Study of Therapeutic Efficacy and Safety of Labetalol and Nifedipine in Management of Preeclampsia, Kempegowda Institute of Medical Sciences, Bangalore, India

Maysam Rowshani*, Keshava H. K.

Abstract

Background: Preeclampsia is a pregnancy-specific disease characterized by development of hypertension (blood pressure levels above 140/90 mmHg) and proteinuria after 20 weeks of pregnancy in women with previously normal blood pressure, sometimes progressing into a multi organ 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 additionally the child and can prompt long term health problems. The present study was undertaken to compare safety and therapeutic effect of labetalol and nifedipine in controlling pregnancy induced hypertension. Objective: To compare efficacy and safety of labetalol and nifedipine in management of preeclampsia in Kempegowda Institute of Medical Sciences, Bangalore, India. Methodology: A medical clinic based forthcoming cross sectional spellbinding investigation was directed on inpatients from OBG department who have been determined to have preeclampsia and admitted to KIMS 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 (%). Result: A complete 60 patients who satisfied the inclusion and exclusion criteria were joined up with the investigation. Determination of maternal age, gravida and pregnancy trimester dispersion among patients indicated lion's share 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 impact for labetalol was 129.88 ± 2.08 mmHg and for nifedipine was 147.91 ± 5.5 mmHg. The mean diastolic blood pressure lowering impact for labetalol and nifedipine was found to be 89.41 ± 4.1 mmHg and 98.33 ± 6.2 mmHg respectively. In current perception, we discovered labetalol was more powerful than nifedipine with P value: < 0.001 (Probability values less than 0.05 were considered significant) which demonstrated huge impact in lowering maternal high blood pressure. In patient`s urine analysis, out of total 60 patients, 29 (48.33%) were double positive for albuminuria pursued 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 observed to be purpose 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

Introduction

Pregnancy is related with significant anatomical, physiological, biochemical and endocrine changes that influence multiple organs and systems. These progressions are basic to assist the lady with adapting to the pregnant state and to help fetal development and survival. Such anatomical and physiological changes may cause perplexity amid clinical examination of a pregnant woman. Essentially, changes in blood biochemistry during pregnancy may make challenges in interpretation of results. On the other hand, clinicians additionally need to perceive pathological deviations in these ordinary anatomical and physiological changes during pregnancy to establish proper activity to improve maternal and fetal result (Niraj Yanamandra and Edwin Chandraharan, 2012).

preeclampsia (PE) is a clinical substance described by either the new onset of hypertension and proteinuria or end organ damage after 20 weeks of gestation. It is one of the real pregnancy-related hypertensive disorders and can happen postpartum. Extra clinical signs and

Maysam Rowshani*, Keshava H. K.

Doctors of pharmacy, Department of pharmacy practice, Visveswarapura institute of pharmaceutical sciences, Bengaluru, India.

*Email: rowshani.maysam@gmail.com

side effects incorporate headache, visual disturbance, epigastric pain, thrombocytopenia, and abnormal liver capacity (Lain and Roberts, 2002). These clinical manifestations are activated by mild to severe microangiopathy of target organs, including the brain, liver, kidney, and placenta. Potential maternal intricacies incorporate pulmonary edema, cerebral hemorrhage, hepatic failure, renal failure, and even death. Potential fetal complications are caused by placental hypo perfusion or the need for preterm delivery.

Traditionally, the clinical conclusion of PE is made when new-onset hypertension in the second 50% of pregnancy is related with new-onset proteinuria. In any case, following the observation that some patients show evidence of multi organ damage without proteinuria, under certain circumstances PE can be diagnosed without proteinuria. In the absence of proteinuria, the conclusion can be made whether any of coming up next is available: abnormal liver function, thrombocytopenia, renal insufficiency, pulmonary oedema, visual impairment, or cerebral symptoms. As indicated by the 2013 report of the American College of Obstetricians and Gynaecologists' Task Force on Hypertension in Pregnancy, PE can be analysed when either (Lain and Roberts, 2002) systolic blood pressure is more noteworthy than or equivalent to 140 mmHg or diastolic blood pressure is more than or equal to 90 mmHg on two events something like 4 h separated in a previously normotensive patient or (American College of Obstetricians and Gynecologists, 2013) systolic blood pressure is more than or equal to 160 mm Hg or diastolic blood pressure is more than or equal to 110 mmHg and hypertension can be affirmed inside minutes to encourage timely antihypertensive therapy. In addition to hypertension, proteinuria must be measured as greater than or equal to 300 mg per 24 h urine specimen, as a protein ratio greater than or equal to 0.3, or as a urine dipstick protein of 1+ (if a quantitative measurement is unavailable) (Cunningham et al., 2010).

Hypertensive disorders confound 5-10% everything pregnancies and together they form one member of deadly triad, along with hemorrhage & infection that contribute enormously to maternal morbidity and death rates (Cunningham et al., 2010). Pregnancy initiated hypertension incorporates a gathering of hypertensive disorders created due to gravid state after 20 weeks of pregnancy. Preeclampsia may be mild or severe. HELLP (Hemolysis, Elevated liver enzymes, Low platelet counts) syndrome is a complication of severe preeclampsia/eclampsia (Brown, Buddle and Farrrell, 1998).

Incidence of Eclampsia in the developed countries is about 1 in 2000 deliveries[3] as compared to developing countries (Douglas KA, Redman, 1994; World Health Organization, 1988; Crowther, 1985; Bergstrom, 1992) where it differs from 1 in 100 to 1 in 1700. Preeclampsia/eclampsia likely records in excess of 50,000 maternal deaths worldwide every year (Lopez-Jaramillo, Casas and Serrano, 2001).

The administration of pre-eclampsia focuses on the control of acute hypertension, the aversion of seizures and timely delivery of the fetus. In a patient with pre-eclampsia who is close or at term (≥ 37 weeks' gestation), when the fetus is mature, delivery is an effective way to treat the disorder and upgrade pregnancy results. In preterm gestations, the risk of continuing the pregnancy in the face of a multisystem disorder must be balanced against the risks of premature birth. Delivery is shown when life-threatening maternal complications are available or looming, for example, extreme hypertension refractory to treatment (which puts the mother at risk of stroke), pulmonary edema, acute renal failure, hepatic rupture or eclampsia (Preeclampsia Complications Royal College of Obstetrics and Gynecology Guideline; Palei et al., 2013; Maged et al., 2013). The essential objective of treating hypertension in patients with pre-eclampsia is to prevent an acute hypertensive crisis, which may prompt intracranial hemorrhage or stroke.

Materials and Methods

This investigation was directed on inpatients of obstetrics and gynecology department of Kempegowda Institute of Medical Sciences, Bangalore, India. A hospital based planned cross sectional illustrative examination to decide viability and safety of labetalol and nifedipine in management of preeclampsia. A total 60patients from the obstetrics and gynecology department of Tertiary Care Hospital who got labetalol and nifedipine for the executives of their preeclampsia and satisfied the inclusion and exclusion criteria were chosen for the examination. The study was conducted for a period of 6 months from June2018 to November 2018.

Study Criteria

- **Inclusion Criteria:** Patients with serious preeclampsia and who admitted to obstetrics and gynecology department of a Tertiary Care Hospital.
- **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.

Descriptive statistical analysis has been carried out in the present study. Data were analyzed using SPSS 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 exhibited on mean ± SD and results of categorical estimations are introduced in Number, percentage (%), Microsoft word and Excel have been used to generate graphs, tables etc.

Result and Discusion

A clinic based imminent cross sectional illustrative examination was directed to determine efficacy and safety of labetalol and nifedipine in management of preeclampsia at obstetrics and gynecology department of tertiary hospital Bangalore, India. All out 60 patients who satisfied the inclusion and exclusion criteria were taken on the examination. Determination of maternal age, gravida and pregnancy trimester distribution among patients indicated greater part of patients 30 (50%) were in age gathering of 25-29 years, 26 (43.33%) were in gravida third (G 3) and 46 (76.67%) were at their 3rd trimester of pregnancy (Table 1).

Table 1: Maternal Age, Gravida and Pregnancy Trimester Distribution

Parameter	Number of Patient (n = 60)	Percentage (%)
Age Distribution (year)		
19 or less	1	1.67
20 to 24	21	35
25 to 29	30	50
30 or more	8	13.33
Gravida		
G 1	12	20
G 2	20	33.33
G 3	26	43.33
G 4 or more	2	3.33
Pregnancy Trimester (week)		
1 to 12	2	3.33
13 to 28	12	20
29 to 40	46	76.67

A study conducted by Lamminpaa R, et al (2012). concluded preeclampsia is more common in women with advanced maternal age and risk of preeclampsia increases with advancing in maternal age. Most observational examinations show a reliably strong positive association between maternal pregnancy body mass index and the risk of preeclampsia. In present examination, body mass index has been partitioned according to 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). Assurance of body mass index conveyance among patients demonstrated larger part of patients 36 (60%) at pre obesity nutritional status pursued by 15 (25%) were at normal weight and 9 (15%) were at obese nutritional status. Study on risk factors for preeclampsia in multigravida women conducted by Parvin Bastani, et al (2008) demonstrated that high maternal age and BMI, history of preeclampsia, positive past medical history and inadequate prenatal care are risk factors for preeclampsia among multigravida women.56 In this study, 40 (66.67%) of patients have stayed 10-20 days at hospital followed by 10 (16.67%) for 21-30 days, 9 (15%) for less than 10 days and 1 (1.67%) for more than a month. Systolic and diastolic blood pressure before receiving antihypertensive medication (Labetalol and Nifedipine) at a day of admission at hospital are shown in Table 5-6, Figure No. 9-10. According to definition criteria for preeclampsia, majority of patient 30 (50%) were above 140 mmHg for systolic blood pressure and 35 (58.33%) patients were above 90 mmHg for diastolic blood pressure. Systolic and diastolic blood pressure of included patients were recorded subsequent to getting antihypertensive medications (Labetalol and Nifedipine). All these data are demonstrated in Table 2, 3

Table 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
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 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
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
90 - 99	29	48.33
100 - 109	7	11.67
110 - 119	0	-
≥ 120	0	-

Table 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	< 0.001*
Labetalol	129.88 ± 2.08	89.41 ± 4.1	≥ 0.040
Nifedipine	147.91 ± 5.5	98.33 ± 6.2	

Table 4 shows comparison of mean systolic/diastolic blood pressure-lowering effects between labetalol and nifedipine antihypertensive medication. In current examination we found, the mean systolic blood pressure lowering impact for labetalol was 129.88 ± 2.08mmHg and for nifedipine was 147.91 ± 5. 5mmHg.The mean diastolic blood pressure lowering impact for labetalol and nifedipine was observed to be 89.41 ± 4.1mmHg and 98.33 ± 6.2 mmHg separately. In current perception, we discovered labetalol was more compelling than nifedipine with P value: < 0.001 (Probability values less than 0.05 were considered significant) which indicated significant effecting lowering maternal high blood pressure (Table 4) 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.[48] We found the average of hemoglobin, platelet count, fasting blood sugar, serum creatinine and blood urea were between normal values, however average level of liver enzyme (Alkaline Phosphatase) found to be high among of patients (Table 9). Study of preeclampsia with hemolysis, elevated liver enzymes, and thrombocytopenia which conducted by Weinstein Louis described elevated liver enzyme is associated with preeclampsia and supportive therapy must be followed to improve maternal and fetal outcome.[57] In patient`s urine investigation, out of total 60 patients, 29 (48.33%) were twofold positive for albuminuria pursued by 13 (21.67%) for triple or progressively positive, 10 (16.67%) for single positive and just 8 (13.33%) indicated 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.

Out of total, sixteen patients complained adverse drugs reactions. In present examination we discovered, labetalol just contributed in four number of all announced adverse effects including hypotension and headache, whereas nifedipine observed to be purpose behind twelve number of adverse effects containing hypotension, heart rate abnormalities and drowsiness (Table 5).

Table 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

Conclusion

Preeclampsia is the most frequently encountered medical disorder in obstetrics practice and remain a major cause of maternal, fetal & neonatal morbidity & mortality. Absolute 60 patients who satisfied the inclusion and exclusion criteria were taken a crack at the examination. The mean systolic blood pressure lowering impact for labetalol was 129.88 ± 2.08 mmHg and for nifedipine was 147.91 ± 5.5 mmHg. In current perception, we discovered labetalol was more powerful than nifedipine with P value: < 0.001 (Probability values less than 0.05 were viewed significant) which indicated 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).

References

American College of Obstetricians and Gynecologists. (2013). Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' task force on hypertension in pregnancy. Obstetrics and gynecology, 122(5), 1122.

Bastani, P., Hamdi, K., & Najafi, H. (2008). Risk factors for preeclampsia in multigravida women. Research Journal of Biological Sciences, 3(1), 148-153.

Bergström, S., Povey, G., Songane, F., & Ching, C. H. O. N. G. (1992). Seasonal incidence of eclampsia and its relationship to meteorological data in Mozambique. Journal of perinatal medicine, 20(2), 153-158.

Brown, M. A., Buddle, M. L., Farrell, T., Davis, G., & Jones, M. (1998). Randomised trial of management of hypertensive pregnancies by Korotkoff phase IV or phase V. The Lancet, 352(9130), 777-781.

Costantine, M. M., & Cleary, K. (2013). Pravastatin for the prevention of preeclampsia in high-risk pregnant women. Obstetrics and gynecology, 121(2 0 1).

Crowther, C. A. (1985). Eclampsia at Harare Maternity Hospital. An epidemiological study. South African medical journal= Suid-Afrikaanse tydskrif vir geneeskunde, 68(13), 927-929.

Cunningham, F. G., Leveno, K. J., Bloom, S. L., Hauth, J. C., Rouse, D. J., & Spong, C. Y. (2010). Pregnancy hypertension. Williams obstetrics, 23, 706.

Lain, K. Y., & Roberts, J. M. (2002). Contemporary concepts of the pathogenesis and management of preeclampsia. Jama, 287(24), 3183-3186.

Lamminpää, R., Vehviläinen-Julkunen, K., Gissler, M., & Heinonen, S. (2012). Preeclampsia complicated by advanced maternal age: a registry-based study on primiparous women in Finland 1997–2008. BMC pregnancy and childbirth, 12(1), 47.

López-Jaramillo, P., Casas, J. P., & Serrano, N. (2001). Preeclampsia: from epidemiological observations to molecular mechanisms. Brazilian journal of medical and biological research, 34(10), 1227-1235.

Palei, A. C., Spradley, F. T., Warrington, J. P., George, E. M., & Granger, J. P. (2013). Pathophysiology of hypertension in pre‐eclampsia: a lesson in integrative physiology. Acta physiologica, 208(3), 224-233.

Preeclampsia Complications Royal College of Obstetrics and Gynecology Guideline. Available at https://www.rcog.org.uk/guidelines.

Redman, C. W. G. (1994). Eclampsia in the United Kingdom. Br Med J, 309, 1395-1400.

World Health Organization. (1988). International Collaborative Study of Hypertensive Disorders of Pregnancy. Geographic variation in the incidence of hypertension in pregnancy. Am J Obstet Gynecol, 158(1), 80-3.

Yanamandra, N., & Chandraharan, E. (2012). Anatomical and physiological changes in pregnancy and their implications. Obstetric and intrapartum emergencies: a practical guide to management, 1.