Original Article

Efficacy of the Labetalol Versus Methyldopa in Pregnancy Induced Hypertension Among Patients Visiting Tertiary Care Hospital

Hajira Khalid[1], Fozia Parveen[2], Amina Begum[3], Aksa Ismail[4], Sadia Detho[5], Ulvina Khalid[6]

[1]Consultant gynecologist, Sindh Government Qatar Hospital Karachi, [2]Professor, Gynae and OBS, Dow University of Health Sciences, [3]Consultant gynecologist, CDF Hospital Hyderabad, [4]Consultant gynecologist, DHQ Hospital Dadu, [5,6]Consultant gynecologist, Dow University of Health Sciences,

Correspondence: *Dr. Hajira Khalid*
Consultant gynecologist,
Govt. Qatar Hospital. Email: drhajirakhalid13@gmail.com

Abstract

Objective: To compare the mean arterial pressure of labetalol versus methyldopa in pregnancy induced hypertension in patients

Methodology: This randomized control trial was done at Gynae unit I civil Hospital Karachi from Jan 2017 to Feb 2018. Women were randomly allocated into two groups, in which 97 women were treated with labetalol and 97 were treated with methyldopa. Outcome was measured in the form of efficacy of the drug by lowering systolic blood pressure less than 140 mmHg and diastolic less than 90 mmHg up to 7 days after starting treatment.

Results: The average age of the patients was 30.14±4.84 years. MAP was significantly better in those women who were treated with labetalol as compared to methyldopa [92.85±8.95 vs. 99.58±7.73 p=0.0005]. Effectiveness was significantly high in labetalol as compare to methyldopa [91.8% vs. 62.9% p=0.0005]

Conclusion: The present study confirms that labetalol is an effective drug for use and quicker in achieving adequate control of blood pressure in pregnancy-induced hypertension.

Key Words: Hypertensive disorder, pregnancy induced hypertension, Labetalol, Methyldopa

Cite this article as: Khalid H, Parveen F, Begum A, Ismail A, Detho S, Khalid U. Efficacy of the Labetalol Versus Methyldopa in Pregnancy Induced Hypertension Among Patients Visiting Tertiary Care Hospital. J Soc Obstet Gynaecol Pak. 2021; 11(2):131-134.

Introduction

The most frequent medical disease in pregnancy is hypertension, which contributes considerably to maternal and perinatal mortality and morbidity.[1] It is estimated that hypertension complicates around 6-10% pregnancies.[2] If it remains uncontrolled, it can lead to complications like pre-eclampsia, eclampsia, fetal growth retardation, abruptio placentae, premature delivery and fetal mortality as well as maternal morbidity and the mortality. Preeclampsia and eclampsia cause a woman's mortality every three minutes around the world.[3,4] In underdeveloped nations such as Latin America, Africa, Asia, and the Caribbean, hypertension in pregnancy is linked to 10-15% of maternal fatalities, whereas eclampsia is linked to 10% of maternal deaths.[5]

As a result, it is critical to keep blood pressure under control in order to reduce risks such as placental abruption, maternal cardiac failure, cerebral hemorrhage, and adverse effects on the uteroplacental circulation and the fetus. The use of antihypertensive agents in pregnancy is controversial. If pharmacological therapy is required in pregnant women with mild to severe hypertension, labetalol, methyldopa, and long-acting nifedipine are appropriate oral antihypertensive medications.[6] Although diuretics have been demonstrated to be effective in the treatment of essential hypertension during pregnancy, they are ineffective in the treatment of pregnancy-induced hypertension. The most widely prescribed antihypertensive medicine is methyldopa, and it has been proven to be beneficial. [7]

Authorship Contribution: All authors are equally participated in Substantial contributions to the conception or design of the work drafting, Final approval of the version to be published, revising it critically for important intellectual content, statistical analysis, Active participation in active methodology

Funding Source: none
Conflict of Interest: none

Received: Oct 8, 2020
Accepted: May 09, 2021

But it has a high incidence of side effects because of its central action, like postural hypotension, constipation, galactorrhoea, postpartum depression, altered sleep pattern and headache, and it takes 24 hours for complete action. NICE recommends Labetalol as a first line antihypertensive for pregnancy induced hypertension, pre-eclampsia and eclampsia, which is a nonspecific alpha and beta blocker that reduces blood pressure by peripheral vasodilation. One study concluded that labetalol is equally efficacious and better tolerated compared to methyldopa in the treatment of pregnancy induced hypertension.[8] Although labetalol is preferred over methyldopa as it is free of the above-mentioned side effects,[9-11] it is still less frequently used in our routine practice. So, the current study is designed to compare the efficacy of labetalol versus methyldopa in pregnancy induced hypertension in our population. Up till now only a few trials have been conducted in Pakistan, so more studies are required to provide local data to develop local guidelines and may help us select one drug over the other for efficient blood pressure control in pregnancy.

Methodology

This randomized control trial, the patients were selected from those attending the antenatal clinics Of Gynae unit I civil Hospital Karachi from 1-jan-2017 to 23- feb-2018

Sample size was calculated through openepi online software version 3.01a. Taking mean arterial pressure in methyldopa group 98.15 and labetalol group 96.90 with 3.44 and 2.70 standard deviation respectively with 80% of power of the test and 95% confidence interval. The total calculated sample size 194 required 97 in each group [10].

Non-probability consecutive sampling was used to select the sample

Inclusion Criteria: Age group: 16-40 years, both primigravida-multiparity, singleton pregnancy, and gestational age: >20 weeks were included

Exclusion Criteria: Patients with bronchial asthma, any preexisting cardiovascular disorder, diabetes mellitus, or multiple pregnancies, as documented by history and medical records, were excluded from the trial.

After all eligibility criteria, obtaining informed consent, taking their demographic details, patient was randomly allocated into two groups by envelope method with single blinding. Envelops was sealed and jumbled up , half containing tab labetalol and half containing tab methyldopa, so one arm was received tab labetalol and other methyldopa. Their initial blood pressure was recorded and respective drug was given. Dose adjustment was done according to blood pressures in initial 24 hours as inpatient up to maximum doses, those who were their blood pressure controlled was recorded, and those who have not achieved blood pressure controlled, and requiring additional antihypertensive treatment was recorded. Outcome was measure in the form of efficacy of the drug by lowering systolic blood pressure less than 140 mmHg and diastolic less than 90 mmHg up to 7 days after starting treatment. Name, age, parity, BMI, gestational age and family history of HTN was recorded in pre-design proforma. Data was analyzed by SPSS version 20. Frequency and percentages was calculated for all categorical variables like family history of hypertension. Mean and standard deviation was conducted for all the variables like BMI, age, gestational age, parity, systolic and diastolic pressure before and after treatment. Independent t test was used to compare mean arterial pressure between groups. Stratification of outcome variable in groups of age, parity, BMI and family history of hypertension was done to control effect modifiers. Post stratification independent t test was applied. P value less than and equal to 0.05 was taken as significant.

Results

A total of 194 women were included in this study. Women were randomly allocated into two groups, in which 97 women were treated with labetalol and 97 were treated with methyldopa. The average age of the patients was 30.14±4.84years. Mean age, gravid, parity, BMI and gestational age with respect to groups are presented in table I.

Table I: Comparison of demographic statistics between groups (n=194)

Variables		Labetalol (n=97)	Methyldopa (n=97)	p-Value
Age (Years)		29.77±4.98	30.52±4.68	0.286
Gravida		2.51±1.64	2.67±1.77	0.503
Parity		1.23±1.29	1.19±1.26	0.823
BMI (kg/m^2)		27.66±2.34	26.90±1.36	0.006
Gestational Age (Weeks)		33.25±2.57	33.07±2.91	0.658
Baseline	SBP (mmHg)	154.95±5.02	155.77±9.66	0.457
	DBP (mmHg)	97.01±5.80	98.76±8.92	0.107
After 7 days	SBP (mmHg)	124.95±10.71	133.61±11.65	0.0005
	DBP (mmHg)	76.80±8.72	82.58±6.65	0.0005

In the labetalol group, the prior history of HTN was 37.14 percent, while in the methyldopa group, it was 53.64 percent. Baseline mean systolic and diastolic blood pressure were not statistically significant between groups, as indicated in table I, however after 7 days, mean systolic and diastolic blood pressure were statistically significant between groups.

Comparison of MAP between groups was significantly better in those women who treated with labetalol as compare to methyldopa [92.85±8.95 vs. 99.58±7.73 p=0.0005]. Efficacy of drug was observed in term of controlling BP<140/90.

Effectiveness was significantly high in labetalol as compare to methyldopa [91.8% vs. 62.9% p=0.0005] as reported in table III. Effect of age, BMI and previous history of HTN was controlled by stratification analysis and found that labetalol was effective to control BP as compare to methyldopa as shown in table II to III respectively.

Table II. Comparison of overall efficacy between groups (n=194)

Efficacious	Labetalol (n=97)	Methyldop (n=97)	Total	P-Value
Yes [BP < 140/90]	89 (91.8%)	61 (62.9%)	150 (77.3%)	0.0005
No [BP ≥ 140/90]	8 (8.2%)	36 (37.1%)	44 (22.7%)	

Table III: Comparison of MAP between groups controlling theeffect of age of the patients (n=194)

Variables		Labetalol		Methyldopa		
		n	Mean+SD	n	Mean+SD	P-Value
Age Groups (Years)	<=30 Years	48	92.91±10.84	45	102.0±8.15	0.0005
	>30 Years	49	92.78±6.713	52	97.50±6.75	0.001
BMI (kg/m^2)	28.5	59	93.23±10.33	71	99.29±7.55	0.0005
	28.6 to 32	38	92.28±6.30	26	100.38±8.29	0.00005
History of hypertension	Yes	53	93.77±7.59	37	99.81±7.53	0.0005
	No	44	91.74±10.33	60	99.44±7.91	0.0005

Discussion

In a country like Pakistan, where the maternal mortality rate remains high despite steady improvement and development in health care, a large section of the population is still without it. Maternal mortality is mostly preventable, according to the analysis of causes of maternal mortality. Hypertensive disorders are thought to complicate about 10% of pregnancies and are a major cause of maternal and foetal morbidity and mortality.[12] The most prevalent medical condition found during pregnancy is hypertension.[13] Worldwide, hypertension is thought to complicate 6–8% of all pregnancies.[14] Preeclampsia and eclampsia are said to cause the death of a woman every three minutes around the world.[15.16] Antihypertensive medications are routinely used to reduce blood pressure and prevent it from growing to negative consequences for the mother and foetus. Antihypertensive drugs decrease the chances of getting severe hypertension in half. [15] If pharmaceutical treatment is needed in pregnant women with mild to severe hypertension, labetalol, methyldopa, and long-acting nifedipine are effective options. 16 A total of 194 women aged 16 to- 40 were involved in this study to assess the mean arterial pressure of labetalol against methyldopa in PIH. Women were randomly divided into 2 groups, in which 97 women received labetalol and 97 received methyldopa treatment.

Advanced maternal age is one of the risk factors that are associated with PIH.[17] The risk of PIH in subsequent pregnancy increases with maternal age 1.3 per 5 years of age). In our study, the mean age in Labetalol group was 29.77 years and in methyldopa group was30.52 years making the average age of the patients 30.14±4.84 years. In the present study, most of the patients in labetalol and methyldopa group were gravida 2+ showing prevalence of multigravida in our study population. PIH has a high rate of recurrence in subsequent pregnancies. Several studies have consistently shown that 30-50 percent of women who had PIH in their first pregnancy also had PIH in their second pregnancy, despite the severity of the disease appearing to decrease.[18] In our study population, previous history of HTN was 37(38.14%) in labetalol group and 53(54.64%) in methyldopa group.

While comparing the mean arterial pressure of labetalol versus methyldopa in PIH in our study, MAP was significantly better in those women who were treated with labetalol as compared to methyldopa [92.85±8.95 vs. 99.58±7.73 p=0.0005]. Our result is supported by many other authors. In a comparable study, El Qarmalawi et al found that 81.4 percent of patients using labetalol showed a substantial drop in MAP, compared to 68.5 percent of patients taking methyldopa.[9] In a similar study, Cruickshank et al. found that labetalol reduced blood pressure in 45 of 51 women (88 percent) within 24 hours. Several other researchers have discovered similar reaction rates, including Lardoux's group at 82 percent and CA Michael at 92 percent. According to Brunton et al[19], labetalol is more effective

than methyldopa in the treatment of mild hypertension in pregnancy, which was also confirmed in our current study.

Conclusion

The present study confirms that labetalol is an effective drug for use and quicker in achieving adequate control of blood pressure in pregnancy-induced hypertension.

References

1. Sibai B M. *Etiology and management of hypertensionand pre-eclampsia.* Am J Obstet Gynecol. 2012;206:4.
2. Bramham K, Nelson-Piercy C, Brown M J. *Postpartum management of hypertension*. BMJ. 2013;346:1-3.
3. Giannubilo SR, Bezzeccheri V, Cecchi S, Landi B, Battistoni GI, Vitali P, et al. *Nifedipine versus I abetalol in the treatment of hypertensive disorders of pregnancy.* Arch Gynecol Obstet. 2012;286:637-42.
4. Khedun SM, Moodley J, Naicker T. *Drug management of hypertensive disorders of pregnancy*. Pharmacol Ther. 1997;7:221-58.
5. Rudra P, Basak S, Patil D, Latoo M Y. *Recent advances in management of pre-eclampsia*. Br J Med Pract. 2011;4(3):a433:14-20.
6. Magee, Laura A.*; von Dadelszen, Peter Management of Hypertension in Pregnancy, Maternal-Fetal Medicine: 2021;3;2;124-135
7. Podymow T, August P. Update on the use of antihypertensive drugs in pregnancy. Hypertension. 2008 Apr 1;51(4):960-9.
8. Verma R, Lahon K, Tonpay SD, Kale VJ, Jain DK. *A comparative randomized contolled parallel group study of efficacy and tolerability of labetalol versus methyldopa in the treatment of new onset hypertension during pregnancy*. Int J Life Sci Pharma Res. 2012;2(1):23-31.
9. El-Qarmalawi AM, Morsy AH, Al-Fadly A, Obeid A, Hashem M. *Labetalol vs. methyldopa in the treatment of pregnancy-induced hypertension*. Int J Gynaecol Obstet. 1995;49:125-30.
10. Subhedar V, Inamdar S, Hariharan C, Subhedar S. *Comparison of efficacy of labetalol and methyldopa in patientswith pregnancy-induced hypertension.* Int J Reprod Contracept Obstet Gynecol. 2013 ;2(1):27-34.
11. Qasim A, Siddiqui MH, Salam J, Nusrat U. *Labetalol versus Methyldopa: efficacy in pregnancy induced hypertension.* Gomal J Med Sci. 2014;12(4)233-6.
12. Chauhan R, Sharma RS, Parashar MK, Chauhan VS. Clinical examination of hypertension in pregnancy. In: Shah MR, editor. Hypertensive disorders in pregnancy. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd; 2007. P. 111-25.
13. Arias F, Daftary SN, Bhide AG. Hypertensive disorders ofpregnancy. In: Dasgupta S, Nasim S, Khanna M, editors.Practical guide to high-risk pregnancy and delivery-a SouthAsian perspective. New Delhi: Elsevier Publication; 2008. p. 397-439.
14. Magee LA, Ornstein MP, Dadelszen P. Fortnightly review: management of hypertension in pregnancy. BMJ. 1999;318:1332-6.
15. Abalos E, Duley L, Steyn DW, Henderson-Smart DJ.Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database Syst Rev.2007;(1):CD002252
16. Brown MA, Hague WM. The detection, investigation and management of hypertension in pregnancy: executive summary. Consensus statement from theAustralasian Society for the Study of Hypertension in Pregnancy. Aust N Z JObstet Gynaecol. 2000;40:133-8.
17. Lamminpää R, Vehviläinen-Julkunen K, Gissler M, Heinonen S. Preeclampsia complicated by advanced maternal age: a registry-based study on primiparous women in Finland 1997–2008. BMC pregnancy and childbirth. 2012 ;12(1):1-5.
18. Lee KW, Ching SM, Ramachandran V, Yee A, Hoo FK, Chia YC, Wan Sulaiman WA, Suppiah S, Mohamed MH, Veettil SK. Prevalence and risk factors of gestational diabetes mellitus in Asia: a systematic review and meta-analysis. BMC pregnancy and childbirth. 2018 Dec;18(1):1-20.
19. Brunton L, Chabner B, Knollman B. Goodman and Gilman's The Pharmacological basis of Therapeutics. (12thedn.), Chapter 12: Adrenergic agonists and antagonists. New York: The McGraw Hill Companies, USA; 2011. P. 328- 429.