and nifedipine and efficacy of both drugs. Blood pressures were measured every 4 hrs using sphygmomanometer and average of three consecutive readings is recorded. The two groups were followed until delivery and are interviewed for any adverse reactions.

Results: The duration of days required for labetalol to normalize the high blood pressure is 5 days (5±2.63 d), and that of nifedipine is 7.5 days (7.5±3.83 d) with P value of 0.0015. Common adverse Drug reactions (ADR's) of the both drugs are pedal edema (50%, 47.36%), headache (44.7%, 26.31%), and orthostatic hypotension (9%, 7%) etc are compared.

Conclusion: Oral Labetalol is more efficacious than Oral Nifedipine, with an exception of more adverse effects and high cost.

Keywords: Preeclampsia, Safety, Efficacy, Labetalol, Nifedipine.

INTRODUCTION

Hypertensive disorders of pregnancy are an important cause of severe morbidity and mortality among both mother and fetus [1]. Pregnant women with hypertension have more chance to develop placental abruption, disseminated intravascular coagulation (DIC), cerebral hemorrhage, hepatic failure and acute renal failure [2].

Hypertensive disorders of pregnancy include Preeclampsia, Eclampsia, Chronic hypertension, gestational hypertension and preeclampsia superimposed on chronic hypertension [3, 4]. Among the pregnancy complicating hypertensive disorders, Preeclampsia and Eclampsia are the major causes of maternal and perinatal mortality and morbidity [1].

Preeclampsia is defined as a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg on 2 occasions at least 4 h apart after 20 w gestation in women with a previously normal blood pressure or ≥160 mmHg systolic or ≥110 mmHg diastolic, confirmed with a short interval (minutes) to facilitate timely antihypertensive therapy and Proteinuria ≥300 mg/24 h or a protein/creatinine ratio≥ 0.3 mg/dl or a dipstick reading of 1+reading [5].

Worldwide about 76,000 pregnant women die each year from preeclampsia and related hypertensive disorders. Fetal mortality rate is thought to be on the order of 5,00,000 per annum [6]. The prevalence of Preeclampsia in developing countries ranges from 1.8% to 16.7% [7]. The Recent United Kingdom (UK) guidelines from the National Institute of Health and Clinical Excellence (NICE) recommend oral Labetalol as the first line choice in the treatment of hypertension in pregnancy [8].

Novelty of the study

Selection of antihypertensive agent is the major issue concerned with pre-eclampsia. National Institute of Health and Clinical Excellence Guidelines suggests that Labetalol, Nifedipine and Methyldopa are preferred choice of drugs. The use of antihypertensive drugs in pregnancy is controversial as most antihypertensive agents used in pregnancy are designated as Category ‘C’ stating that human studies are lacking. Clinicians vary in their choice of treatment for hypertension in pregnancy and there is uncertainty regarding potential benefits and harms of using antihypertensive drugs in pregnancy.

A meta-analysis study of Randomized controlled trials conducted for the assessment of efficacy, side effects and perinatal outcome of nifedipine compared with other antihypertensives for treating severe preeclampsia in pregnant women concluded that nifedipine is associated with greater effective control of blood pressure and prolongation of gestation, compared with other antihypertensive for women with severe preeclampsia [9].

A prospective study conducted in 2012 evaluated the effectiveness and safety of oral Labetalol and oral Nifedipine in pregnant women with Pregnancy induced hypertension (PH) and concluded that labetalol is more effective than Nifedipine in controlling blood pressure whereas tachycardia (11 %) and occipital headache are more common with nifedipine [10]. Despite of various clinical trials conducted, there is seldom robustness in the treatment guidelines of preeclampsia. Therefore our study focuses on an assessment of safety and efficacy of oral labetalol and oral nifedipine in the control of hypertension in pregnancy.

MATERIALS AND METHODS

A Prospective Observational Study has been carried out on Comparison of Safety and Efficacy of oral Labetalol and oral Nifedipine in Pre-eclampsia patients in Obstetrics and Gynecology Department at Government General Hospital, Guntur for 6 months from 1st March 2014 to 31st August 2014.

The study is completely inpatient based; primary data was generated by studying patients admitted for the management of preeclampsia. Inclusion Criteria is pregnant women of age between
Blood pressure doesn’t decrease even after increasing the dose to maximum, additional antihypertensive agent is added and the treatment is considered as failure.

Investigations Considered are complete hemogram, Liver function tests (LFT’s), Renal function tests (RFT’s), Serum uric acid, Fundoscopy, Ultrasound scan. Those patients with impending eclampsia were given Magnesium sulphate. Decision to continue with conservative management of pregnancy or to deliver and mode of delivery is made depending on maternal and fetal indications. Then patients were followed until delivery and the various modes of delivery were noted. The patients were interviewed for the drug adverse effects. Later consultation was made with the physician and the data were documented. Finally, the documented data was analyzed using Microsoft excel version and statistical methods (t test) to find p value to compare the two treatment groups.

RESULTS

A comparative study consisting of 152 pregnant women, 76 pregnant women with pre eclampsia treated with Labetalol(Group A) and 76 pregnant women with preeclampsia treated with Nifedipine(Group B) is undertaken to study the safety & efficacy of the drugs. Both the two groups had comparable demographics and their characteristics are represented in table 1.

On comparison of common adverse effects of the both drugs, Labetalol and Nifedipine, we found Pedal edema (50%, 47.36%), Headache (28.94%, 26.31%), Sweating (23.68%, 15.78%), Orthostatic Hypotension (21.05%, 10.52%), Blurred Vision (21.05%, 2.63%), Chills and Rigors (15.78%, 7.89%), Facial Edema (15.78%, 7.89%), Dizziness (10.52%, 10.52%), Nausea & Vomiting (10.52%, 0), Bronchospasm (7.89%, 2.63%), Fever (7.89%, 5.26%) respectively. We found Labetalol (Group A) has experienced more adverse effects than Nifedipine and is as shown in fig. 3 and in table 2.
for Labetalol is 120 h (120±63.12) and 180 h for Nifedipine (180±91.92) with P value of 0.0015 and are as listed in table 3. There is significant difference between both the treatment groups.

Table 2: Comparison of adverse effects of oral labetalol and nifedipine

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>Labetalol (n=76)</th>
<th>Nifedipine (n=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No of Patients</td>
<td>Percentage</td>
</tr>
<tr>
<td>Pedal Edema</td>
<td>38</td>
<td>50</td>
</tr>
<tr>
<td>Headache</td>
<td>22</td>
<td>28.94</td>
</tr>
<tr>
<td>Sweating</td>
<td>18</td>
<td>23.68</td>
</tr>
<tr>
<td>Orthostatic Hypotension</td>
<td>16</td>
<td>21.05</td>
</tr>
<tr>
<td>Blurred Vision</td>
<td>16</td>
<td>21.05</td>
</tr>
<tr>
<td>Chills &amp; Rigors</td>
<td>12</td>
<td>15.78</td>
</tr>
<tr>
<td>Facial Edema</td>
<td>12</td>
<td>15.78</td>
</tr>
<tr>
<td>Dizziness</td>
<td>8</td>
<td>10.52</td>
</tr>
<tr>
<td>Nausea &amp; Vomiting</td>
<td>8</td>
<td>10.52</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>6</td>
<td>7.89</td>
</tr>
<tr>
<td>Fever</td>
<td>6</td>
<td>7.89</td>
</tr>
<tr>
<td>Cough</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anasarca</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Periorbital Edema</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*n-samplesize

Table 3: Comparison of efficacy of labetalol and nifedipine

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Labetalol (n=76)</th>
<th>Nifedipine (n=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration in days</td>
<td>5</td>
<td>7.5</td>
</tr>
<tr>
<td>Duration in Hours</td>
<td>120</td>
<td>180</td>
</tr>
<tr>
<td>mean±SD (d)</td>
<td>5±2.63</td>
<td>7.5±3.83</td>
</tr>
<tr>
<td>mean±SD (h)</td>
<td>120±63.12</td>
<td>180±91.92</td>
</tr>
<tr>
<td>P value: 0.0015</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SD: Standard Deviation,*n-Sample Size.

DISCUSSION

The Cochrane review on drugs for the treatment of very high blood pressure in pregnancy concluded that until better evidence is available, the choice of antihypertensive should depend on the clinician's experience and familiarity with a particular drug [11].

The appropriate selection of antihypertensive in pre-eclampsia is controversial in the literature. Most commonly preferred choice of antihypertensive is Labetalol, Methyldopa, and Nifedipine in pre-eclampsia [12].

As per the National Institute for Health and Clinical Excellence (NI CE) guidelines for hypertension in pregnancy, the preferred choice of drug is oral Labetalol to oral nifedipine and Methyldopa [8].

Main findings

In our study, we included 152 pregnant women with Group A(n=76), Group B(n=76). Group A is treated Labetalol and Group B with Nifedipine. Treatment Strategies are Labetalol 100 mg twice daily, Maximum Dosage 2400 mg/day; Nifedipine 10 mg Thrice a day (TID), Maximum Dosage 120 mg/day. If there is seldom improvement to normal dosage, the dosage was increased in increments to both treatment groups. Pregnant women were monitored for Blood Pressure every 4 h and adverse effects frequently. Based on the statistics, we observed that Labetalol is more effective than Nifedipine in controlling blood pressure whereas the safety concern, nifedipine has less frequency of side effects than labetalol.

Strengths and Limitations

The strengths of our study are the generalizability of results is due to the diversity of the study population from various regions and unbiased since there is no loss of data as it is a prospective study and there exists a chronological relationship between drug exposure and outcome.

The limitations of our study are Study population is heterogeneous which includes both proteinuric and non-proteinuric pregnant women with high blood pressure and Blood pressure considered is
the highest single reading recorded among all four hourly measurements for the entire day.

**Interpretation**

The results of our study are similar to that of a prospective, randomized, open labeled study, the use of oral labetalol with oral nifedipine in hypertensive urgencies in the emergency department of obstetrics conducted by McDonald AJ et al. The pretreatment Blood pressure for labetalol was 195/127 mmHg which decreased to 154/100 mmHg and of nifedipine was 198/128 mm Hg, alleviated to 163/100 mm Hg (P>2). No significant side effects occurred with either drug. Labetalol is effective when compared to nifedipine in pregnancy induced hypertensive emergencies [13].

However, they diverge from a Meta-analysis Study conducted by Liu QQ et al, the study includes the assessment of the efficacy, side effects and perinatal outcome of nifedipine compared with other antihypertensives.

Compared with other antihypertensives, nifedipine contributed greater efficacy in controlling blood pressure (OR = 2.65, 95%CI: 1.65-4.25, P<0.01) [9].

A recent prospective study conducted by Nita K. Patela et al. in 2012 to evaluate the comparative effectiveness and safety of nifedipine, methylopro and labetalol monotherapy in patients with Pregnancy induced hypertension (PIH) concluded that Labetalol was more effective than methylopro and nifedipine in controlling blood pressure in patients with Pregnancy induced hypertension (PIH) providing sustenance for our study [10].

There was no major adverse event attributed to either drug regimens. Our data supports recent guidelines and expert opinion that oral labetalol is the suitable first-line antihypertensive for hypertensive emergencies of pregnancy.

**CONCLUSION**

From our study, we observed that Oral Labetalol is more efficacious than Oral Nifedipine, with an exception of more adverse effects and high cost. Hence most of the Health care professionals preferring Nifedipine to Labetalol. However, due to inter individual variation, prevalence of side effects may vary and due to their lesser severity, it’s better to opt labetalol for effective control of blood pressure in preeclampsia.

**Practical and research recommendations**

In order to have an appropriate therapeutic decision making, further studies should be performed in the future with large homogenous study population for better results.

**ABBREVIATION**


**Details of ethics approval**

Ethics Committee, Guntur Medical College and Govt. General Hospital, Guntur–522004, AP, India

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**CONFLICT OF INTERESTS**

Declared None

**REFERENCES**


