IOSR Journal Of Pharmacy
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
www.iosrphr.org Volume 4, Issue 7 (July 2014), PP. 34-37

Comparitive study of nimodipine versus Nifedipine in the treatment of hyperstion in pregnancy

Dr.Veena B.T.[1], Dr.Suvarna R[2]

[1]*Dr.Veena B.T., Assistant Proffessor of Obstetrics & Gynaecology, Kempegowda Institute of Medical Science and Research Centre, Bangalore.*
[2]*Dr.Suvarna R, Proffessor of Obstetrics & Gynaecology, Kempegowda Institute of Medical Science and Research Centre, Bangalore.*

ABSTRACT: *Hypertensive disorders of pregnancy complicates about 7-10% pregnancy. Various anti-hypertensives have been tried to control the pressure without much affecting the maternal and fetal health. The present study, compare the effect Nimodipine and Nifedipine in controlling blood pressure during pregnancy.*

Aims & Objectives: *To control the efficacy of Nimodipine and Nifedipine in control of blood pressure during pregnancy and to assess the effects of drug on maternal and fetal outcome.*
Methodology: Eligible women are randomly assigned and treated with tablet Nimodipine 30mg 8th hourly (Group A) and Nifedipine 10mg 8th hourly (Group B). Each group has 50 patients and further sub-divided as diastolic BP between 100-109mm of Hg and 110mm Hg and above. Relevant statistical analysis was applied and results were interpreted.

RESULTS: *Both groups are comparable in terms of systolic and diastolic blood pressure control. Group A had minimal side effects like headache, flushing and hypotension for about 2%. Perinatal outcomes were comparable between the two groups with 96% carry home baby rate in Group A and 88% in group B, which are also comparable.*
Conclusion: Nimodipine is comparable with Nifedipine and can be used as an alternative drug in the treatment of hypertension in pregnancy as it is safe, effective and with minimal side effects.
As it is more expensive than Nifedipine in country like India, Nifedipine continues to be the first line drug.

KEYWORDS: *Diastolic blood pressure; Nifedipine; Nimodipine;*

Brief Description about the need for the Study: WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT - Previously illustrated literatures have demonstrated the effect of Nimodipine / Nifedipine with regard to its action as anti-hypertensives, in pre-eclampsia or in chronic hypertension which is correlated in the present study.Nifedipine is the drug which is very commonly used in the oral formulation, one of its known adverse effects being sudden hypotension and hence not recommended in many countries and proved by many literatures was also considered for study to formulate the drug regimens.

WHAT THIS STUDY ADDS: The present study is dedicated to consider the two (calcium channel blockers) drugs in the form of oral preparations, their effect on prolongation of pregnancy and benefit to the fetus with respect to the maturity along with its action as anti-hypertensive. This study also specifically shows that non-proteinuric patients have better control of blood pressure than the proteinuric patients, hence can be used more specifically in non-proteinuric patients.

Summary : This is a comparative study of Nimodipine and Nifedipine in the treatment of hypertension of in pregnancy undertaken in Department of OBG at KIMS Hospital and Research Centre from Mar 2004 – Mar 2006.The study was to evaluate the anti-hypertensive effects of both the drugs, to reduce maternal complications as a result of hypertension and to attain greater fetal maturity by prolongation of pregnancy without compromising on uterine blood flow and fetalwell being. Nifedipine was taken as the reference drug to evaluate the effects of trial drug Nimodipine in terms of the above parameters.A protocol was drawn for the investigations to be done in these patients and the administration of drugs was standardized. The patients were followed up until delivery.In the present study, it was found that there was an effective reduction in blood pressures in both groups. There was no maternal mortality in either group. Prolongation of the pregnancy was also possible in cases with mild to moderate hypertension and better neo-natal outcome was noted in both the groups.

There were minimal and mild side effects in Nimodipine group and none discontinued treatment during the period. Thus the compliance from the patient was good.

I. INTRODUCTION

Hypertensive disorders of pregnancy complicates about 7-10% of pregnancies[1]. Severe hypertension increases maternal mortality and morbidity due to cerebrovascular accidents, pulmonary oedema and placental abruption. Several anti-hypertensive drugs have been tried in the pregnancy considering various factors in the pregnancy. Methyldopa, Labetalol and Nifedipine(Dihydro-piridine group[2]) are commonly in use at present. But in developing countries, Labetalol is not used as first line drug due to cost constraints and Methyldopa, which is an established first line drug takes longer time to act and on the other hand Nifedipine, which is used for both acute and chronic hypertensions has long side effects like rapid drop in the pressure following medication, complications like Myocardial infarction and Congestive cardiac failure[3]. It has been banned in countries like Australia.Nimodipine (Dihydro-piridine group) is one more anti-hypertensive drug with similar mechanism of action as Nifedipine and lowers the blood pressure more gradually, hence overcomes the known side effects of Nifedipine and also helps to increase cerebral perfusion pressure[4].

Aims & Objectives

[1] To compare the efficacy of Nimodipine and Nifedipine in the control of blood pressure during pregnancy.
[2] To assess the maternal and fetal side effects of the drugs.

II. METHODOLOGY

This study was completely in-patient based. Primary data was generated by studying patients admitted for the management of pregnancy-induced hypertension (PIH) at the KempeGowda Institute of Medical Sciences, Bangalore for a period of two years from March 2004 to March 2006.On admission, detailed history, clinical examination and investigation related to PIH are done.Inclusion Criteria: All pregnant women with diastolic blood pressure (DBP) more than 100 mm Hg on atleast 2 occasions 4 hours apart after 20 weeks of gestation.Exclusion Criteria: Heart disease including ischaemic heart disease, Haemotological disorders, Liver disease and History of intolerance / hypersensitivity to dihydropyridine groups of drugs.

Total of 100 patients with diagnosis of PIH were randomized in to 2 groups of 50 each. After informed written consent, Group A received Nimidipine 30 mg 8^{th} hourly and Group B received Nifedipine 10 mg 8^{th} hourly alternatively with matching distribution. Each group was further sub-divided as DBP between 100-109 mm Hg and above 110 mm Hg.All patients BP measurement was done at rest, in sitting or 15 degree lateral recumbency. Two consecutive readings 4 hours apart and with Korotkoffs phase-V were used to determine DBP.Aim of the treatment was to maintain the DBP between 90–100. Patients with gestational age of less than 34 weeks, and those with impending eclampsia / eclampsia were given $MgSO_4$ as per Zuspans regimen.
Decision to continue with conservative management of pregnancy or to deliver and mode of delivery was made depending on maternal and fetal indications. Patients were followed until delivery, indication for induction, mode of delivery, fetal and maternal outcome and side effects of the drug if any during the treatment were noted.Relevant statistical methods were applied depending on the type of data that were generated. Chi-Square test, Fischer exact test, Student t test (Paired), Effect size and Statistical software namely SPS 11.0 and Systat 8.0 were used for the analysis.

III. RESULTS

The age, parity, pre-treatment risk factors that affect the maternal and fetal outcome, NST, additional drugs like $MgSO_4$ and Phenobarbitone used on the patients of both the groups were matched. The gestational age at presentation in either group is as follows.

Table 1: Gestational Age at Presentation

Gestational age at presentation in weeks	Group A (n=50)		Group B (n=50)	
	Number	%	Number	%
20-24	-	-	1	2
25-28	2	4	2	4
29-32	2	4	12	24
33-36	17	34	21	42
37-40	29	58	13	26
>40	-	-	1	2

The maximum number of cases was between 37-40 weeks of gestation in Group A and 33-36 in Group B.

Table 2: Diastolic BP at Presentation

Diastolic BP in mm Hg	**Group A (n=50)**		**Group A (n=50)**	
	Number	**%**	**Number**	**%**
100-109	30	60	25	50
110 and above	20	40	25	50
Inference	Diastolic BP at presentation is statistically similar between two groups with p=0.315			

Table 3: Division of patients into Non-proteinuric and Proteinuric cases

Non-proteinuric and Proteinuric cases	**Group A (n=50)**		**Group A (n=50)**	
	Number	**%**	**Number**	**%**
Non-Proteinuric	32	64	26	52
Proteinuric (Significant proteinuria ≥ 300 mg/L)	18	36	24	48
Inference	Non-proteinuric and Proteinuric is comparable between the two groups (p=0.548)			

Table 4: Mean Pattern of Blood pressure (Post-treatment)

Study Period	**Systolic Blood pressure mm HG (Mean ± SD)**		**Diastolic Blood pressure mm HG (Mean ± SD)**	
	Group A	**Group B**	**Group A**	**Group B**
0 hour	150.72±10.38	155.47±10.96	104.88±6.07	107.24±7.32
8 hour	143.28±9.04	144.61±6.72	97.76±6.48	98.24±6.81
24 hour	140.44±10.02	145.38±10.60	94.12±8.52	96.96±6.57
48 hour	138.55±9.66	141.71±13.08	91.70±7.01	94.29±10.46
72 hour	135.77±11.48	139.52±10.14	89.71±9.97	94.96±10.89
Student t (0 hour - 72 hour)	t=7.406 p<0.001	t=4.838 p<0.001	t=9.755 p<0.001	t=4.613 p<0.001
Effect size	1.36	1.51	1.89	1.34

Table 5: Comparison Apgar score between groups

Apgar Score	**Apgar at 1 minute**		**Apgar at 5 minute**	
	Group A	**Group B**	**Group A**	**Group B**
	N=49	**N=46**	**N=49**	**N=46**
> 7.0	40 (81.6%)	37 (80.4%)	44 (89.8%)	40 (86.9%)
7 - 4	7 (14.3%)	6 (13%)	3 (6.1%)	4 (8.7%)
< 4.0	2 (4.1%)	3 (6.5%0	2 (4.1%)	2 (4.3%)
Inference	Apgar score at 1 and 5 minutes are comparable between the two groups (p>0.05)			

Table 6: Birth weight distribution

Birth weight distribution	**Group B**			**Group B**		
	Non-proteinuric	**Proteinuric**	**Total**	**Non-proteinuric**	**Proteinuric**	**Total**
< 1500	-	4	4 (8%)	4	8	12 (24%)
1501 - 2000	3	3	6 (12%)	5	11	16 (32%)
2001 - 2500	10	2	12 (24%)	6	3	9 (18%)
2501 - 3000	17	2	19 (38%)	7	3	10 (20%)
3001 - 3500	6	2	8 (16%)	1	-	1 (2%)
> 3500	1	-	1 (2%)	1	1	2 (4%)
Inference	Proteinuric patients had more LBW babies compared to non-proteinuric patients					

IV. DISCUSSION

The present study compares Nifedipine, which is the commonly used anti-hypertensive with Nimodipine in terms of control of blood pressure during pregnancy and their maternal and fetal side effects and neo-natal outcome. The diastolic pressure at presentation was 100-109 mm Hg in 60% of the patients in Group A and 50% of the patients in Group B. Diastolic BP of 110 mm Hg and above was present in 40% of patients in Group A and 50% of patients in Group B with significant proteinuria in 36% in Group A and 48% in Group B. Ferrazzani& Associates, 1990 showed that, risk of perinatal morbidity and mortality is increased when hypertension in pregnancy is associated with proteinuria[5].In 10% of non-proteinuric patients and 12% of proteinuric patients in Group A, BP was not under control even after 48 hours. In 8% of non-proteinuric and 20% of proteinuric patients in Group B, BP was not under control even after 48 hours. This is comparable in both the groups (p=0.454). These patients with uncontrollable BP were given $MgSO_4$ and pregnancy was terminated.In Gita Banerjee and co-author's study (2000)[6] using Nimodipine, there was more fall in MAP after 72 hours in the non-proteinuric than in the proteinuric group. This study too has found similar results.Present study using Nifedipine and Nimodipine can be compared to KaterinaFenakle at al study (1991)[7], who used Nifedipine in their study.

There was adequate control of blood pressure (consistently below 160/110 mm Hg). Mean prolongation in both the groups is around 6 days, whereas in the above study, it was 15 days. The longest duration of prolongation of pregnancy was 30 days in both groups. Prolongation of pregnancy in days is statistically comparable between both the groups with p=0.611.Minimal side effects like headache and flushing were in Group A, which were tolerable. Group B did not have any side effects. Hypotension with Systolic BP < 90 mm Hg was seen in 1 patient after delivery.Post-treatment complications like hypotension were seen in 2% and 2% patients had pleural effusion in Group A. Postpartum impending eclampsia and Abruptio Placenta (Grade 0) were noticed in Group B in 2% of the cases.In majority of patients, pregnancy was prolonged for 1-3 days and it was prolonged beyond 2 weeks in 12% in Group A and 14% in Group B, which were comparable to other studies[8].56% in Group A and 62% in Group B required induction, majority of them for uncontrolled hypertension. Elective CS was done in 20% and 16% of patients in Group A and Group B respectively. Type of delivery was comparable between the two groups.Over 80% of new born had Apgar score of >7. Apgar score at 1 and 5 minutes were comparable between the two groups with p>0.05. Proteinuric patients in both the groups and low birth weight babies compared non-proteinuric patients. Birth weight distribution was comparable between both the two groups. 40% and 44% in Group A and B respectively were admitted to NICU which are comparable. Majority of the babies were admitted to NICU in view of preterm, intrapartum asphyxia and meconium aspiration, which correlates with many other studies[9, 10].One baby in Group A died due to intra ventricular haemorrhage. Two babies died in Group B were preterm, one had necrotizing enterocolitis and the other had severe birth asphyxia.

V. CONCLUSION

In the treatment of hypertension in pregnancy, Nimodipine and Nifedipine were equally effective in the control of blood pressure, both systolic and diastolic. This control was better in the non-proteinuric patients. With effective control of blood pressure, the pregnancy could be prolonged thus enhancing fetal maturity.There was no difference in both the groups with regard to obstetric interventions, NICU admissions and birth apgar and birth weight.Hence to conclude Nimodipine is a safe effective oral drug that can be offered to an alternative to Nifedipine in the management of PIH. As it is comparatively much more expensive than Nifedipine, in developing countries, Nifedipine continue to be preferred first line drug.

REFERENCES

[1]. Sibai BM. Pre-clampsia-Eclampsia. Current problems in obstetrics Gynaecology and Fertility 1990, 13, 1-45.

[2]. Goodman & Gilman's. The pharmacological basis of Therapeutics. 10th edition. Page 853-860.

[3]. Tripathi KD. Essentials of Medical Pharmacology, 4th edition, updated Reprint 2001, Chapter 35. Antianginaland other anti-ischaemic drugs. Pg. 528-533.

[4]. Fernando Arias. Practical guide to high-risk pregnancy and delivery. Second edition, 2001. In: pre-eclampsia and eclampsia, 183-210.

[5]. Ferrazzani S, Caruso A, De Carolis S, Martino IV, Mancuso S, Proteinuria and outcome of 444 pregnancies complicated by hypertension. Am J ObstetGynecol 1990; 162; Pg. 366.

[6]. Gita Banerjee (Basu), DebdulalChatterjee, AlokenduChatterjee, Partha Mukherjee, Chandana Das. A randomized controlled Trial on use of Nimodipine in mild PIH. J ObstetGynecol India. 52(4): 2002 July/August; Pg. 44-46.

[7]. KaterinaFenakel, Gabriel Fenakel, ZVI Appelman, Samuel Lurie, ZVI Katz and ZEEV Shoham. Nifedipine in the treatment of severe pre-eclampsia. ObstetGynecol 1991; 77:331 Pg 331-337.

[8]. Gruppo Di Studio, Hypertension in the Gravidanza. Nifedipine versus expectant management in mild to moderate hypertension in pregnancy. Br J ObstetGynaec. July 1998; Vol.105, Pg. 718-722.

[9]. Anthony J, Mantel G, Johanson R, Dommisse J. The haemodynamic and respiratory effects of interavenousNimodipine used in the treatment of eclampsia. Br J ObstetGynecol India. 52(4): 2002 July / August; Pg. 44-46.

[10]. Dasgupta S.Antiserotoninergic effect of Nimodipine in the management of pregnancy induced hypertension, Obstetrics, Dasgupta, 2001. Recent advances edited by DipikaDekha.