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COMPARISON STUDY OF THERAPEUTIC EFFICACY AND SAFETY OF LABETALOL AND NIFEDIPINE IN MANAGEMENT OF PREECLAMPSIA, TERTIARY CARE HOSPITAL, BANGLORE, INDIA

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ABSTRACT

Objectives: *to evaluate safety of labetalol and nifedipine in management of preeclampsia. And to compare efficacy of labetalol and nifedipine for management of preeclampsia. Tertiary Care Hospital, Banglore, India.* ***Method:*** *A hospital based prospective cross sectional descriptive study was conducted on inpatients from OBG department who have been diagnosed with preeclampsia and admitted to Aster CMI tertiary care Hospital Bangalore. Demographic details (Name, age) of patient were collected. Admission, discharge date, diagnosis of the patient and drug data (Brand and generic name) of antihypertensive drugs (labetalol, nifedipine) prescribed, dose frequency, route of administration, dose were recorded. Blood pressure at day of admission was recorded and compare with mean blood pressure after receiving labetalol and nifedipine. Data were analyzed using statistical software. Probability values (p value) less than 0.05 were considered significant. Quantitative variables have been indicated in mean ± SD. Results of continuous measurements are presented on mean and results of categorical measurements are presented in Number, percentage (%).* ***Results:*** *A total 60 patients who fulfilled the inclusion and exclusion criteria were enrolled in the study. Determination of maternal age, gravida and pregnancy trimester distribution among patients showed majority of patients 30 (50%) were in age group of 25-29 years, 26 (43.33%) were in gravida third (G 3) and 46 (76.67%) were at their 3rd trimester of pregnancy. Determination of body mass index distribution demonstrated majority of patients 36 (60%) at pre-obesity nutritional status. In this study we found, the mean systolic blood pressure lowering effect for labetalol was 129.88 ± 2.08 mmHg and for nifedipine was 147.91 ± 5.5 mmHg. The mean diastolic blood pressure lowering effect for labetalol and nifedipine was found to be 89.41 ± 4.1 mmHg and 98.33 ± 6.2 mmHg respectively. In current observation, we found labetalol was more effective than nifedipine with P value: < 0.001 (Probability values less than 0.05 were considered significant) which showed significant effect in lowering maternal high blood pressure. In patient`s urine analysis, out of total 60 patients, 29 (48.33%) were double positive for albuminuria followed by 13 (21.67%) for triple or more positive, 10 (16.67%) for single positive and only 8 (13.33%) showed negative albuminuria. In present study, labetalol only contributed in four numbers of all reported adverse effects including hypotension and headache, whereas nifedipine found to be reason for twelve numbers of adverse effects containing hypotension, heart rate abnormalities and drowsiness.* ***Conclusion:*** *Labetalol was safer and more effective than nifedipine in lowering blood pressure in patients with pregnancy-induced hypertension/preeclampsia.*

KEY WORDS

Preeclampsia, Antihypertensive Drugs, Labetalol, Nifedipine and Tertiary Care Hospital.

INTRODUCTION

Pregnancy is associated with profound anatomical, physiological, biochemical and endocrine changes that affect multiple organs and systems. These changes are essential to help the woman to adapt to the pregnant state and to aid fetal growth and survival. Such anatomical and physiological changes may cause confusion during clinical examination of a pregnant woman. [1]

Preeclampsia is a pregnancy-specific disease characterized by development of hypertension (blood pressure levels above 140/90 mmHg at two successive measurements at a 4-hour interval) and proteinuria after 20 weeks of pregnancy in women with previously normal blood pressure, sometimes progressing into a multiorgan cluster of varying clinical features such as edema, visual disturbance, and headache and epigastric pain. It can affect the mother's kidneys, liver, and brain. The condition can be fatal for the mother and/or the baby and can lead to long-term health problems. [2]

In industrialized countries preeclampsia complicates approximately 3-5% of pregnancies and represents one of the most common causes of maternal mortality and severe maternal morbidity including eclampsia, placental abruption, pulmonary edema, and acute renal failure. Infants of mothers with preeclampsia are at approximately 2-fold higher risk of neonatal death. [3] The prevalence of preeclampsia in developing countries ranges from 1.8% to 16.7 %. [4]

Pathophysiological evidence characterizing preeclampsia as a condition of excessive systemic inflammation. Conditions such as asthma and obesity, which are both associated with inflammation, increase the risk of preeclampsia. Recent work suggests that women with moderate to severe asthma symptoms, regardless of asthma diagnosis or treatment, are at Severe pre-eclampsia/eclampsia with blood pressure readings ≥ 160/110 mmHg is associated with increased risks of complications like hypertensive encephalopathy, intra-cranial hemorrhage and eclampsia. The reduction of blood pressure to levels below 150/100 mmHg is necessary to reduce complications. [6]

Although preeclampsia is unique to pregnancy, it shares biological and pathological similarities as well as many risk factors (e.g., obesity, diabetes, dyslipidemia, hypertension, etc.) with adult cardiovascular diseases (CVD). Endothelial dysfunction and inflammation are fundamental mechanisms for the initiation and progression of both atherosclerosis and preeclampsia. [7] Women with chronic hypertension prior to pregnancy are at increased risk of a number of complications, including superimposed preeclampsia, preterm delivery, fetal growth restriction or demise, placental abruption, heart failure, and acute kidney failure. [8]

The management of pre-eclampsia focuses on the control of acute hypertension, the prevention of seizures and timely delivery of the fetus. In a patient with pre-eclampsia who is near or at term (≥ 37 weeks gestation), when the fetus is mature, delivery is an effective way to treat the disorder and optimize pregnancy outcomes. In preterm gestations, the risk of continuing the pregnancy in the face of a multisystemic disorder must be balanced against the risks of premature birth.

Delivery is indicated when life-threatening maternal complications are present or impending, such as severe hypertension refractory to treatment (which places the mother at risk of stroke), pulmonary edema, acute renal failure, hepatic rupture or eclampsia. The primary goal of treating hypertension in patients with pre-eclampsia is to prevent an acute hypertensive crisis, which might lead to intracranial hemorrhage or stroke. [9-11]

MATERIALS AND METHODS

1 Place of Study

This study was conducted on inpatients of obstetrics and gynecology department of Tertiary Care Hospital, Bangalore, India.

2 Study Design

A hospital based prospective cross sectional descriptive study to determine efficacy and safety of labetalol and nifedipine in management of preeclampsia.

3 Sample Size

A total 60patients from the obstetrics and gynecology department of Tertiary Care Hospital who received labetalol and nifedipine for management of their preeclampsia and fulfilled the inclusion and exclusion criteria were selected for the study.

4 Study Criteria

I) Inclusion Criteria

Patients with severe preeclampsia and who admitted to obstetrics and gynecology department of a Tertiary Care Hospital, Aster CMI Hospital, Bangalore, India

II) Exclusion Criteria

- Patients with essential hypertension.
- Patient with H/O Cardiac disease, Bronchial asthma, Hematological disorder, Allergy to labetalol or nifedipine, Diabetic and Liver disorders.

5 Study Procedures

I) Patient Enrollment

A hospital based prospective cross sectional descriptive study was conducted on inpatients from obstetrics and gynecology department who have been diagnosed with preeclampsia and admitted to tertiary care Hospital Bangalore.

II) Data Collection

Data has been collected with respect to:

- Demographic details: Names, age, sex of patients
- Prescribed drug data: Name of drugs prescribed, dose of drugs, dose frequency, route of administration.

RESULT AND DISCUSION

Most observational studies demonstrate a consistently strong positive association between maternal pregnancy body mass index and the risk of preeclampsia. In present study, body mass index has been divided as per world health organization criteria into below 18.5 (underweight), 18.5–24.9 (normal weight), 25.0–29.9 (pre-obesity) and 30.0 or more (obese). Determination of body mass index distribution among patients showed majority of patients 36 (60%) at preobesity nutritional status followed by 15 (25%) were at normal weight and 9 (15%) were at obese nutritional status (Table No. 1)

Table No. 1: Maternal Body Mass Index Distribution

Body Mass Index	Nutritional Status	Number of Patient (n = 60)	Percentage (%)
Below 18.5	Underweight	0	-
18.5–24.9	Normal Weight	15	25.00
25.0–29.9	Pre-obesity	36	60.00
30.0 or more	Obese	9	15.00

Table No. 4 shows comparison of mean systolic/diastolic blood pressure-lowering effects between labetalol and nifedipine antihypertensive medication. In current study we found, the mean systolic blood pressure lowering effect for labetalol was 129.88 ± 2.08mmHg and for nifedipine was 147.91 ± 5.5 mmHg. The mean diastolic blood pressure lowering effect for labetalol and nifedipine was found to be 89.41 ± 4.1mmHg and 98.33 ± 6.2 mmHg respectively. In current observation, we found labetalol was more effective than nifedipine with *P* value: < 0.001 (Probability values less than 0.05 were considered significant) which showed significant effect in lowering aternal high blood pressure.

Table No. 2: Maternal Systolic and Diastolic Blood Pressure after Administration of Labetalol

Systolic Blood Pressure (mm Hg)	Number of Patient (n = 60)	Percentage (%)
120 – 129	27	45.00
130 – 139	26	43.33
140 – 149	7	11.67
150 – 159	0	-
≥ 160	0	-
Diastolic Blood Pressure (mm Hg)	**Number of Patient (n = 60)**	**Percentage (%)**
80 – 89	43	71.67
90 – 99	16	26.67
100 – 109	1	1.67
110 – 119	0	-
≥ 120	0	-

Table No. 3: Maternal Systolic and Diastolic Blood Pressure after Administration of Nifedipine

Systolic Blood Pressure (mm Hg)	Number of Patient (n = 60)	Percentage (%)
120 - 129	15	25.00
130 - 139	31	51.67
140 - 149	14	23.33
150 - 159	0	-
≥ 160	0	-
Diastolic Blood Pressure (mm Hg)	**Number of Patient (n = 60)**	**Percentage (%)**
80 – 89	24	40.00
90 – 99	29	48.33
100 – 109	7	11.67
110 – 119	0	-
≥ 120	0	-

Systolic and diastolic blood pressure of included patients was recorded after receiving antihypertensive medications (Labetalol and Nifedipine). All these data are demonstrated in Table No. 2-3

Table No. 4: Comparison of Maternal Systolic/Diastolic Blood Pressure-Lowering Effects between Antihypertensive Medication Labetalol and Nifedipine

Medication and Mean ± SD Blood Pressure			P value
	Mean ± SD for SBP	Mean ± SD for DBP	
Labetalol	129.88 ± 2.08	89.41 ± 4.1	< 0.001*
Nifedipine	147.91 ± 5.5	98.33 ± 6.2	≥ 0.040

* Significant (p value: p ≤ 0.01)

Similar finding correlates with the study of comparative evaluation of antihypertensive drugs in the management of pregnancy-induced hypertension, labetalol was more effective than methyldopa and nifedipine in controlling blood pressure in patients with pregnancy-induced hypertension. (12)

In patient`s urine analysis, out of total 60 patients, 29 (48.33%) were double positive for albuminuria followed by 13 (21.67%) for triple or more positive, 10 (16.67%) for single positive and only 8 (13.33%) showed negative albuminuria. A study of microalbuminuria in pregnancy as a predictor of preeclampsia showed urinary micro-albumin excretion when used as a single test appeared to predict preeclampsia with a high sensitivity. (13)

Out of total, sixteen patients complained adverse drugs reactions. In present study we found, labetalol only contributed in four number of all reported adverse effects including hypotension and headache, whereas nifedipine found to be reason for twelve number of adverse effects containing hypotension, heart rate abnormalities and drowsiness (Table No. 5). Mode of child delivery is shown in Table No. 6.

Table No.5: Comparison Number of Patients with Adverse Drug Reaction

Adverse Drug Reactions	Labetalol	Nifedipine
Hypotension	1	7
Heart Rate Abnormalities	0	4
Headache	3	0
Drowsiness	0	1
Total	4	12

Table No. 6: Mode of Delivery of Patients

Mode of Delivery	Number of Patients	Percentage (%)
Spontaneous Vaginal Delivery	35	58.33
Vacuum/Forceps	8	13.33
Caesarean Section	3	5.00
Twin Delivery	0	-
Undelivered	14	23.33

CONCLUSION

Preeclampsia is the most frequently encountered medical disorder in obstetrics practice and remain a major cause of maternal, fetal & neonatal morbidity & mortality. Total 60 patients who fulfilled the inclusion and exclusion criteria were enrolled in the study. The mean systolic blood pressure lowering effect for labetalol was 129.88 ± 2.08 mmHg and for nifedipine was 147.91 ±5.5 mmHg. In current observation, we found labetalol was more effective than nifedipine with P value: < 0.001 (Probability values less than 0.05 were considered significant) which showed significant effect in lowering maternal high blood pressure. We concluded labetalol was safer and more effective than nifedipine in lowering blood pressure in patients with pregnancy induced hypertension (preeclampsia).

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