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Research Article

THE ROLE OF ORAL LABETALOL AND NIFEDIPINE IN THE TREATMENT OF PREGNANCY-INDUCED HYPERTENSION

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ABSTRACT

Hypertensive disorders are the most common medical disorders encountered during pregnancy and are responsible for 15% of the maternal deaths in India. According to American College of Obstetricians and Gynecologists (ACOG) hypertension in pregnancy is defined as systolic blood pressure (SBP) of 140 mm Hg or higher and Diastolic blood pressure (DBP) of 90 mmHg or higher after 20 weeks of gestation with previous normal BP. The aim of this study is to evaluate the role of oral Labetalol and Nifedipine in the management of pregnancy-induced hypertension. The study designed as a prospective observational study. A specially designed data entry form was used to enter all patient data like Name, Age, Past Medical & Medication history, obstetric history, Lab values, Blood pressure, Immunization status, Current treatment & Drug related problems. Pregnant women with pregnancy-induced hypertension prescribed with either Labetalol or Nifedipine were selected. Main outcome measures include monitoring of side effects of Labetalol and Nifedipine and efficacy of both drugs. Blood pressures were measured using sphygmomanometer. The two groups were followed until delivery and are interviewed for any side effects. In conclusion Labetalol is very effective in controlling pregnancy-induced hypertension, with an exception of high cost. Nifedipine remains a better alternative because of its rapidity in action in controlling blood pressure even in hypertensive emergencies very effectively.

KEYWORDS: *Hypertensive Disorders, Efficacy, Labetalol, Nifedipine.*

INTRODUCTION

Hypertensive disorders represent one of the most common medical complications of pregnancy [1, 2]. Hypertensive disorders of pregnancy occur in about 10% of all pregnant women around the world. Preeclampsia affects 3–5% of pregnancies. Along with preeclampsia, other diseases which are included in the group of hypertensive disorders of pregnancy are eclampsia, gestational hypertension and chronic hypertension.

In Asia and Africa, nearly one tenth of all maternal deaths are associated with hypertensive disorders of pregnancy. In India, the incidence of preeclampsia is reported to be 8-10% among the pregnant women. According to a study, the prevalence of hypertensive disorders of pregnancy was 7.8% with preeclampsia in 5.4% of the study population in India.

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Women who develop severe hypertension during pregnancy may experience adverse eff ects similar to those associated with mild preeclampsia [2-4]. In the mother, these may range from elevated liver enzymes to renal dysfunction; and in the fetus, from preterm delivery to intrauterine restriction of fetal growth [3, 4].

Hypertensive disorders are the most common medical disorders encountered during pregnancy and are responsible for 15% of the maternal deaths in India [5]. According to American College of Obstetricians and Gynaecologists (ACOG) hypertension in pregnancy is defined as systolic blood pressure (SBP) of 140 mm Hg or higher and Diastolic blood pressure (DBP) of 90 mmHg or higher after 20 weeks of gestation with previous normal BP [6]. The main goal of treatment is to safeguard the mother from the development of acute complication like cerebro-vascular accidents, eclampsia, target organ damage and maternal mortality while delivering a healthy Infant [7]. National Institute for Health and Clinical Excellence guidelines 2010 recommend use of intravenous Hydralazine, oral Nifedipine and intravenous Labetalol for treatment of severe hypertension in pregnancy._Different anti-hypertensive drugs available are: Methyldopa, Beta-blocker including Labetalol, Calcium channel blocker (Nifedipine) Hydralazine, Nitroglycerine. Sisson *et al.* [8], studied Hydralazine versus Labetalol for management of hypertension. They concluded that

Labetalol is safe and effective anti- hypertensive for management of severe hypertension.

Treating the hypertension does not alter the progression of disease. However it has been shown that early treatment decreases not only the frequency of hypertensive crisis, but also the rate of neonatal complications. Antihypertensive medications are mainly used to prevent or treat severe hypertension, to prolong pregnancy for as long as safely possible thereby maximizing the gestational age of the infant, and to minimize fetal exposure to medications that may have adverse effects. During pregnancy, the challenge is in deciding when to use antihypertensive medications, and what level of blood pressure to target. The antihypertensive drugs that may be used in pregnancy are methyldopa, beta blockers, calcium channel blockers and vasodilators [9].

Till date, there have not been many randomized clinical trials comparing these two agents. Hence this study was conducted to compare the efficacy safety and side-effects of Labetalol and Nifedipine, mode of delivery in two groups, fetal outcome in patients receiving either Labetalol or Nifedipine.

METHODOLOGY

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 Karuna medical college Hospital, Vilayodi, Chittur Palakkad district Kerala for a period of six months from November 2018 to April 2019. The study protocol was approved by ethical committee of the institution (IHEC/08/2018) and the written informed consent was taken from all the study participants.

Inclusion criteria for the study were patients with gestational hypertension whose blood pressure recordings are ≥140/90mmHg, Patients with gestational age from 20years to menopause, Gestational period of 14 to 39 weeks.[2nd &3rd trimester]. The Patients receiving more than one anti-hypertensive drug, Patients with previous history of heart diseases, liver diseases, and renal diseases are excluded, Allergy to Labetalol or Nifedipine, 1st trimester, Patients with protein in urine were excluded from our study.

On admission, detailed patient case history was collected which includes the details like age, obstetrics and gynecological history, past medical history, past medication history, blood pressure, socio economic status. The recorded blood pressure was collected. After diagnosing PIH written informed consent was taken and study group were treated with either Labetalol or Nifedipine. Pregnant women receiving Labetalol 100mg twice daily were considered as group A and who received Nifedipine 10mg thrice a day were considered as group B. Follow-up was done for 3 weeks by considering the blood pressure level along with that the complications by the drug was analyzed by using the data collection form. Numerical data obtained were statistically analysed with suitable statistical software. Descriptive statistics including means and standard deviations were calculated for all the variables. Differences among categorical variables analyze by using two-way ANNOVA.

RESULT AND DISCUSSION

A total of 89 patients with pregnancy induced hypertension were enrolled in the study and randomly divided in to two groups. Among them 56 were treated with Labetalol [Group A] and 33 were treated with Nifedipine [Group B] was undertaken to study the safety and efficacy of the drugs.

The demographic and clinical characteristics of the two groups at the time of enrolments, the majority of the pregnant women belong to age group of 20-25years and many of them are primigravidas in this category. In our study, we observed that 20-25years aged pregnant women are more prominent with pregnancy induced hypertension (Table 2).

Gestational age is a measure of the age of a pregnancy which is taken from the woman's last menstrual period (LMP), or the corresponding age of the gestation as estimated by a more accurate method if available. Such methods include adding 14 days to a known duration since fertilization. Among our study population, 75 % of patient in Labetalol and 69.7% of patient in Nifedipine was belonged to the above 30 weeks of the gestational week (Table 3).

In biology and human medicine says that the gravidity and parity are the number of times is or has been pregnant and carried the pregnancies to a viable gestational age. In our study population, Nifedipine 45.45% (n=15), Labetolol 42.85% (n=24) of patients belongs to Primi, followed by Nifedipine 39.39% (n=13), Labetolol 35% (n=20) of patients were belongs to the group of Gravidae 2 and Nifedipine 15.15% (n=05), Labetolol 21.42 (n=12) of patients are Gravidae 3 (Table 4).

Edema (swelling) during pregnancy is quite common. The amount of swelling, however, might vary according to the time of the day and weather. It might increase in the evening and in warmer temperatures. About half of all pregnant women experience it around their ankles, feet, and legs especially in the last few months of pregnancy. When compared with nifedipine group, Labetalol group having more number (Grade 1- 21.43% and Grade 2 – 26.79%) of patients affected pedal edema. Thereby confirming a relation between PIH and pedal edema. There is no significant difference in pedal edema incidence between the two study groups. Thereby showing either Labetalol or Nifedipine is not a predisposing factor to pedal edema (Table 5).

Table No. 1: Age Wise Distribution

Age in years	Nifidipine		Labetolol	
	Frequency (n=33)	Percentage (%)	Frequency (n=56)	Percentage (%)
20-25	16	48.48	34	60.71
26-30	14	42.42	11	19.64
>30	3	9.09	11	19.64

Table No. 2: Gestational Age at presentation

Gestational week	Nifedipine (n=33)		Labetatol (n=56)	
	Frequency (n=33)	Percentage (%)	Frequency (n=56)	Percentage (%)
20-25	5	15.15	6	10.71
26-30	5	15.15	8	14.28
>30	23	69.7	42	75.01

Table No. 3: Distribution of Cases According to Parity

PARITY	Nifedipine (n=33)		Labetatol (n=56)	
	Frequency (n=33)	Percentage (%)	Frequency (n=56)	Percentage (%)
Primi	15	45.45	24	42.85
Gravidae 2	13	39.39	20	35.71
Gravidae 3	5	15.15	12	21.42

Table No. 4: Distribution of Cases According to Pedal Edema

Pedal Edema	Nifedipine (n=33)		Labetatol (n=56)	
	Frequency (n=33)	Percentage (%)	Frequency (n=56)	Percentage (%)
Grade 1	9	27.27	12	21.43
Grade 2	7	21.21	15	26.79
Grade 3	-	-	-	-

Table No. 5: Distribution of Cases According to Mode of Delivery

Mode of delivery	Labetalol (n =56)		Nifedipine (n=33)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
Spontaneous vaginal delivery	18	32.14	13	39.39
Induction of labour	11	19.64	4	12.12
Acceleration of vaginal delivery	7	13.35	2	6.06
Instrumental delivery	2	3.57	3	9.09
Caesarean section	18	32.14	11	33.33

Vaginal delivery the baby is born through the birth canal. It's hard to know when exactly you will go into labour, but most women give birth at around 38-41 weeks of pregnancy. There are several benefits in vaginal delivery, shorter hospital stays, lower infection rates, quicker recovery; babies born vaginally have a lower risk of respiratory problems. In our study population, 34.83% of women were delivered by spontaneous vaginal delivery.

A caesarean section or C-section is the delivery of a baby through a surgical incision in the mother's abdomen and uterus. In certain circumstances, a C-section is scheduled in advance. Caesarean section was done in 32.58% of women. C-section was done because of several reasons, previous surgery, C-Sections, or other uterine conditions and Baby is in breech (bottom first) or transverse (sideways) position and placenta previa (when the placenta is low in the uterus and covers the cervix).

Figure 1 shows that the mean blood pressure before starting the treatment in group B was 156.06/93.33 mmHg and group A was 147.14/93.75 mmHg and after treatment the mean blood pressure in group 1 was reduced to 129.39/80.60 mmHg and in group 2 was 131.60/82.67 mmHg.

Side effects depends on many different factors, which can be generally grouped as patient-related, drug-related, and environmentally or socially-related. Side effects can be caused by all kinds of medicines, including prescription and over-the-counter medicines, complementary medicines including herbal preparations, vitamins, and some products dispensed by naturopaths and other practitioners of complementary medicine. Death can also occur in severe cases.

On individual assessment of the side effects of Labetalol and Nifedipine, patients on Labetalol has experienced side effects mostly dizziness ,excessive tiredness, nausea, headache ,tingling of scalp, light-headedness etc and side effects observed mostly due to Nifedipine are dizziness, excessive tiredness, headache, nausea, muscle cramps etc.
On comparing both the drugs, Labetalol and Nifedipine, we found both the drugs are showing almost similar side effects dizziness [73.21%,87.87%] excessive tiredness [76.78%,60.60%], nausea [42.85%,48.48%], headache [41.07%, 42.42%] heart burn [17.85%, 57.57%] light-headedness [28.57%,27.27%], tingling of scalp [28.57%, 27.27%] stomach upset [16.07%, 12.12%] stuffy nose [17.85, 6.06], fast heart beat [14.28%, 15.15%], muscle cramps [12.5%, 27.27%] constipation [10.7%, 9.09%] cough [8.9%, 3.03%] fatigue [0%,3.03%] (Table 6).

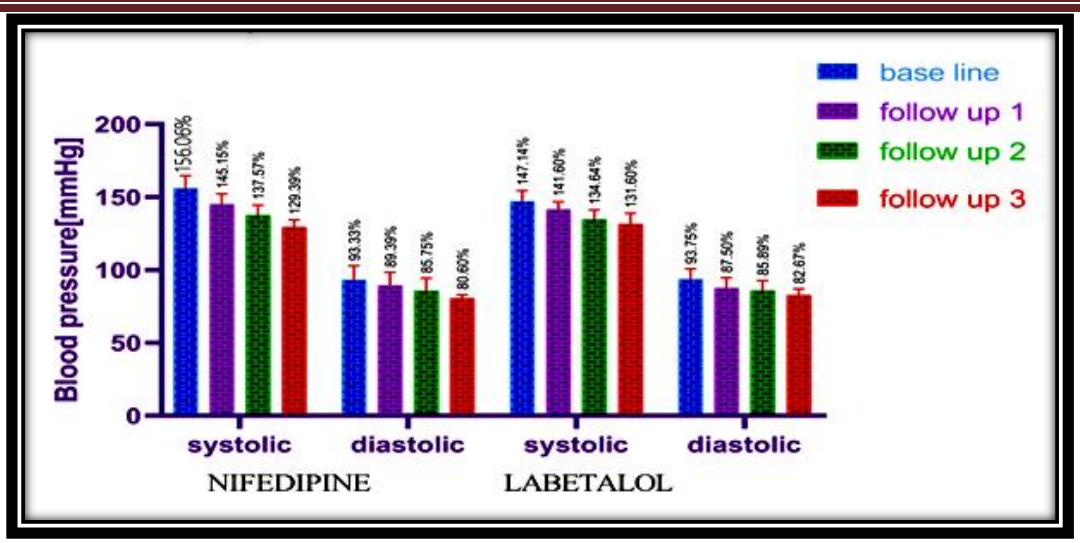

Fig. 1: Distribution of Cases According to Mean Blood Pressure Before and After Treatment

Table No. 6: Distribution of Cases According to Side Effects

Adverse effects	Labetalol		Nifedipine	
	Frequency	Percentage (%)	Frequency	Percentage (%)
Dizziness	41	73.21	29	87.87
Tingling of scalp	16	28.57	9	27.27
Lightheadedness	16	28.57	9	27.27
Excessive tiredness	43	76.78	20	60.60
Headache	23	41.07	14	42.42
Stomach upset	9	16.07	4	12.12
Stuffy nose	10	17.85	2	6.06
Nausea	24	42.85	16	48.48
Heart burn	10	17.85	19	57.57
Fast heart beat	8	14.28	5	15.15
Muscle cramps	7	12.5	9	27.27
Constipation	6	10.7	3	9.09
Cough	5	8.9	1	3.03
Fatigue	0	0	1	3.03

CONCLUSION

A hypertensive disorder of pregnancy is one of the life threatening complications encountered in obstetrics. Management of hypertension in pregnancy is a challenging task, because drastic reduction of BP leads to uteroplacental insufficiency & that may lead to intrauterine fetal death and continuation of pregnancy with severe hypertension leads to adverse feto-maternal outcome. Therefore, there is a need for an ideal antihypertensive agent for effective control of severe hypertension in pregnancy. In conclusion Labetalol is very effective in controlling pregnancy induced hypertension, with an exception of high cost. Nifedipine remains a better alternative because of its rapidity in action in controlling blood pressure even in hypertensive emergencies very effectively

Limitation:

Smaller population and shorter duration of the study is one of the limitations. We can't able to differentiate whether the side effects shown by the pregnant women are due to pregnancy or the impact of drug. Wide research studies with appropriate study design is needed to find if any casual association between pregnancy and prescribed drugs with the shown outcome.

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