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Original Article

Evaluation of the Comparative Effectiveness of Labetolol and Methyldopa in the Treatment of Pregnancy Induced Hypertension

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Abstract

Objective: To compare effectiveness of labetolol and methyldopa in the treatment of pregnancy induced hypertension.

Methods: This randomized controlled trial was carried out in the Obstetrics & Gynaecology Department at a Tertiary Care Hospital in Rahim Yar Khan from September 2022 to March 2023. The study involved a total of 84 patients, with 42 patients in each group (Labetalol and Methyldopa). Inclusion criteria encompassed patients aged 20 to 40 years, with gestational age ≥ 20 weeks, and diagnosed with Pregnancy induced hypertension (PIH). The study aimed to compare the effectiveness of Labetalol and Methyldopa in treating PIH.

Results: The mean age for the Labetalol group is 29.48 with a standard deviation (SD) of 6.500, while the Methyldopa group has a mean age of 31.55 with an SD of 5.844. The mean gestational age for the Labetalol group is 28.38 weeks with an SD of 4.732, and for the Methyldopa group, it is 29.64 weeks with an SD of 4.509. In the Labetalol group, 38 out of 42 patients (90.5%) experienced efficacy, compared to 30 out of 42 (71.4%) in the Methyldopa group. The P-value of 0.049 suggests that the difference in efficacy between the both study groups is statistically significant, favouring Labetalol as the more effective treatment for pregnancy-induced hypertension.

Conclusion: Our study strongly suggests that Labetalol is more effective than Methyldopa in treating pregnancy-induced hypertension, particularly in older age groups. Future research is needed to explore side-effect profiles for a comprehensive understanding.

Key words: PIH, efficacy, labetalol, methyldopa.

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Introduction

Pregnancy-induced hypertension is characterized by a systolic blood pressure (SBP) equal to or exceeding 140 mmHg, a diastolic blood pressure (DBP) equal to or exceeding 90 mmHg, or a combination of these two. It is crucial to monitor both systolic and diastolic levels to accurately diagnose Pregnancy-Induced Hypertension (PIH), which manifests after the 20th week of gestation in women who previously had normotensive readings. PIH is broadly categorized into gestational hypertension, pre-eclampsia, and eclampsia.[1,2]

Pregnancy-induced hypertension (PIH) poses a significant risk for neonatal and maternal health. According to 2011-2013 data, the United States reported a pregnancy-related mortality ratio of 17.0 deaths per 100,000 live births. Notably, this ratio had a disproportionate impact on non-Hispanic black women, who experienced a 3.4 times higher rate compared to non-Hispanic white women. The leading causes of these maternal deaths included cardiovascular conditions (15.5%), pre-existing medical conditions (14.5%), infections (12.7%), hemorrhage (11.4%), and cardiomyopathy (11.0%).[3,4]

The high prevalence of PIH necessitates meticulous management to prevent severe complications such as fetal growth retardation, eclampsia, pre-eclampsia, premature delivery, abruptio placentae and increased rates of fetal and maternal mortality.[5]

Managing blood pressure during pregnancy remains

a contentious area, fraught with debates and uncertainties over the optimal use of antihypertensive medications.[6] Mild to moderate hypertension, characterized by a systolic pressure between 140-190 mm Hg and a diastolic pressure between 90-109 mm Hg, may be treated with targeted pharmacological interventions.[7] Severe hypertension, indicated by a systolic pressure above 160mm Hg and diastolic above 110 mm Hg, necessitates more aggressive therapeutic strategies. The overarching goal of antihypertensive treatment is to lower blood pressure levels, thus extending the duration of the pregnancy and mitigating the risk of severe hypertension.[5]

Among the antihypertensive agents like long-acting nifedipine, labetalol and methyldopa are generally considered appropriate for treating hypertension in pregnancy.[8] Labetalol, a combined alpha and beta adrenoceptor blocker, is globally recognized for its efficacy and can be administered either orally or intravenously depending on the severity of PIH.[9] Methyldopa has also received widespread acceptance and is supported by extensive research as an effective medication for managing hypertension during pregnancy.[10]

The management of hypertension in pregnancy is a multifaceted issue that requires early detection, proper diagnosis, and careful choice of treatment methods to ensure the well-being of both the mother and the fetus. A comparison between labetalol and methyldopa, two of the frontline antihypertensive agents, can yield valuable insights and guide best practices in the treatment of pregnancy-induced hypertension. Further research in this field will contribute to reducing the global burden of hypertensive disorders in pregnancy.

While labetalol is recognized as more effective than methyldopa in managing pregnancy-induced hypertension, the specific efficacy differences across various patient subgroups remain underexplored. Our study addresses this gap by stratifying data based on age, gestational age, and parity, providing insights into contexts where labetalol demonstrates a significant advantage, such as in older patients (p=0.023) and primipara women (p = 0.013), while also highlighting scenarios where methyldopa remains viable. These findings contribute to personalized treatment approaches and evidence-based decision-making, particularly in settings where methyldopa is more accessible. Additionally, our study focuses on short-term efficacy rather than long-term neonatal outcomes, ensuring its applicability to immediate clinical management of pregnancy-induced hypertension.

Methods

The study was conducted in the Department of Obstetrics & Gynaecology at a Tertiary Care Hospital In Rahim Yar Khan. It spanned from September 2022 to March 2023.

The sample size consisted of 84 patients, with each group containing 42 patients. It was calculated based on a Level of confidence (α) of 5%, Power of study (1-β) of 90%, anticipated population proportion P-I (labetalol group) of 91.8%, and anticipated population P-II (methyldopa group) of 62.9%. A non-probability consecutive sampling was used, and the study was designed as a randomized controlled trial.

The inclusion criteria comprised patients with pregnancy-induced hypertension as per the operational definition, those aged between 20 and 40 years, and having gestational age ≥ 20 weeks. Exclusion criteria were patients with a history of cardiac disease and diabetes mellitus, renal or thyroid disease, or those taking any other antihypertensive therapy.

The study was conducted after approval from the hospital's Ethical Committee (ERB CMH-RYK-00101) dated 30 Aug 2022. Informed consent was obtained, and patients' details, including gestational age and parity were recorded on a proforma. Patients aged 20-40, with specific blood pressure criteria, were selected. Fetal monitoring was done through clinical recording and CTG. Patients were randomly assigned to either Labetalol group or Methyldopa group based on drawn slips. Treatment efficacy was evaluated after 72 hours.

Pregnancy-Induced Hypertension was defined as an elevated blood pressure of 160/100 mmHg or higher, measured on two separate occasions four hours apart, occurring after the 20th week of gestation. Pregnancy-Induced Hypertension was defined as an elevated blood pressure of 140/90 mmHg or higher, measured on two separate occasions four hours apart, occurring after the 20th week of gestation. The efficacy of the drug was assessed 72 hours post-initiation of treatment, based on its ability to reduce the blood pressure to levels below 140/90 mmHg.

The collected data were entered into SPSS version 24 and analyzed. Mean and SD were calculated for age and gestational age. Frequencies were calculated for efficacy and parity. The efficacy of treatment between Labetalol group and Methyldopa group was compared using the chi-square test. Stratification in relation to age, parity, and gestational age was done, and post-stratification chi-square test was applied. A P-value of less than 0.05 was taken as significant.

Results

Total 84 patients (42 patients in each group) of pregnancy induced hypertension were selected.

Participants in the two groups were matched to minimize bias through strict inclusion criteria and random allocation. Both groups were comparable in terms of key

demographic and clinical features, including age (mean age 29.48 ± 6.50 in the Labetalol group vs. 31.55 ± 5.84 in the Methyldopa group, $p > 0.05$) and gestational age (28.38 ± 4.73 weeks vs. 29.64 ± 4.51 weeks, $p > 0.05$). Randomization ensured equal distribution of potential confounders, such as parity and gestational age, between the groups. Additionally, stratified analyses by age, gestational age, and parity further validated the comparability of the groups and ensured that observed differences in efficacy were not due to baseline imbalances. We believe this approach effectively minimized bias and enhanced the validity of our findings.

The mean age for the Labetalol group is 29.48 with a standard deviation (SD) of 6.500, while the Methyldopa group has a mean age of 31.55 with an SD of 5.844. The mean gestational age for the Labetalol group is 28.38 weeks with an SD of 4.732, and for the Methyldopa group, it is 29.64 weeks with an SD of 4.509.

Table 1 shows the comparative effectiveness of Labetalol and Methyldopa for treating hypertension in pregnancy. In the Labetalol group, 38 out of 42 patients (90.5%) experienced efficacy, compared to 30 out of 42 (71.4%) in the Methyldopa group. The P-value of 0.049 suggests that the difference in efficacy between the two groups is statistically significant, favouring Labetalol as the more effective treatment for pregnancy-induced hypertension.

Table 2 stratifies the data by age groups. Among the younger age group (20-30 years), Labetalol appears to be more effective with 17 out of 21 patients (81.0%) experiencing efficacy, as opposed to 12 out of 18 (66.7%) for Methyldopa. However, the P-value of 0.465 suggests that this difference is not statistically significant. In the older age group (31-40 years), Labetalol was effective for all 21 patients (100.0%), which was significantly better than Methyldopa's efficacy in 18 out of 24 patients (75.0%), supported by a P-value of 0.023.

Table 3 stratifies the data by gestational age. In both gestational age groups, Labetalol appears to be more effective, but the differences did not reach statistical significance, as indicated by the P-values of 0.147 and 0.297 for the 20-28 week and 29-36 week groups, respectively.

Table 1: *Comparison of efficacy between both groups*

Group	Efficacy		Total	P value
	Yes	No		
Labetalol group	38 (90.5%)	4 (9.5%)	42	0.049
Methyldopa group	30 (71.4%)	12 28.6%	42	

Table 4 categorizes the data by parity. Among primipara women, Labetalol was significantly more effective with a P-value of 0.013; 22 out of 23 (95.7%) experienced efficacy, compared to 11 out of 18 (61.1%) in the Methyldopa group. Among multipara women, there was no significant difference in efficacy between Labetalol and Methyldopa, as indicated by a P-value of 1.00.

Table 2: *Stratification in relation to age*

Age groups	Group	Efficacy		Total	P value
		Yes	No		
20-30 Years	Labetalol group	17 (81.0%)	4 (19.0%)	21	0.465
	Methyldopa group	12 (66.7%)	6 (33.3%)	18	
31-40 years	Labetalol group	21 (100.0%)	0	21	0.023
	Methyldopa group	18 (75.0%)	6 (25.0%)	24	

Table 3: *Stratification in relation to gestational age*

Gestation group	Study group	Efficacy		Total	P value
		Yes	No		
20-28 weeks	Labetalol group	21 (95.5%)	1 (4.5%)	22	0.147
	Methyldopa group	13 (76.5%)	4 (23.5%)	17	
29-36 weeks	Labetalol group	17 (85.0%)	3 (15.0%)	20	0.297
	Methyldopa group	17 (68.0%)	8 (32.0%)	25	

Table 4: *Stratification in relation to parity*

Parity	Study group	Efficacy		Total	P value
		Yes	No		
Primipara	Labetalol group	22 (95.7%)	1 (4.3%)	23	0.013
	Methyldopa group	11 (61.1%)	7 (38.9%)	18	
Multipara	Labetalol group	16 (84.2%)	3 (15.8%)	19	1.00
	Methyldopa group	19 (79.2%)	5 (20.8%)	24	

Discussion

The focal point of our research was to rigorously evaluate the efficacy of Labetalol and Methyldopa in the treatment of pregnancy-induced hypertension. With a sample size of 84 participants, equally divided between the two treatment arms, our study has elucidated a statistically significant advantage for Labetalol (P=0.049).

The 90.5% efficacy rate for Labetalol that we observed shares a compelling concordance with the 88% reported

by Easterling T et al.[11] This parallelism lends additional credence to the hypothesis that Labetalol offers a quantifiable advantage in treating pregnancy-induced hypertension. The slight difference in percentages could be attributed to sampling variance or demographic factors, warranting future multi-center trials for validation.

Rauf H et al.[12] reported a 75% efficacy rate for Methyldopa, which slightly outperformed our result of 71.4%. While this might hint at the efficacy of Methyldopa, it is crucial to consider that Rauf H et al. also discussed a lower side-effect profile for Methyldopa, a variable our study did not explore. The absence of side-effect evaluation in our study highlights the need for comprehensive analyses that factor in both efficacy and adverse effects to derive a rounded clinical recommendation.

Our data align remarkably well with the balanced efficacy representation offered by Qasim A et al.[13]—80% for Labetalol and 70% for Methyldopa. Beyond mere numbers, our stratified analysis added an intricate layer by illustrating Labetalol's pronounced efficacy among older demographics (P=0.023), thereby enriching the existing understanding of patient-specific drug responses.

Both our study and Molvi SN et al.[14] independently identified a discernible advantage for Labetalol among subjects in the older age group (31-40 years), validating the robustness of this age-specific efficacy trend. This adds another dimension to prescribing practices, suggesting that Labetalol may be particularly advantageous in managing hypertension in older pregnant women.

Contrary to the findings of Verma RE et al.,[15] who reported age-independent efficacy, our study illustrated age-dependent variations, especially favoring Labetalol in older demographics. This discrepancy forms a critical research question: Could the varied findings be attributed to sample characteristics, or do they signify a genuine divergence that necessitates further studies?

The superiority of Labetalol in reducing both SBP and DBP at 72 h, as seen in our study, resonates with Lomte D et al.'s[16] findings. Such a synchronized pattern further entrenches Labetalol as a more potent antihypertensive agent, although it does beg the question of the long-term sustainability of these reductions.

Conclusion

Our study provides compelling evidence for the superior efficacy of Labetalol over Methyldopa in managing pregnancy-induced hypertension. Our findings align well with existing literature, while also presenting nuanced insights into age-dependent efficacy, particularly favoring Labetalol among older patients. However, the study does not explore side-effect profiles, which warrants future comprehensive research. Overall, Labetalol emerges as a promising treatment option, yet further multi-centric studies are essential for evidence-based guidelines.

Ethical Approval: The IRB/EC approved this study via letter no.CMH-RYK-00101.

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Authors' Contribution

UIK: Conception
SU, JN: Design of the work
ZS, SG, FM: Data acquisition, analysis, or interpretation
SU, ZS, FM: Draft the work
UIK, SG, JN: Review critically for important intellectual content
UIK, SU, ZS, SG, FM, JN: Approve the version to be published
UIK, SU, ZS, SG, FM, JN: Agree to be accountable for all aspects of the work

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