Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Der Pharmacia Lettre, 2011, 3(3): 383-387
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-5071
USA CODEN: DPLEB4

Evaluation on efficacy of Methyldopa monotherapy and combination therapy with Nifedipine in pregnancy-induced hypertension

Jayasutha J*[1], Ismail A.M[2] and Senthamarai R[2]

[1]*Department of Pharmacy Practice, SRM College of Pharmacy, Kancheepuram District, Tamilnadu, India*
[2]*Periyar College of Pharmaceutical Sciences for Girls, Tiruchirapalli, Tamilnadu, India*

ABSTRACT

To find the effectiveness of methyldopa and methyldopa in combination with nifedipine to treat pregnancy-induced hypertension (PIH). A prospective study was conducted involving 105 pregnant women having PIH diagnosed after 20 weeks of gestation between May 2009 and Jan 2010. Patients were divided into two groups according to severity of the disease, Group 1 contains 55 patients (mild hypertension) and Group 2 contains 50 patients (moderate to severe hypertension). Group 1 was treated with methyldopa and Group 2 was treated with methyldopa and nifedipine. On treatment with methyldopa, the mean systolic and diastolic blood pressure were found to decrease from 150.6 ± 6.9 to 121.2 ± 6.29 and 96 ± 6.21 to 82 ± 7.14 respectively. For the group of patients treated with methyldopa and nifedipine, the mean systolic and diastolic blood pressure were changed from 170.5 ± 17.4 to 126 ± 8.83 and 112.5 ± 11.05 to 85 ± 6.88 respectively. Methyldopa was effective in controlling mild pregnancy induced hypertension and methyldopa with nifedipine as a combination was effective in controlling moderate to severe hypertension of both preeclampsia and pregnancy induced hypertension patients.

Keywords: Pregnancy-induced hypertension; Methyldopa; Nifedipine.

INTRODUCTION

Pregnancy induced hypertension (PIH) is a form of high blood pressure in pregnancy. PIH is a potentially life-threatening disorder that usually develops late in the second trimester or in the third trimester. Pregnancy induced hypertension occurs in about 5 percent to 8 percent of all pregnancies [1] and [2]. Hypertensive disorders remain a major cause of perinatal and maternal

morbidity and mortality worldwide, because of complications such as preeclampsia, eclampsia, fetal growth retardation, and premature birth or abruptio placentae [3] and [4]. Pregnancy-induced hypertension (PIH) will occur after 20weeks of gestation having blood pressure ≥140/90 mm Hg without proteinuria, with resolution to baseline by 12wks postpartum. Preeclampsia, the non convulsive form of PIH with proteinuria. Preeclampsia may be mild or severe. HELLP (Hemolysis, elevated liver enzyme, low platelet count) syndrome is a complication of severe preeclampsia or eclampsia [5]. Methyldopa is regarded as first line, first choice of drug to treat hypertension during pregnancy. It is the only drug which has been fully assessed and shown to be safe for mother, neonate, and infant [8]. Oral nifedipine appears to be an effective antihypertensive agent in preeclamptic hypertensive emergencies [9]. Hence in our study, we evaluated the effects of methyldopa and methyldopa with nifedipine in pregnancy induced hypertension.

MATERIALS AND METHODS

A prospective study was conducted with 105 pregnant women having PIH between May 2009 and Jan 2010. Permission for the study was obtained from clinical ethics committee and scientific boards of the participating hospital. Informed consent form was obtained from all participating pregnant women, after they had been given oral and written information about study protocol. Women consented to participate in the study on their admission to hospital or as outpatient. For inclusion in the study, the following criteria were required, 1) Pregnant women with hypertension diagnosed after 20 weeks of gestation ≥ 140 / 90 mm Hg, 2) Bad obstetric history due to pregnancy-induced hypertension. Criteria for exclusion were 1) Cases where medical termination of pregnancy is planned before 20 weeks of gestation, 2) Normal pregnant women, 3) Pre existing hypertension/ renal disease/ immunological disorder. Eligible womens were divided into two groups according to severity of the disease, Group 1 contains 55 patients (mild hypertension) and Group 2 contains 50 patients (moderate to severe hypertension). Group 1 was treated with methyldopa and Group 2 was treated with methyldopa and nifedipine. Methyldopa was started at 250mg - 500mg two – four times a day (Maximum dose 2g / day). Nifedipine was started at 20 mg two-three times a day (Maximum dose 60 mg / day). Women with early onset, severe preeclampsia were admitted for inpatient monitoring in a high risk obstetric ward. Women with mild pregnancy-induced hypertension were not necessary to admit in the hospital, they were treated as outpatient. Complete demographic details such as age, chronicity of disease, family history of PIH, past obstetric history of PIH, and gravida was obtained in a suitably designed patient profile form for all 105 patients. Maternal monitoring for inpatient included 2-hourly blood pressure measurement (Mercury sphygmomanometer) daily and hemoglobin, hematocrit, renal function test, liver function test were all performed twice weekly. Doppler ultrasonography was performed twice in a week in order to evaluate the fetal growth. Analysis of urine albumin was done in both the groups. Outpatient monitoring was performed at ‘obstetric special care clinic’ once fortnightly/monthly as the case may be. Here also similar approach to monitor blood pressure was performed and hemoglobin, hematocrit, urine analysis for albumin, renal function test, liver function test and ultrasonography was performed once in a month/two months.

Statistical method: Data are analyzed using column statistics and Student “t” test

RESULTS AND DISCUSSION

A total of 105 patients meeting the study criteria were enrolled into the study. Out of which 55 patients were in Group 1 and 50 patients were in Group 2. All fifty five patients (100%) in Group 1 had pregnancy-induced hypertension and fourty two patients (82%) in Group 2 had preeclampsia and remaining eight patients (18%) had pregnancy-induced hypertension. Fourteen women (25%) in Group 1 and eleven women (22%) in Group 2 had family history of preeclampsia or hypertension. Twenty eight (51%) in Group 1 and eighteen women (36%) in Group 2 had experienced previous preeclampsia or hypertension. It is clear that patients who had hypertension or preeclampsia in their previous pregnancy were more prone to develop hypertension in their next pregnancy. Kirsten Duckitt [6] reported that the risk of pre-eclampsia is increased in women with a previous history of pre-eclampsia.The demographic details of women on admission are shown in Table 1.

Table: 1 Demographic details of women in Group 1 and Group 2

Characteristics	Group 1	Group 2
Age (years)	28 ± 4	25 ± 4
Primigravidas (%)	70	82
Multigravidas (%)	30	18
Gestational entry (week)	28 ± 6	32 ± 5

From the Table 1, it is clear that primigravidas were more common in both the groups than multigravidas. From Table 2, we could find that in the patients of mild hypertension (Group 1), methyldopa reduces the systolic and diastolic blood pressure with the mean change of 29.3% and 14%. For patients with moderate to severe hypertension (Group 2), methyldopa with nifedipine reduces the systolic and diastolic blood pressure with the mean changes of 44.5% and 27.5%.

Table: 2 Mean ± SD and Mean Changes of Systolic and Diastolic Blood Pressure (mm Hg) in Group 1 and Group 2

Blood Pressure	Group 1		Mean Change	Group 2		Mean Change
	Before treatment	After treatment		Before treatment	After treatment	
Systolic Blood Pressure	150.6 ± 6.9	121.3 ± 6.29	29.3*	170.5±17.47	126±8.83	44.5*
Diastolic Blood Pressure	96 ± 6.21	82 ± 7.14	14*	112.5±11.05	85±6.88	27.5*

*P-value * <0.0001 Vs Before treatment using Student "t" test*

The laboratory data of patients in Group 1 includes hemoglobin (Hb), hematocrit (Hct), Serum glutamic oxaloacetic transaminase (SGOT), Serum glutamic pyruvic transaminase SGPT), alkaline phosphatase, uric acid, creatinine, platelet count. The mean ± SD of Hb, Hct and platelet count were 12.3 ± 0.94, 36.4 ± 3.7 and 2.86 ± 0.67. The mean ± SD of liver function test which includes SGOT, SGPT, alkaline phosphatase were 22.5 ± 5.87, 20.9 ± 5.80 and 213.7 ± 35.6 respectively. The mean ± SD of renal function test such as uric acid and creatinine were 2.76 ± 1.55 and 0.79 ± 0.27. No albuminuria was observed in patient with PIH.

All laboratory data in Group 1 were almost normal. Table 3 shows abnormal laboratory data of patient in Group 2 which was reduced after significant reduction in blood pressure. It's found that there is no significant increase in Hb, Hct, and Platelet count. But there is significant decrease in liver function test (SGOT, SGPT and alkaline phosphatase) and renal function test (uric acid and creatinine) after treatment. Table 3 also shows that drastic reduction in urine albumin after treatment. This is due to the combination of methyldopa with nifedipine. Methyldopa with nifedipine was effective in improving renal function and liver function test but no significant improvement in hematological test was observed. Ismail AAA [11] proved that Nifedipine decreased blood pressure and improved kidney functions without affecting the umbilical artery blood flow in cases of preeclampsia

Table: 3 Special investigational results of patients in Group 2. Values are given as mean ± SD, mean changes and P – value of laboratory values (Group 2).

S. No.	Parameters	Before treatment	After treatment	Mean Change
1.	Urine Albumin (mg/24hr urine sample)	810 ±219.8	105 ±176.14	705***
2.	Hb (mg/dl)	10.64 ± 1.69	11.01±1.499	-0.365$^{(NS)}$
3.	Hct (%)	32.9 ±5.1	33.8 ±4.49	-0.91$^{(NS)}$
4.	SGOT (U/L)	34.5±8.28	28.65 ±5.79	6**
5.	SGPT (U/L)	30.7 ±11.16	23.7 ±8	7**
6.	Alkaline phosphatase (U/L)	361.65 ±173.8	270.8 ±70.65	90.85*
7.	Uric acid (mg/dl)	6.16 ±0.975	5.46 ±0.669	0.7*
8.	Creatinine (mg/dl)	1.105 ±0.397	0.84 ±0.253	0.265*
9.	Platelet count (lakh/cu.mm)	2.88 ±0.67	2.93 ±0.63	-0.047$^{(NS)}$

<0.01 Significant; ** <0.001 Very significant; * <0.0001 Highly significant; NS - Non significant*
Hb - hemoglobin; Hct - hematocrit; SGOT - serum glutamyl oxaloacetic transaminase; SGPT - Serum glutamyl pyruvic transaminase

From Table 4, we could find that major maternal complications are experienced by patients in Group 2 because 82% of patients in Group 2 had preeclampsia. Proteinuria significantly increases the risk of maternal complications. Lakshmi Seshadri [10] reported that the onset of proteinuria is associated with a steep increase in risks to the mother and fetus.

Table: 4 Maternal complications

Complications	Group 1 (n=55)	Group 2 (n=50)
Placental abruption	0	1
HELLP syndrome	0	1
Elevated liver enzymes	0	36
Abnormal renal function test	0	39
Proteinuria	0	42
Death	0	0
Eclampsia	0	0

(Some patients experienced > 1 complicatins)
HELLP - hemolysis, elevated liver enzymes, low platelet count.

CONCLUSION

From the results, we could derive that methyldopa is effective in controlling mild hypertension and methyldopa with nifedipine is found to be effective in controlling moderate to severe hypertension of both preeclampsia and pregnancy induced hypertension patients perhaps due to additive effect. Methyldopa is quite effective in preventing preeclampsia and methyldopa with nifedipine is effective in preventing eclampsia.

Acknowledgement
I submit my deepest thanks to Dr. S. Chandra Kumar, M.D., Chairman and Dr. A. Meenakshi Sundari, M.D., DGO (Obstetrician and Gynecologist), Kaveri Medical Center Hospital and KMC Speciality Hospital, Tiruchirappalli, India for granting permission to carry out this study at their hospital.

REFERENCES

[1] Durig P, Ferrier C, Schneider H. Ther Umsch **1999** Oct; 56 (10) : 561-71.
[2] Remuzzi G, Ruggenenti P. Am J Kidney Dis. **1991** Sep;18(3):285-305.
[3] James M. Roberts, Gail Pearson, Jeff Cutler Hypertension **2003**; 41: 437.
[4] Khan KS, Wojdyla D, Say L, Gülmezoglu AM et al. Lancet **2006**; 367(9516): 1066-74.
[5] Bethesda, Maryland. Am J Obstet Gynecol **2000**; 183(1): S1-22
[6] Kirsten Duckitt, Deborah Harrington. BMJ **2005**; 330: 565.
[7] Sonia Hernández -Díaz, Sengwee Toh, Sven Cnattingius. BMJ **2009**; 338: 2255.
[8] Redman CWG, Beilin LJ, Bonnar J, Ounsted MK. Lancet **1976**; 2: 753-756.
[9] James A. Scardo, Stephen T. Vermillion, Barbara B. Hogg Am J Obstet Gynecol **1996**; 175(2): 336-340.
[10] Lakshmi Seshadri and Indira Venkataraman. The Journal of Reproductive Medicine **1997**; 42 (2): 88-90.
[11] Ismail AAA**,** Medhat I, Tawfic TAS and Kholeif A, Int J Gynaecol Obstet**1993**; 1 (40): 39-43.