Section: Obstetrics & Gynecology

Original Research Article

COMPARE THE ANTI-HYPERTENSIVE EFFICACY OF ORAL LABETALOL AND ORAL NIFEDIPINE IN MILD PREECLAMPSIA.

Surayya Tahseen[1], Juveriya[2], Hafsa Younus[3], Amtul Aziz Safiya[4], Sofia Sumain[5], Asma Hafeez[6]

[1]*Associate Professor, Department of Obstetrics & Gynecology, Deccan College of Medical Sciences, Hyderabad, Telangana, India.*
[2]*Senior Resident, Department of Obstetrics & Gynecology, Deccan College of Medical Sciences, Hyderabad, Telangana, India.*
[3,4,5,6]*Postgradute, Department of Obstetrics & Gynecology, Deccan College of Medical Sciences, Hyderabad, Telangana, India.*

Received *: 15/12/2023*
Received in revised form *: 04/02/2024*
Accepted *: 20/02/2024*

Corresponding Author:
Dr. Surayya Tahseen
Associate Professor, Department of Obstetrics & Gynecology, Deccan College of Medical Sciences, Hyderabad, Telangana, India..
Email: drsurtah@yahoo.com.

DOI: 10.5530/ijmedph.2024.1.65

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2024; 14 (1); 356-364

ABSTRACT

Background: Aim: This study is to compare the anti-hypertensive efficacy of Tablet Labetalol and Tablet. Nifedipine in mild preeclampsia.

Material and Methods: The study was conducted at the Deccan College of Medical Sciences (Owaisi Hospital and Research Centre and Princess Esra Hospital) both the hospitals attached from January 2021 to June 2022. 100 antenatal women with mild preeclampsia were selected. Informed consent taken. 50 women were given Tablet Labetalol. 50 women were treated with Tablet Nifedipine.

Results: This study was conducted on a total of 100 antenatal mild preeclamptic women to compare the anti-hypertensive efficacy of T. Labetalol and T. Nifedipine. The maternal and fetal outcomes were also studied. Patients were divided into two groups 50 each. Group A Received T. Labetalol and group B received T. Nifedipine. Blood pressure and feto maternal status were serially monitored. Termination was done at 37 completed weeks gestation or when the patient progressed to severe preeclampsia. The average dose required for T. Labetalol was 300 mg and 30 mg for T. Nifedipine. In both the groups, all 50 patients had adequate control of blood pressure. Inspite of adequate control the disease progressed in both groups. In group A (T. Labetalol) 14% progressed to severe pre-eclampsia. In group B (T. Nifedipine) 20% progressed to severe pre-eclampsia. Among the babies delivered, in group A 86% were term babies and 8% required SNN admission. In group B 80% were term babies and 10% required SNN admission. Comparing the two groups, group B had significantly higher number of side effects when compared to group A. None of the patients developed grave complications such as HELLP syndrome, pulmonary edema, coagulopathy, postpartum collapse, eclampsia. The maternal mortality was nil. Thus when patients with preeclampsia are identified and treated atan earlier stage the morbidity and mortality associated with preeclampsia can be significantly reduced.

Conclusion: From this study it is prudent that both T. Labetalol and T. Nifedipine are equally efficacious in the control of hypertension in mild preeclampsia.

Keywords: Preeclmpsia, Labetalol, Nifedipine, HELLP syndrome, Maternal Complications.

INTRODUCTION

Hypertensive disorders complicate 5-10 % of all pregnancies. Preeclampsia is identified in 3.9% of all pregnancies! (Williams 26th). Hypertensive disorders include preeclampsia, gestational hypertension, and chronic hypertension and complicate up to 10percent ofpregnancies. As a group, they are onemember ofthe deadly triad-along with haemorrhage and infection-that contributes greatly to maternal morbidity.[1]

In developed countries 16% of maternal deaths were due to hypertensive disorders. In India around 18-

15% of maternal deaths were due to hypertensive disorders. Importantly half of these deaths were preventable.[2]

Preeclampsia is best described as a pregnancy-specific syndrome that can affect virtually every organ system. Although preeclampsia is more than simply gestational hypertension with proteinuria, the appearance of protein remains a primary diagnostic criterion. It is an objective marker and reflects the system-wide endothelial leak that characterizes the preeclampsiasyndrome.[3]

Preeclampsia can be divided into early onset <34 weeks late onset >34 weeks, preterm onset <37 weeks, and term onset >37 weeks. Preeclampsia is hypertension with proteinuria after 20 weeks of gestation in women with previously normal blood pressure which returns to normal within 12 weeks gestation". Preeclampsia is defined as hypertension associated with proteinuria, greater than 0.3 g/L in a 24-hour urine collection or 1+ by qualitative urine examination two times 6 hours apart, after 20 weeks of gestation.[4]

Proteinuria is defined as 24-hour urinary protein excretion exceeding 300mg, and urine protein: creatinine ratio of ≥ 0.3, persistent 30 mg/dl (1+) in dipstick two times 6 hours apart.

Diagnosis of gestational hypertension is made in women whose systolic blood pressure reaches 140 mm of hg and above or when diastolic blood pressure reaches 90mmhg and above, for the first time after 20 weeksgestation, without proteinuria. The blood pressure returns to normal by 12 weeks postpartum.

Abnormal laboratory findings in tests of renal, hepatic and haematological function increase the certainty of preeclampsia. Preeclampsia often affects young and nulliparous women. The incidence ismarkedly influenced by race, ethnicity and has genetic predisposition. Other risk factors include obesity, multifetal gestation, thrombophilia's.[5]

Taking into consideration the various devastating complications ofPreeclampsia such as abruption, eclampsia, HELLP syndrome, cerebrovascular accidents and various neonatal complications, the need tocurtail this disease from progressing is evident. Hence, we are committed to identify pregnant women with preeclampsia, manage them and thereby prevent adverse maternal and fetal outcome.

In India the most commonly used antihypertensives in pregnancy are methyldopa, labetalol and nifedipine. Previously the most commonly used drug wasmethyl dopa.[6]

Now a days methyl dopa has been largely replaced byT.Labetalol and T.Nifedipine, due to its slower onset of action. Both T.Labetalol and T.Nifedipine are rapid in onset and effective in the treatment of hypertension. They have minimal maternal and fetal side effects.

Hence this study is to compare the anti-hypertensive efficacy of T.Labetalol and T.Nifedipine in mild preeclampsia. The feto maternal outcome were also studied.

Aims and Objectives

- To compare the anti- hypertensive efficacy of Tablet Labetelol withTablet Nifedipine in pre-eclampsia.
- To study the maternal and perinatal outcome in preeclampsia following treatment with Tablet Labetalol and Tablet Nifedipine.

MATERIAL AND METHODS

Inclusion Criteria

- All antenatal women with gestational age 20 weeks till term whosetwo Blood Pressure recordings are >140/90mmhg recorded more than 4 hours apart.
- Patients who give consent...

Exclusion Criteria

- Gestational hypertension
- Multifetal gestation
- Haemophilia
- Eclampsia
- Chronic hypertension
- Patients who have IUD at presentation.
- Patients who do not give consent.

Associated co morbidities-heart disease, diabetes mellitus, bronchialasthma, gestational diabetes mellitus, renal disease, thyrotoxicosis.

Materials and Methods

The study was conducted at the Deccan College of Medical Sciences (Owaisi Hospital and Research Centre and Princess Esra Hospital) both the hospitalsattached from January 2021 to June 2022.

100 antenatal women with mild preeclampsia were selected. Informed consent taken. 50 women were given T.Labetalol. 50 women were treated with T.Nifedipine.

Thorough history and clinical examination were done. Once the diagnosis of preeclampsia was made, all patients were admitted. Investigations such as complete blood count, peripheral smear, blood sugar, liver function test, renal function test, prothrombin time, clotting time, bleeding time, fundus examination of eye, ultrasound abdomen were done.

Patients with blood pressure 140/90 mm of Hg and above were started on antihypertensive drug (NICE Guidelines 2011). In Group A, 50 patients were given T. Labetalol. In Group B, 50 patients were treated with T. Nifedipine.

Serial monitoring of blood pressure was done. Antihypertensive efficacy and feto maternal outcomes were monitored.

Control aimed to keep systolic BP <140 mm Hg and diastolic between 80-90 mmHg (NICE Guidelines, UK-2011).

In Group A, T.Labetalol was started with a dose of 100 mg.Blood pressure was measured 2nd hourly and the dose was increased by 100 mg every 6th hourly until adequate control was achieved. The next day the total dose required was divided and given as twice daily dosage. The same dose was continued thereafter from the 2nd day of treatment. Then blood pressure

was measured four times a day. The maximum dose of tab.labetelol given was 200mg TDS.

In Group B, T.Nifedipine was started at dose of 10 mg, blood pressure was measured 2nd hourly, dose increased by 10mg 6th hourly until adequate control was achieved. Total dose was divided as thrice daily dosage from the 2nd day. The same dose continued thereafter. Blood pressure was measured four times a day. The maximum dose of tab.nifedipine given was 20mg TDS.

Patients were enquired about imminent symptoms; body weight and urine albumin were checked every day.

Antenatal Steroids were given to patients with gestational age between 28 to 34 weeks for fetal lung maturity.

Patients were counselled well about the complications and the need forgood compliance. In patients with gestational age was less than 37 weeks, once

adequate control was achieved and if the patient is compliant for follow up, patients were discharged.

Patients were followed up in antenatal OPD every week by measuring blood pressure and repeating all investigations. Patients were warned about imminent symptoms and were asked to report immediately.

Pregnancy was terminated at 37 weeks gestation. Patients who developed Severe preeclampsia were terminated. Patients diagnosed for the first time after 37 weeksgestation were also terminated.

Antihypertensive efficacy, disease progression, gestational age at delivery, drug side effects and neo natal complications were documented.

Immediately following delivery blood pressure was measured every 2 hours for 24 hours. There after BP was measured four times a day. The antihypertensive was continued if BP was ≥ 140/90 mmHg.

Patients were discharged on the 5th postnatal day if BP was under control. Patients who were on antihypertensive during the postnatal period wereadvised to continue the drug till 12 weeks postpartum and then taperedaccording to their blood pressure.

Patients were helped to make their choice about contraception.

Patients were followed up every week in postpartum centre until 12 weeks postpartum.

RESULTS

There was no statistical difference between both groups. Hence both groups were comparable.

Most common in age group in both groups were between 21 and 25 years. [Table 1]

BMI

There was no statistical difference between both groups. Hence both groups were comparable.

In both the groups most of the patients were overweight with BMI more than 25. [Table 2]

GRAVIDA

In group A majority 52% were primigravida.

In group B majority 48% were primigravida. [Table 3]

GESTATIONAL AGE

In group A majority were diagnosed between 34 and 36 weeks.

In group B majority were diagnosed between 34 and 36 weeks. [Table 4]

Majority of the patients required dose between 200 and 400 mg. [Table 5]

Majority of the patients required dose between 20 and 30 mg. [Table 6]

CONTROL OF BLOOD PRESSURE

In group A all 50 patients had adequate control of blood pressure.

In group B all 50 patients had adequate control of blood pressure. [Table 7]

Among the patients in group A taking Tab. Labetalol 14% progressed to severe preeclampsia.

Among the patients in group B taking Tab. Nifedipine20% progressed to severe preeclampsia.

The difference was not statistically significant. [Table 8]

WORSENING OF PROTEINURIA

In group A 2% had worsening of proteinuria. They developed urine albumin 2+.

In group B 6% had worsening of proteinuria. Of which 4% developed urine albumin 2+. Remaining 2% developed urine albumin 3+.

The Difference Was Not Statistically Significant. [Table 9]

DEVELOPMENT OF UTERO PLACENTAL INSUFFICIENCY

In group A 2% progressed by developing IUGR. 4% developed oligohydramnios. 2% had intrauterine death of the fetus.

In group B 6% progressed by developing IUGR. 6% developed oligohydramnios.

The difference was not statistically significant. [Table 10]

DEVELOPMENT OF PAPILLEDEMA

In group A 2% of the patients developed papilledema.

In group B none of the patients developed papilledema. The difference was not statistically significant. [Table 11]

ONSET OF IMMINENT ECLAMPSIA

In group A and Group B 2% of the patients had imminent eclampsia. [Table 12]

DRUG SIDE EFFECTS

In group A none of the patients developed drug side effects.

In group B 12% of the patients had side effects. Of which 6% had headache. 4% had palpitation and 2% had giddiness.

There was statistically significant difference between the two groups.

Group B had significantly higher side effects than group A. [Table 13]

GESTATIONAL AGE AT DELIVERY

In group A 86% delivered at term.

In group B 80% delivered at term.

There was no significant difference between the two groups. [Table 14]

CAESAREAN SECTION

In group A 24% delivered by caesarean section. Among them 14% emergency section and 10% were taken up as elective section.

In group B30% delivered by caesarean section. Among them 18% emergency section and 12% were taken up as elective section. [Table 15]

MODE OF DELIVERY VAGINAL DELIVERY

In group A 76% patients delivered vaginally. Of which 12% had instrumental delivery.

In group B 70% patients delivered vaginally. Of which 12% had instrumental delivery. [Table 16]

NEONATAL OUTCOME

In group A 43 (96%) were term babies. In group B 40 (80%) were term babies.

In both the groups all term babies had birth weight more than 3 kg.

There was no statistical difference in the neonatal outcome. [Table 17]

BIRTH WEIGHT OF BABIES

In group A among the 14% pre term babies delivered 6% had birth weight less than 2 kg and the remaining 8% had birth weight between 2 and 2.5 kg.

In group B among the 20% pre term babies delivered 8% had birth weight less than 2 kg and the remaining 12% had birth weight between 2 and 2.5 kg.

In both the groups, all term babies had birth weight more than 2.5kg. [Table 18]

NEONATAL ADMISSION

In group A 4 (8%) babies born had neonatal admission.

In group B 5 (10%) babies born had neonatal admission.

There was no statistical difference between the two groups.

The most common reasons being RDS and TTN. [Table 19]

POSTPARTUM FOLLOW UP

In group A 48 patients (96%) did not require anti-hypertensive in their postpartum period. Remaining 2 patients (4%) required treatment.

In group A 48 patients (96%) did not require anti-hypertensive in their postpartum period. Remaining 2 patients (4%) required treatment. [Table 20]

Table 1: Age of the Patient

Age	Group A		Group B		Total		Statistical Interference
	(n=50)	(%)	(n=50)	(%)	(n=100)	(%)	
Below 20yrs	4	8.0%	3	6.0%	7	7.0%	
21 to 25yrs	26	52.0%	25	50.0%	51	51.0%	
26 to 30yrs	12	24.0%	12	24.0%	24	24.0%	X^2=.385 Df=3.943>0.05 Not Significant
31yrs & above	8	16.0%	10	20.0%	18	18.0%	

Table 2: BMI of The Patientage of the Patient

BMI	Group A		Group B		Total		Statistical Interference
	(n=50)	(%)	(n=50)	(%)	(n=100)	(100%)	
Below 18	7	14.0%	8	16.0%	15	15.0%	
18 – 24	19	38.0%	16	32.0%	35	35.0%	X2=.404 Df=2.817>0.05 Not Significant
Above 25	24	48.0%	26	52.0%	50	50.0%	

Table 3: Obstetric Score of the Patient

Obstetric Score	Group A		Group B		Total		Statistical Interference
	(n=50)	(%)	(n=50)	(%)	(n=100)	(100%)	
G1	26	52.0%	24	48.0%	50	50.0%	
G2	14	28.0%	16	32.0%	30	30.0%	X2=.480 Df=3.923>0.05 Not Significant
G3	7	14.0%	8	16.0%	15	15.0%	
G4	3	6.0%	2	4.0%	5	5.0%	

Table 4: Gestational Age at Diagnosis

Gestational age at diagnosis	Group A		Group B		Total		Statistical Interference
	(n=50)	(%)	(n=50)	(%)	(n=100)	(100%)	
28 – 33 weeks	10	20.0%	10	20.0%	20	20.0%	
34 – 36 weeks	30	60.0%	30	60.0%	60	60.0%	X2=.000 Df=21.000>0.05 Not Significant
Term	10	20.0%	10	20.0%	20	20.0%	

Table 5: Required Dose of the Drug – Group A T. Labetalol

	Group A	
Dose (mg)	**(n=50)**	**(100%)**
200	17	34.0%
300	13	26.0%
400	11	22.0%
500	7	14.0%
600	2	4.0%

Table 6: Required Dose of the Drug – Group B T. Nifedipine

	Group A	
Dose (mg)	**(n=50)**	**-100%**
20	14	28.00%
30	24	48.00%
40	12	24.00%

Table 7: Control of Bloodpressure

Control BP	Group	A	Group	B	Total		Statistical Interference
	(n=50)	(100%)	(n=50)	(100%)	(n=100)	(100%)	
Control	50	100.0%	50	100.0%	100	100.0%	Nil

Table 8: Progression Top Severe Pre-Eclampsia

	Group A	(%)	Group B	(%)	Total	(%)	Statistical Interference
	No=50		**No=50**				
progression to severe pre-eclampsia	7	14	10	20	17	17	X2=0.870 DF=20.602>0.05 Not Significant

Table 9: Woresning of Proteinuria

Proteinuria >2+	Group	A	Group	B	Total		Statistical Interference
	(n=50)	**(%)**	**(n=50)**	**(%)**	**(n=100)**	**(100%)**	
2+	1	2.0%	2	4.0%	3	3.0%	X2=1.375 Df=2.503>0.05 Not Significant
3+	0	0%	1	2.0%	1	1.0%	

Table 10: Development of Utero Placental Insufficiency

IUGR/Oligohy-dramnios/IUD	Group	A	Group	B	Total		Statistical Interference
	(n=50)	**(%)**	**(n=50)**	**(%)**	**(n=100)**	**(%)**	
IUGR	1	2.0%	3	6.0%	4	4.0%	
Utetro Placental insufficiency	2	4.0%	3	6.0%	5	5.0%	X2=2.244 Df=3.523>0.05 Not Significant
IUD	1	2.0%	0	.0%	1	1.0%	

Table 11: Development of Papilledema

Papilledema	Group	A	Group	B	Total		Statistical Interference
	(n=50)	**(%)**	**(n=50)**	**(%)**	**(n=100)**	**(%)**	
	1	2.0%	0	.0%	1	1.0%	X2=1.010 Df=1.315>0.05 Not Significant

Table 12: Onset of Imminent Eclampsia

Imminent Eclampsia	Group	A	Group	B	Total		Statistical Interference
	(n=50)	**(%)**	**(n=50)**	**(%)**	**(n=100)**	**(%)**	
1	1	2.0%	1	2.0%	2	2.0%	X^2=.000 Df=11.000>0.05 Not Significant

Table 13: Drug Side Effects

Chi-square test

Drug side effects	Group	A	Group	B	Total		Statistical Interference

	(n=50)	(%)	(n=50)	(%)	(n=100)	(%)	
Giddiness	0	0%	1	2.0%	1	1.0%	
Palpitation	0	0%	2	4.0%	2	2.0%	X2=11.383 Df=3.049>0.05 Significant
Headache	0	0%	3	6.0%	3	3.0%	

Table 14: Gestational Age at Delivery

Chi-square test

Gestational age at delivery	Group	A	Group	B	Total		Statistical Interference
	(n=50)	(%)	(n=50)	(%)	(n=100)	(%)	
28 to 33 weeks	3	6.0%	4	8.0%	7	7.0%	
34 to 36 weeks	4	8.0%	6	12.0%	10	10.0%	X^2=.651 Df=2.722>0.05 Not Significant
Term	43	86.0%	40	80.0%	83	83.0%	

Table 15: Mode of Delivery

Chi-square test

	Group	A	Group	B	Total		Statistical Interference
	(n=50)	(%)	(n=50)	(%)	(n=100)	(%)	
Vaginal	38	76.0%	35	70.0%	73	73.0%	
Emergency	7	14.0%	9	18.0%	16	16.0%	X2=.464 Df=2.793>0.05 Not Significant
Elective	5	10.0%	6	12.0%	11	11.0%	

Table 16: Mode of Delivery Vaginal Delivery

Chi-square test

Vaginal	Group	A	Group	B	Total		Statistical Interference
	(n=50)	(%)	(n=50)	(%)	(n=100)	(%)	
Labour natural	4	8.0%	5	10.0%	9	9.0%	
Labour natural with episiotomy	28	56.0%	24	48.0%	52	52.0%	X^2=1.095 Df=4.895>0.05 Not Significant
Outlet forceps delivery	4	8.0%	3	6.0%	7	7.0%	
Vacuum delivery	2	4.0%	3	6.0%	5	5.0%	

Table 17: Neonatal Outcome

Chi-square test

	Group	A	Group	B	Total		Statistical Interference
	(n=50)	(%)	(n=50)	(%)	(n=100)	(%)	
Preterm	7	14.0%	10	20.0%	17	17.0%	
Term	43	86.0%	40	80.0%	83	83.0%	X^2=.638 Df=21.424>0.05 Not Significant

Table 18: Birth Weight of Babies

Chi-square test

Birth Weight(kg)	Group	A	Group	B	Total		Statistical Interference
	(n=50)	(%)	(n=50)	(%)	(n=100)	(%)	
>2.5kg	43	86.0%	40	80.0%	83	83.0%	
2 to 2.5kgs	4	8.0%	6	12.0%	10	10.0%	X^2=.651 Df=2.722>0.05 Not Significant
>2kgs	3	6.0%	4	8.0%	7	7.0%	

Table 19: Neonatal Admission

Chi-square test

Neonatal admission	Group	A	Group	B	Total		Statistical Interference
	(n=50)	(100%)	(n=50)	(%)	(n=100)	(100%)	
Yes	4	8.0%	5	10.0%	9	9.0%	X^2=1.111 Df=2.132>0.05 Not Significant

Table 20: Postpartum Follow UP

Chi-square test

Postnatal	Group	A	Group	B	Total		Statistical Interference
	(n=50)	(%)	(n=50)	(%)	(n=100)	(%)	
Yes	2	4.0%	4	8.0%	6	6.0%	X^2=.709 Df=1.400>0.05 Not Significant

DISCUSSION

This study compares the efficacy of two antihypertensives, T.Labetalol andT.Nifedipine in preeclampsia. The drug side effects and feto maternal outcome were also studied.

100 patients were included in the study. 50 patients were assigned to take T.Labetalol and 50 patients were assigned to take T.Nifedipine. Both groups were similar in age group, BMI and gestational age at diagnosis.

Regarding the obstetric score, most of the patients in both groups were primi gravida.

In group A, that is patients on T.Labetalol the dose required to achieve adequate control of blood pressure ranged from 200mg upto 600mg per day. 34% of the patients required 200mg, 26% of the patients required 300mg, 22% of them required 400mg, 14% required 500mg, 4% required 600mg.

In group B, that is patients on T.Nifedipine the dose required ranged from 20mgto 40 mg per day. 28% of the patients were controlled with 20mg, 48% were controlled with 30mg, 24% were controlled with 40mg.

In both the groups adequate control of blood pressure was achieved. There by proving that both T.Labetalol and T.Nifedipine are equally efficacious.

This result is consistent with a meta-analysis by Prof. Peter Von Dadelszen et al. (2007). Here the efficacy of oral labetalol and nifedipine were analysed in mild preeclampsia. They have proved that both the drugs are effective, safe and rapid in their onset of action.

This is also consistent with the study by Bharathi et al.(2009).[7] Here antihypertensive efficacy in mild preeclampsia was studied and it was provedthat both T.Labetalol and T.Nifedipine are equally effective.

In contrary to this study, Patel NK et al. (2012 Dec),[8] have proved that T.Labetalol has better efficacy than T.Nifedipine in preeclampsia.

Even though adequate control of blood pressure was achieved in boththe groups the basic pathology behind the disease could not be altered. Thisis evident because in both the groups few patients progressed to severepreeclampsia with adequate blood pressure control.

In group A patients (T.Labetalol) 14% progressed to severe preeclampsia. Among them 2% had worsening of protienuria, 8% had uteroplacental insufficieny which was evident by the onset of oligohydramnios (4%), IUGR (2%) and intrauterine death of the fetus (2%), 2% developed papilledema and 2% developed imminent eclampsia.

In group B patients (T.Nifedipine) 20% progressed to severe preeclampsia. Among them 6% had worsening of proteinuria, 6% hadoligohydramnios, 6%had IUGR and remaining 2% of them developed imminent symptoms.

Thus even though the rate of disease progression to severe preeclampsiawas higher in group B, it was not statistically significant.

Regarding the drug side effects, in group A patients who took T.Labetalol none of them developed any side effects. In group B patients who took T.Nifedipine 12% of them developed side effects.

This difference was statistically significant. The most common side effect being headache (6%) followed by palpitation (4%) and giddiness (2%). Thus proving that T.Labetalol was well tolerated and without any side effects.

In the same study by Bharathi et al,[7] both drugs had side effects butthe side effects were higher in T.Nifedipine group .Similar to our study the most common side effect with T.Nifedipine was headache .But in contrary to this study ,where there was no side effects with T.Labetalol,in the studyby Bharathi et al. the most common side effect with T.Labetaolol was headache.

In group A patients taking T.Labetalol 86% of them delivered at term gestation. Rest of the 14% delivered preterm as pregnancy was terminated due to progression to severe preeclampsia, among which 8% delivered between 28 and 33 weeks gestation and the rest 6% were between 34 and 37 weeks gestation.

In group B patients taking T.Nifedipine 80% of them delivered at term gestation. Rest of the 20% delivered preterm as pregnancy was terminated dueto progression to severe preeclampsia. Among which 8% delivered between 28 and 33 weeks gestation and 12% delivered between 34 and 37 weeks.

Thus in both the groups majority delivered at term. There was no significant difference in the gestational age at delivery between both the groups.

In group A patient ,76% had vaginal delivery and 24% had caesarean section. In group B patients, 70% had vaginal delivery and 30% ha Regarding the neonatal outcome, in group A 86% were term babies and 14% were preterm babies. Among the 14%, 8% had birth weight between 2 and 2.5 kg. The remaining 6% had birth weight less than 2 kg.

In group B 80% were term babies and 20% were preterm babies. Among the 20%, 12% had birth weight between 2 and 2.5 kg. The remains 8% had birth weight less than 2 kg.

In group A 8% of the babies were admitted in NICU and in group B 10% of the babies were admitted in NICU. The most common reason being respiratory distress of new born due to pre maturity. Thus in both the groups there is no significant difference in the

neonatal outcome. This is consistent with the results of study by E.J.Waterman et al (2004),[9] which showed that there are no differential effects on utero placental or fetal hemodynamics with the use of T.Labetalol and T.Nifedipine in hypertension in pregnancy. The same study proved no differential effects on neonatal outcome including birth weight.

In contrary to this, the study by Patel NK et al.(2012) 10 the neonatal outcome was better with T.Labetalol as there was lower incidence of respiratory distress of new born. This is because T.Labetalol maintains adequate placental perfusion and there by tissue oxygenation.

Post-partum follow of patients in both the groups, 4% patients in group A (T.Labetalol) and 6% patients in group B (T.Nifedipine) required continuation of antihypertensive in the post-partum period.

In this study none of the patients developed life threatening complication of preeclampsia such as coagulopathy, eclampsia, pulmonary edema, HELLP syndrome and postpartum colapse. There was no maternal mortality in this study.

Sibai and Cunningham reviewed a number of worldwide studies and concluded that the incidence of pre-eclampsia in nulliparous was more than that for multiparous.[11]

This is consistent with the results of the study by Waterman EJ et al,[9] which showed that there are no detrimental effects uteroplacental or fetal, hemodynamics with the use of labetalol and nifedipine in pregnancy. The same study proved no detrimental effects on neonatal outcome including birth weight 56.

Prakash et al., found that preeclampsia was more common in primigravida than multi gravida. In both study groups, majority cases were diagnosed at 34-36 weeks of gestation (75% in group 1 & 70% in group 2). It is consistent with this study.[10]

Rose et al., in their study found that more cases belonged to 34-36 weeks of gestation Study by Amulya C et al., found that at the time of admission more cases were belonging to more than 34 weeks of gestation.

Study by Patel NK et al,[10] stated that Tab. Labetalol is more effective than Tab. Nifedipine in mild preeclampsia. Study by Peter von Dadelszen et al. proved that Tab.Labetalol and Tab.Nifedipine are effective and safe in management of preeclampsia.[12]

A meta-analysis by Peter von Dadelszen et al, and with the study by Bharathiet al, where they have proved that both the drugs are effective, safe and rapid in their onset of action.[12]

Bharathi et al both the drugs had side effects but they were higher in nifedipine group. Similar to our study the most common side effect with nifedipine was headache.

Patel NK et al, showed that the neonatal outcome was better with labetalol as there was lower incidence of respiratory distress of newborn, which is inconsistent to our study.[10]

For a woman near term, with a soft, partially effaced cervix, even a milder degreeof preeclampsia probably carries more risk to the mother and her fetus-newborn than does induction of labor. A randomized trial of 756 women withpreeclampsia supported delivery after 37 weeks' gestation.

Barton and coworkers reported excessive neonatal morbidity in women delivered before 38 weeks despite having stable, mild, non proteinuric hypertension.[13]

Another Dutch study-HYPITAT-II-randomly assigned women with non-severe hypertension between 34 and 37 weeks to immediate delivery or to expectant management. Immediate delivery reduced the risks for adverse maternal outcomes-. 1 versus 3. 1 percent. However, it increased the risk for neonatal respiratory distress syndrome-5.7 versus 1.7 percent.

To assess this approach, 1182 nulliparas with mild gestational hypertension-20 percent had proteinuria-were managed with home health care (Barton, 2002).[14] Their mean gestational ages were 32 to 33 weeks at enrollment and 36 to 37 weeks at delivery. Severe preeclampsia developed in approximately 20 percent, about 3 percent developed HELLP syndrome, and two women had eclampsia. Perinatal outcomes were generally good. In approximately 20 percent, there was fetal-growth restriction, and the perinatal mortality rate was 4.2 per 1000 births.

The use of antihypertensive drugs to prolong pregnancy or modify perinatal outcomes in pregnancies complicated by various hypertensive disorders has been ofconsiderable interest. Drug treatment for early mild preeclampsia has been disappointing. Sibai and colleagues (1987a) reported that women given labetalol had significantly lower mean blood pressures. However, mean pregnancy prolongation, gestational age at delivery, and birthweight did not differ between groups. The cesarean delivery rate and the number of newborns admitted to special-care nurseries were also similar. The frequency of growth-restricted neonates was doubled in women given labetalol-19 versus 9 percent.[14]

Similar conclusions were reached by Abalos and associates (2014), who reviewed 49 randomized trials of active antihypertensive therapy compared with either no treatment or placebo given to women with mild-to-moderate gestational hypertension.[4]

Theoretically, antihypertensive therapy has potential application when severe preeclampsia develops before intact neonatal survival is likely. Such management is controversial, and it may be dangerous. In one of the studies, Sibai and the Memphis group (1985) attempted to prolong pregnancy because of fetal immaturity in 60 women with severe preeclampsia between 18 and 27 weeks. The results were disastrous. The perinatal mortaltiy rate was 87 percent. Although no mothers died, 13 suffered placental abruption, 10 had eclampsia, three developed renal failure, two had hypertensive encephalopathy, one had an intracerebral hemorrhage, and another had a ruptured hepatic hematoma.[15]

Memphis group redefined criteria and performed a randomized trial of aggressive versus expectant management for 95 women who had severe preeclampsia but with more advanced gestations of 28 to 32 weeks (Sibai, 1994). Women with HELLP, syndrome were excluded from this trial. Aggressive management included (steroid) glucocorticoid administration for fetal lung maturation followed by delivery in 48 hours. Expectantly managed women were observed at bed rest and given either labetalol or nifedipine orally for severe hypertension. In this study, pregnancy was prolonged for a mean of 15.4 days in the expectant management group. An overall improvement in neonatal outcomes was also reported.[16]

Sibai and Barton (2007b),[17] reviewed expectant management of severe preeclampsia from 24 to 34 weeks. More than 1200 women were included, and although the average time gained ranged from 5 to 10 days, the maternal morbidity rates were formidable.

Serious complications in some of these and in later studies included placental abruption, HELLP syndrome, pulmonary edema, renal failure, and eclampsia.

The MEXPRE Latin Study was a multicenter trial that randomly assigned 267 women with severe preeclampsia at 28 to 32 weeks to prompt delivery or to expectant management (VigilDe Gracia, 2013).[18] The perinatal mortality rate approximated 9 percent in each group, the composite neonatal morbidity outcome was not improved with expectant management. On the other hand, fetal-growth restriction-22 versus 9 percent-and placental abruption-7.6 versus 1.5 percent-were significantly higher in the group managed expectantly.

In conclusion, the present network meta-analysis suggests similar efficacy between nifedipine, hydralazine and labetalol in the treatment of severe hypertension in pregnancy. The above drugs may also be useful in treating hypertension in severe pre-eclampsia. Moderate quality of evidence was observed for direct comparison pooled estimate between labetalol and hydralazine but was either low or very low for othercomparisons. Negligible differences were observed in the individual safety profile.

CONCLUSION

From this study it is prudent that both T.Labetalol and T.Nifedipine are equallyefficacious in the control of hypertension in mild preeclampsia. In both the groups, there was progression to severe preeclampsiain an average of 16% of the patients even though their blood pressure was under control. There by showing that the pathology of disease was not altered significantly in both the groups.Regarding the drug side effects and tolerability, T.Labetalol was significantly better than T.Nifedipine.There was no significant difference in the neonatal outcome between the two groups.Thus T.Labetalol is a better alternative to T.Nifedipine, as it had lesser side effect profile.But in a limited resource setting, T.Nifedipine is an equally effective, cheap and easily available drug for preeclampsia.

Conflict of Interest: None

Funding Support: Nil

REFERENCES

1. Cunningham et al:Williams obstetrics. 23rd edition, 34: 706.
2. Maternal mortality associated with hypertensive disorders of pregnancy in Asia. BJOG: Volume 99: Issue 7,2005
3. Park: Text book of community medicine 22nd edition, 10:515.
4. ACOG Practice Bulletin: Diagnosis and management of preeclampsia.No 33. Jan 2002. ACOG. Int J GynaecolObstet 77:67-75.
5. Fernando Arias: High Risk Pregnancy and Delivery. 3rd edition, 16:414.
6. Steven G.Gabbe: Obstetrics normal and problem pregnancies. 6th edition,33:866-867.
7. Bharathi et al:Comparisonofantihypertensive efficacy. Pharmacologyonline 3:670-678, 2009.
8. Nita K patel et al: Comparitive evaluation of a anti-hypertensive drugs in preeclampsia. Int J Basic Clin Pharmacol 1(3):174-177, 2012.
9. E.J.Water man et al. Hypertension in pregnancy. Vol 23, 2: 155-169,2004
10. Patel NK, Gadhavi M, Gorasia D, Pandya MR. Comparative evaluation of antihypertensive drugs in the management of pregnancy-induced hypertension. Int J Basic Clin Pharmacol. 2012;1(3):174-7.
11. Sibai BM: Diagnosis and management of gestational hypertension andpreeclampsia ObstetGynecol 1 02:181, 2003.
12. Von Dadelszen P, Ornstein MP, Bull SB, Logan AG, Koren G, Magee LA. Fall in mean arterial pressure and fetal growth restriction in pregnancy hypertension: a meta-analysis. Lancet. 2000; 355:87-92.
13. Barton JR, O' JM, NK, J DL, S BM. Mild gestational hypertension remote from term: progression and outcome. Am J Obstet Gynecol. 2001; 184:979–983. doi:10.1067/mob.2001. 112905..
14. Sibai BM, Barton JR: Expectant management of severe preeclampsia remote from term: patient selection, treatment and delivery indications. Am J ObstetGynecol 1 96:514, 2007b.
15. 15.Sibai BM, Mercer B, Sarinoglu C: Severe preeclampsia in the second trimester: recurrence risk and long-term prognosis. Am J ObstetGynecol 1 65: 1 408, 1991.
16. Martin IN]r: Severe systolic hypertension and the search for safer motherhood. Semin Perinatol 40(2):1 1 9, 2016
17. Sibai BM: Diagnosis and management of gestational hypertension andpreeclampsia. ObstetGynecol 1 02: 181, 2003.
18. Vigil-De Gracia P, Ludmir]. Perinatal and hemodynamic evaluation of sildenafil citrate for preeclampsia treatment: a randomized controlled trial. ObstetGynecol 128(5): 1 181, 20 16.