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Original Article

Evaluation of Efficacy and Safety of Methyldopa and Labetalol in the Management of Pregnancy Induced Hypertension

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Abstract

The aim of the study was to compare the efficacy and compliance of methyldopa and labetalol in controlling blood pressure in pregnancy induced hypertension (PIH). A total of 120 patients having pregnancy induced hypertension (PIH) were taken and divided in to two groups. Group A was given Tab. Methyldopa 250mg and group B Tab. Labetalol 100 mg. In both the groups pre and post treatment blood pressure was measured on day 2nd, 7th and day 21st was compared. Reduction of blood pressure and side effects of methyldopa and labetalol were observed. The mean pre treatment blood pressure in group A was 157/104±10 mmHg which was reduced to 137/89±10 mmHg on 48th hours, 127/85±10 mmHg by 7th day and 120/78±10 mmHg by the 21st day. In group B mean pre treatment blood pressure was 162/108±10 mmHg which was reduced to 130/84±10 mmHg on 48th hours, 122/80±10 mmHg by 7th day and 115/74±10 mmHg by the 21st day. Methyldopa and Labetalol have effectively controlled the blood pressure in pregnancy induced hypertensive patients. The level of blood pressure in pregnancy induced hypertensive patients in both Methyldopa and Labetalol treated groups were significantly reduced after intervention but no statistically significant difference was observed between the two groups. The present study indicates that both Methyldopa and Labetalol reduced the blood pressure in PIH patients.

Keywords: Antihypertensive, Labetalol, Methyldopa, Pregnancy, Hypertension.

Introduction

Maternal mortality rate is high in Bangladesh despite progress and development in health care facilities. The analysis of causes of maternal deaths highlight the fact that majority of these deaths are preventable. Hypertension disorders seem to complicate approximately 10% of pregnancies and are important causes of maternal morbidity and mortality.[1] Globally around 6-8% of pregnancies are complicated by hypertension.[2,3] Hypertension is the most common medical problem encountered during pregnancy[4]. During this period the maternal and fetal condition are monitored along with control of hypertension.[5] The risk of developing complications of hypertension is reduced to half by using antihypertensive medications.[6] A wide spectrum of antihypertensive agents represents the key of successful treatment of pregnancy induced hypertension (PIH) and provide opportunity of choice.[7] Today, though medications are available and widely used for the treatment of PIH, the physicians still have to deal with many challenges. Antihypertensive drugs are often used to lower blood pressure with the aim of preventing its progression to adverse outcomes.[8,9] Methyldopa and Labetalol are acceptable oral antihypertensive medications in pregnant women with hypertension. Very little work was done in the past regarding comparative study of efficacy and safety of the above mentioned drugs. At the same time, results were not unambiguous. In the face of the conflicting results, the present study was undertaken to find the efficacy and safety of Methyldopa and Labetalol in PIH.

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Material and methods

The study was a comparative intervention of two antihypertensive drugs (Methyldopa & Labetalol) among pregnant women carried out in the department of Pharmacology, Sir Salimullah Medical College and Mitford Hospital & Shaheed Suhrawardy medical college hospital after approval from institutional Ethical committee. Study period was from July 2016 to June 2017. It was an open label trial.All pregnant women with PIH attending outpatient department of Gynecology and obstetrics Mitford hospital & Shaheed Suhrawardy medical college hospital who received methyldopa and labetalol were the study population. All pregnant women within 20th to 38th weeks of pregnancy with blood pressure more than 140/90 mmHg without any anti hypertensive drug at the time of enrollment were included in this study. Pregnant women having proteinuria, preeclampsia, diabetes mellitus, bronchial asthma, thyrotoxicosis, haematological disorder, multiple gestations were excluded from this study. The study group consisted of patients selected on the basis of inclusion and exclusion criteria. All patients were divided and randomized into two

groups, Group- A and Group-B. Group A consisted of 60 patients and received Tab. Methyldopa 250-500 mg twice daily. Group B consisted of 60 patients and received Tab Labetalol 100-400 mg twice daily. Before giving antihypertensive drugs blood pressure and pulse rate were recorded and urinary albumin was examined. Blood pressure was measured by using sphygmomanometer with patient in recumbent position after 20min rest. Patients were followed up at 48th hour, 1st week and 3rd week after initiation of treatment. At each follow up visit, patients BP was measured and maternal side effects such as hypotension, headache, flushing, nausea, vomiting after starting the antihypertensive drugs were observed and recorded.

Statistical analysis

Data was expressed as mean ± SD. Statistical analysis was done by using statistical package of social sciences (SPSS) for windows version 21. Unpaired 't' test was used as the tests of significance and P value <0.05 was considered as significant, P value <0.01was considered as moderately significant, P <0.001 was considered as highly significant and P > 0.05 was considered as not significant.

Results

Results were discussed in table. Table (I) shows the selected demographic characteristic of all pregnancy induced hypertensive patients. Considering demographic characteristics, there was no significant difference between the Methyldopa and Labetalol treated groups.

Before administration of methyldopa blood pressure level (mean±SD) was 157/104±10 mmHg which was reduced to 137/89±10 mmHg on 48th hours, 127/85±10 mmHg by 7th day and 120/78±10 mmHg by the 21st day (Table II). This change was statistically significant (P<.05). In labetalol treated group pretreatment blood pressure (mean ±SD) was 162/108±10 mmHg which was reduced to 130/84±10 mmHg on 48th hours, 122/80±10 mmHg by 7th day and 115/74±10 mmHg by the 21st day (Table III). This change was statistically significant too. But after intervention no statistically significant difference was found in between the two groups (p>.05).

Both Methyldopa and Labetalol were well tolerated by patients of the present study. Headache, drowsiness and postural hypotension were statistically significant in Methyldopa treated group and weakness was common in labetalol treated group. No serious adverse effects were seen in both the groups that needed dose adjustment or withdrawal of the drug.

Table 1: Selected demographic Characteristics of both groups before intervention

Characteristics	Methyldopa Group-A Mean±SD (n=60)	Labetalol Group-B Mean ± SD (n=60)	P-Value
Age (year)	25.20 ± 5.01	25.60 ± 5.21	0.669[a]
Gravida	1.51 ± 0.87	1.85 ± 1.19	0.089[Ø]
Gestational Age	32.05 ± 4.01	32.61 ± 4.09	0.446[a]
Body Weight (kg)	63.1 ± 9.5	64.8 ± 8.7	0.870[a]

n= number of patients in each group, values are expressed as mean ±SD, Ø chi squared test (x^2) was done to analyze the data, 'a' data was analyzed by using unpaired t -Test, P-value <0.05 = statistically significant.

Table 2: Effect of methyldopa at interval on Blood Pressure

Variables	Group-A (Methyldopa treated) (n = 60)		[G]p value	% Change
Systolic/ Diastolic Blood Pressure (mmHg)	Pre treatment 157±7.9/ 104±8.07	48 hr after treatment 137±6.65/ 89±13.17	<.001/ .001	30
	48 hr after treatment 137±6.65/ 89±13.17	7th day after treatment 127±7.2/ 85±5.95	<0.001/ 0.039	25
	7th day after treatment 127±7.2/ 85±5.95	21 day after treatment 120±6.38/78±5.14	.001/ .004	20

n= Number of patients in each group, values are expressed as mean ±SD, data was analyzed by using p value<.05 = statistically significant, [G]p= in each group as compared to baseline (Paired t-test).

Table 3: Effect of labetalol at interval on Blood Pressure

Variables	Group- B (Labetalol treated) (n = 60)		[G]p value	% Change
Systolic/ Diastolic Blood Pressure (mmHg)	Pre treatment 162±9.57/ 108±8.50	48 hr after treatment 130±7.13/ 84±6.7	<0.001/ <.001	35.42
	48 hr after B 130±7.13 /84±6.7	7th day after R 127±7.2/ 85±5.95	<.001/ .001	31
	7th day after R 122±8.7/ 80±7.13	21 day after treatment 115±5.97/ 74±6.09	<.001/ <.001	30

n= Number of patients in each group, values are expressed as mean ±SD, data was analyzed by using p value<.05 = statistically significant, [a]p = in each group as compared to baseline (Paired t-test).

Table 4: Inter group comparison of two drugs (Methyldopa and Labetalol) on blood pressure

Variables	Group-A (Methyldopa treated) (n=60)		Group B (labetalol treated)	P[b]
Systolic/ Diastolic Blood Pressure (mmHg)	Pre treatment	157±7.9/ 104±8.07	167±9.57/ 108±8.5	35.42
	48 hr after treatment	137±6.65/ 89±13.17	130±7.13/ 84±6.7	31
	7th day after treatment	127±7.2/ 85±5.95	115±5.97/ 74±6.0	30

n=number of patients in each group. P[b]= inter group comparison at baseline and after intervention (unpaired t-test)

Table 5: Distribution of the respondents by adverse drug reaction in both groups (n=120)

Adverse drug reaction	Group		p-value
	Methyldopa (n=60)	Labetalol (n=60)	
Headache	14 (23.3)	5 (8.3)	0.024*
Drowsiness	13 (21.7)	2 (3.3)	0.002**
Weakness	3 (5.0)	5 (8.3)	0.464[ns]
Postural hypotension	8 (13.3)	2 (3.3)	0.048*
Depression	4 (6.7)	1 (1.7)	0.171[ns]
Nausea	7 (11.7)	6 (10.0)	0.769[ns]
Vomiting	4 (6.7)	3 (5.0)	0.697[ns]

Chi-square test was done to measure the level of significance.

Discussion

In the present study pre and post treatment systolic and diastolic blood pressures were measured and compared between Methyldopa and Labetalol treated group on 2nd, 7th and 21st day after drug treatment. The mean pre treatment blood pressure in group A was 157/104±10 mmHg which was reduced to 137/89±10 mmHg on 48th hours, 127/85±10 mmHg by 7th day and 120/78±10 mmHg by the 21st day. In group B mean pre treatment blood pressure was 162/108±10 mmHg which was reduced to 130/84±10 mmHg on 48th hours, 122/80±10 mmHg by 7th day and 115/74±10 mmHg by the 21st day. The study observed the beneficial effects of Methyldopa and labetalol in controlling blood pressure. Both the drugs significantly reduced the blood pressure and then maintained normal BP level. In a study conducted by Cruickshank et al. (1992) labetalol did control the blood pressure in 45 among the 51 treated women (88%).[10] Several other workers have found similar response rates- Lardoux group 82%, CA Michel 92%. In Michael CA (1982) 81.4% patients receiving labetalol caused significant fall in BP as compared to methyldopa treated group which were(68.5% patients).[11] Brunton et al. (2011) stated that both methyldopa and labetalol provided efficient control of BP in PIH which also agrees with the past study. Cosme et al (2000) stated that both Metyldopa and Labetalol are equally effective in controlling blood pressure in pregnancy.McCowan et al (1998) found that Methyldopa and labetalol are equally effective in lowering pregnancy induced high blood pressure.[12] Koopmans et al (2009) stated that Methyldopa had particular benefit among PIH women in case of perinatal outcome and preterm delivery.[13] A prospective study conducted by Nita et al (2012) stated that Labetalol was more effective than Methyldopa in controlling blood pressure in patients with PIH.[14] Moll et al (1973) found that both the drugs were equally effective in controlling pregnancy induced blood pressure.[15] Regarding drug related adverse effects most common adverse effect was headache, 14 (23.3%) patients in methyldopa group and5 (8.3%) on labetalol treated group. The other adverse effects included drowsiness, postural hypotension which was more in patient treated with methyldopa. The incidence of side effects such as nausea, vomiting was similar in both groups. However statistically significant difference in adverse effect found in headache, drowsiness and postural hypotension. The other adverse effects were statistically insignificant. Study conducted by Verma et al. (2012) stats that adverse effects observed were lower in labetalol group compared to methyldopa group.[16] In a study by El-Qarmalawi et al. (1995) patients receiving methyldopa complained of side effects such as drowsiness (22.2%), headache (14.8%), nasal congestion (7.4%), postural hypotension (5.6%). Six patients in labetalol group complained of dyspnoea, no other side effects were noticed.[17]

Conclusion

Both Methyldopa and Labetalol have effectively controlled the blood pressure in pregnancy induced hypertensive patients. No significant change is observed between the two groups, although considering percentage changes of effects produce by the Labetalol appears better.

Ethical consideration

Ethical approval was taken from the ethical review committee of Sir Salimullah Medical College and written consent was taken from the patient with proper explanation. Besides these the participants had rights to withdraw them from the study at any point of time. It was assured that all records were kept confidential.

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