Original Article

Comparison of Outcome of Oral Nifedipine versus Intravenous Hydralazine as Antihypertensive Therapy in the Management of Patients with Severe Preeclampsia

Shagufta Awais[1], Ulfat Naseem[2], Tahira Khalid[3], Afifa Akbar Ali[4], Zonara Qamar[5], Saniya Khalid[6]

[1]Registrar Bahria International Hospital, Rawalpindi, [2]Senior Registrar Ahmad medical complex, Rawalpindi
[3]Associate Prof Federal General Hospital, Chak Shehzad, [4]Registrar Holy Family Hospital Rawalpindi
[5]Consultant Gynaecologist THQ Kotli Sattian, Rawalpindi, [6]Consultant gynaecologist Alsuffah Hospital

Correspondence: *Dr. Shagufta Awais*
Registrar Bahria International Hospital, Rawalpindi
Email: drshagy145@gmail.com

Abstract

Objective: To compare the outcome of oral nifedipine versus intravenous hydralazine as antihypertensive therapy for the management of severe pre-eclampsia

Methodology: This randomized controlled trial study was conducted at Obstetrics & Gynecology Department, Allama Iqbal Memorial Teaching Hospital, Sialkot from August 2020 to February 2021. Total 70(35 in each group) participants with sever preeclampsia were enrolled. All the patients were divided into Group A (oral nifedipine) or Group B (IV hydralazine). All the patients in Group-A were given oral nifedipine in the form of 10 mg tablets and every 15 minutes up to five doses or the desired blood pressure achieved. Group B patients received intravenous hydralazine injections in a dosing regimen of 5 mg IV every 15 minutes, up to a maximum of five doses or until the desired blood pressure was achieved. The clinical response to therapy for both drugs was assessed in terms of outcome. The comparison of outcomes was tested for significance using a t-test. Effect modifiers such as age, gestational age, parity, and BMI were controlled for by stratification. Post-stratification t-tests were applied, and a p-value of ≤ 0.05 was considered significant.

Results The mean time to achieve desired blood pressure in oral nifedipine group was 51.68±5.96 minutes and 39.78±5.15 minutes in IV hydralazine group with a p-value of 0.0001, which is statistically significant. The mean number of doses required to achieve desired blood pressure in oral nifedipine group was 5.13±0.72 and 3.80±0.43 in IV hydralazine group with a p-value of 0.00001, which is statistically significant.

Conclusion This study provides evidence supporting the use of either hydralazine or nifedipine for controlling blood pressure in acute hypertensive emergencies during pregnancy. It suggests that hydralazine may be more effective, with side effects being non-significant.

Keywords: Severe Preeclampsia, Oral Nifedipine, IV Hydralazine.

Cite this article as: Awais S, Naseem U, Khalid T, Ali AA, Qamar Z, Khalid S. Comparison of Outcome of Oral Nifedipine versus Intravenous Hydralazine as Antihypertensive Therapy in the Management of Patients with Severe Preeclampsia. J Soc Obstet Gynaecol Pak. 2023;13(3):344.

Introduction

Severe preeclampsia is a disorder of pregnancy characterized by elevated blood pressure (≥160/110mmHg) and proteinuria (>0.3 g/24 h) after 20 weeks gestation.[1] It has considerable adverse impacts on maternal, fetal, and neonatal health especially in low-resource countries.[2] Incidence of preeclampsia is estimated about 3–10 % of all pregnancies worldwide and approximately 12 to 25% of fetal growth restriction and 15 to 20% of all preterm births are attributable to preeclampsia.[3] According to the previously published studies, eclampsia is responsible for around 34% of maternal deaths in pregnant women.[4] Delivery of the fetus and placenta represents the only definitive treatment for preeclampsia. However, this option is unfortunately not available for many patients diagnosed before the baby reaches full-term. Consequently, treatment primarily focuses on managing symptoms while closely monitoring for the development of complications. The overarching objective in managing preeclampsia is to maintain the woman's blood pressure

Authorship Contribution: [1,4]Substantial contributions to the conception or design of the work; or the acquisition, analysis, or [2]interpretation of data for the work, [3]critical revision of the manuscript for important intellectual content, [5,6]Active participation in active methodology,

Funding Source: none
Conflict of Interest: none

Received: Feb 20, 2023
Accepted: Sept 01, 2023

within the normal range through the use of antihypertensive medications, while also aiming to prevent complications such as eclampsia.[5]

Intravenous hydralazine, labetalol and short acting orally administered nifedipine are amongst the most commonly used anti-hypertensive to control acute hypertensive crises in pregnancy.[6] Hydralazine had long been the preferred drug; however, confidence in its efficacy has waned over the past decade due to mounting evidence of heightened maternal and fetal complications associated with its usage. These include maternal hypotension, increased rates of cesarean sections, placental abruption, maternal oliguria, and adverse effects on fetal heart rate.[7] Oral nifedipine emerges as an alternative option for the management of these patients. Its benefits include low cost, quick start, prolonged action, and oral administration. On the other hand, when used in conjunction with magnesium sulfate, it can result in abrupt maternal hypotension, fetal distress due to placental hypoperfusion, palpitations, and temporary neuromuscular weakness.[8]

Few studies have compared the effectiveness of oral nifedipine with intravenous hydralazine in pre-eclamptic women. Bashir S et al in their recent study compare the efficacy of Hydralazine with Nifedipine in women with severe pre-eclampsia and they found that the mean time to achieve effective blood pressure control in Hydralazine group was 68.33±15.16 and Nifedipine group was 110.17±43.69 (p=0.001). Sudden fall of blood pressure was observed in 6.7% of Hydralazine group and 16.7% of Nifedipine group (p=0.22).[9] In another comparative study, Sabir S et al compared oral nifedipine with intravenous hydralazine to control hypertensive emergencies of pregnancy and found that hydralazine achieved the desired blood pressure in 41.1±20.2 minutes as compared to nifedipine which controlled in 57.9±28.8 minutes. Few doses were required to control BP in case of hydralazine 2.74±1.35 doses as compared to nifedipine which required 3.86±1.45 doses.[10] The study aim to see the difference in outcome of oral nifedipine and intravenous hydralazine as antihypertensive therapy for the management of severe pre-eclampsia.

Methodology

The study was Randomized Controlled Trial which was conducted at Obstetrics & Gynecology Department, Allama Iqbal Memorial Teaching Hospital, Sialkot. Duration of study was six months i.e August 20, 2020 to February 20, 2021. The sample size of 70 (35 in each group) was calculated by using 95% confidence interval with 80% margin of error and taking an expected mean time to achieve the desired blood pressure as 68.33±15.16 minutes with hydralazine as compared to nifedipine which controlled in 110.17±43.69 minutes.[9] Non-probability consecutive sampling technique was used for data collection purpose. Inclusion Criteria included Maternal age between 20 to 35 years, Singleton pregnancy, Gestational age >20 weeks and patients with severe preeclampsia; whereas exclusion criteria included patients having history of cardiac arrhythmias, history of cardiac failure, wheezy chest, hypersensitivity to either nifedipine or hydralazine and patients who are not willing to participate in the study.

Study was conducted after approval of synopsis and permission from ethical committee of hospital. An informed written consent was taken by the trainee researcher from the patients. Total 70 (35 in each group) participants who fulfilled the inclusion criteria were enrolled for the study. After enrolling for study, all the patients were divided into Group A (oral nifedipine) or Group B (IV hydralazine) using lottery method. Baseline demographic details, clinical history, physical examination and blood pressure were taken. Severe pre-eclampsia was defined as systolic blood pressure of >160 mmHg and/or diastolic blood pressure 110 mmHg recorded on at least two separate occasions at least two to four hours apart checked by the trainee researcher at the time of routine checkup after 20th week of pregnancy in previously normotensive female. It was further elaborated by the 24 hours collection of urine. Pre-eclampsia was confirmed if there was presence of ≥300 mg protein in a 24 hour collection of urine. Outcome was assessed by the mean time needed and number of doses required for effective BP control i.e. systolic BP <140 mmHg and diastolic <90 mmHg. After thorough examination and clinical workup, all the patients in Group-A were given oral nifedipine in the form of 10 mg tablets and every 15 minutes upto five doses or the desired blood pressure achieved. Group-B patients received intravenous hydralazine injection in a dose regimen of 5 mg I/V, every 15 minutes upto five doses or desired blood pressure achieved. Patients were advised to start routine medication after that. Clinical response to therapy for both drugs was calculated in term of outcome as per operational definition. Patients who did not respond to given treatment or developed complications, were excluded from study and managed efficiently as per standard guidelines. Data were recorded on a specially pre-designed proforma. All the data were

entered & analyzed by using SPSS (version 25.0). Mean and Standard Deviation was calculated for quantitative variables like age, gestational age, BMI, time to achieve desired blood pressure and number of doses required for desired blood pressure. Frequency and Percentages were calculated for qualitative variables like parity. The comparison of outcome was tested for significance by t-test. Effect modifiers like age, gestational age, parity and BMI were controlled by stratification. Post-stratification t-test was applied. P-value ≤ 0.05 was considered significant.

Results

Total 70 patients with severe preeclampsia were included in the study, divided into Group A (oral nifedipine) and Group B (IV hydralazine). Demographic characteristics such as mean age, age distribution, gestational age, BMI status, and gravidity were assessed. (Table I).

In Table II, oral nifedipine achieved desired blood pressure in 51.68±5.96 minutes compared to 39.78±5.15 minutes for IV hydralazine (p=0.00001). The mean number of doses required were 5.13±0.72 for oral nifedipine and 3.80±0.43 for IV hydralazine (p=0.00001), which is statistically significant.

Table I: Descriptive statistics of variables.

		Groups		Total
		Oral Nifedipine	IV Hydralazine	
Age groups	20-27 years	15 (42.9%)	14 (40.0%)	29 (41.4%)
	28-35 years	20 (57.1%)	21 (60.0%)	41 (58.6%)
	Total	35	35	70
Gestational Age (wks)	<38 weeks	21 (60.0%)	16 (45.7%)	37 (52.9%)
	>38 weeks	14 (40.0%)	19 (54.3%)	33 (47.1%)
	Total	35	35	70
BMI	Normal	22 (62.9%)	21 (60.0%)	43 (61.4%)
	Overweight	13 (37.1%)	14 (40.0%)	27 (68.6%)
	Total	35	35	70
Parity	Primigravida	19 (54.3%)	20 (57.1%)	39 (55.7%)
	Multigravida	16 (45.7%)	15 (42.9%)	31 (44.3%)
	Total	35	35	70

Table II: Comparison of outcomes among both the groups.

Outcomes	Groups		P-value
	Oral Nifedipine	IV Hydralazine	
Time to achieve desired blood pressure	51.68±5.96	39.78±5.15	0.0001
No. of doses required to achieve desired blood pressure	5.13±0.72	3.80±0.43	0.0001

Discussion

Hypertensive disorders complicate 12 – 22% of all pregnancies, making them one of the leading causes of maternal and fetal morbidity and mortality. In a minority of cases, hypertension is accompanied by proteinuria, indicating a multisystem disease known as pre-eclampsia. If not diagnosed and managed promptly, pre-eclampsia can lead to serious consequences. To mitigate adverse outcomes associated with this multi-organ disease, enhanced community health education, prenatal care, and obstetrical facilities are vital for the well-being of both mothers and babies. "Hypertensive crises in pregnancy are associated with an increased risk of stroke. Therefore, lowering blood pressure is considered of utmost importance in these patients. Although existing research is mostly focused on parenteral antihypertensive agents, in resource-limited settings, oral agents can also be used. The results shown in our study were similar to the meta-analysis conducted by Magee et al. [11,12] NHEBP has regarded hydralazine as the drug of choice, with long experience of safety and efficacy.[13] Hydralazine has the advantage that it can be easily administered to unconscious, semi-conscious eclamptic, and restless patients, whereas this is not possible with nifedipine in such cases. Duley et al[14] conducted a meta-analysis that included 24 randomized trials and found that the data was insufficient for final conclusions of comparative effect of antihypertensive agent and that the choice of antihypertensive agents should depend on the familiarity of the adverse effects of the drug, and this conclusion was also reached by Noronha-Neto et al in their study.[15] Nifedipine controls the acute hypertension and preterm labour in pregnancy effectively. Few case reports of use of nifedipine with magnesium sulphate have reported transient neuromuscular weakness.[16] In this study it was found out that hydralazine is more effective drug for control of

blood pressure in acute emergencies as compared to oral nifedipine as the time and number of doses to achieve target blood pressure was in the given time limit. The effectiveness of nifedipine has also been supported by Shekhar et al, Raheem et al, Rezaei et al, in their individual studies.[16,17,18] In our study no significant maternal or fetal adverse effects were shown in both groups and same results were shown in other studies done by Vermillion et al.[19] In this study, mean time to achieve desired blood pressure in oral nifedipine group was 51.68±5.96 minutes and 39.78±5.15 minutes in IV hydralazine group. Mean number of doses required to achieve desired blood pressure in oral nifedipine group was 5.13±0.72 and 3.80±0.43 in IV hydralazine group with a p-value of 0.0001, which is statistically significant. Few studies have compared the effectiveness of oral nifedipine with intravenous hydralazine in pre-eclamptic women. Bashir.S et al in their recent study compare the efficacy of Hydralazine with Nifedipine in women with severe pre-eclampsia and they found that the mean time to achieve effective blood pressure control in Hydralazine group was 68.33±15.16 and Nifedipine group was 110.17±43.69 (p=0.001). Sudden fall of blood pressure was observed in 6.7% of Hydralazine group and 16.7% of Nifedipine group (p=0.22).[20] In another comparative study, Sabir.S et al compared oral nifedipine with intravenous hydralazine to control hypertensive emergencies of pregnancy and found that hydralazine achieved the desired blood pressure in 41.1±20.2 minutes as compared to nifedipine which controlled in 57.9±28.8 minutes. Few doses were required to control BP in case of hydralazine 2.74±1.35 doses as compared to nifedipine which required 3.86±1.45 doses.[21]

Conclusion

This study provides evidence favoring the utilization of either hydralazine or nifedipine for controlling blood pressure during acute hypertensive emergencies in pregnancy. Hydralazine emerges as the more efficacious option, with side effects deemed insignificant.

References

1. Garovic VD, August P. Preeclampsia and the Future Risk of Hypertension: The Pregnant Evidence. Curr Hypertens Rep. 2013;15:10-2.
2. Ngwenya S. Severe preeclampsia and eclampsia: incidence, complications, and perinatal outcomes at a low-resource setting, Mpilo Central Hospital, Bulawayo, Zimbabwe. Int J Womens Health. 2017;9:353-7.
3. Jeyabalan A. Epidemiology of preeclampsia: Impact of obesity. Nutr Rev. 2013;71:10-3.
4. Khowaja AR, Qureshi RN, Sheikh S. Community's perceptions of pre-eclampsia and eclampsia in Sindh Pakistan: a qualitative study. Reprod Health. 2016;13:36-9.
5. Salam RA, Das JK, Ali A, Bhaumik S, Lassi ZS. Diagnosis and management of preeclampsia in community settings in low and middle-income countries. J Family Med Prim Care. 2015;4:501-6.
6. Holbrook B, Nirgudkar P, Mozurkewich E. Efficacy of hydralazine, labetalol and nifedipine for the acute reduction of severe hypertension in pregnancy: a systematic review. Am J Obstet Gynaecol. 2015;212:S286–7.
7. Shekhar S, Gupta N, Kirubakaran R, Pareek P. Oral nifedipine versus intravenous labetalol for severe hypertension during pregnancy: a systematic review and meta-analysis. BJOG. 2016;123:40–7.
8. Gavit Y, Sharma D, Dixit PV. A comparative study of oral nifedipine and intravenous labetalol in control of acute hypertension in severe pre-eclampsia and eclampsia. Int J Reprod Contracept Obstet Gynecol. 2018;7:719-24.
9. Bashir S, Cheema AA, Mazhar R, Rehman A. The efficacy of hydralazine and nifedipine in the management of severe pre-eclampsia. Ann KEMU. 2013;19:164-8.
10. Sabir S, Yasmin S, Abbas G. Comparison of oral nifedipine with intravenous hydralazine for acute hypertensive emergencies of pregnancy. J Postgrad Med Inst. 2016;30:328-30.
11. Magee LA, Abalos E, von Dadelszen P, Sibal B, Easterling T, Walkinshaw S et al. How to manage hypertension in pregnancy effectively. Br J Clin Pharmacol. 2011;72:394– 40.
12. Magee LA, Cham C, Waterman EJ, Ohlsson A, von Dadelszen P. Hydralazine for treatment of severe hypertension in pregnancy: meta-analysis. Br Med J. 2003;327:955-60.
13. Duley L. Handerson-Smart DJ. Mehar S. Drugs for the treatment of very high blood pressure during pregnancy. Cochrane Database Syst Rev. 2006;3:CD001449.
14. Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy (Review). Cochrane Library. 2007;4:1–82.
15. Noronha Neto C, de Souza AS, Amorim MM. Preeclampsia Treatment according to scientific evidence. Rev Bras Ginecol Obstet. 2010;32:459–68.
16. Shekhar S, Sharma C, Thakur S, Verma S. Oral nifedipine or intravenous labetalol for hypertensive emergency in pregnancy: a randomized controlled trial. Obstet Gynecol. 2013;122:1057-63.
17. Raheem IA, Saaid R, Omar SZ, Tan PC. Oral nifedipine versus intravenous labetalol for acute blood pressure control in hypertensive emergencies of pregnancy: a randomised trial. Br J Obstet Gynaecol. 2012;119:78-85.
18. Rezaei Z, Sharbaf FR, Pourmojieb M, Youefzadeh-Fard Y, Motevalian M, Khazaeipour Z et al. Comparison of the efficacy of nifedipine and hydralazine in hypertensive crisis in pregnancy. Acta Med Iran. 2011;49:701-6.
19. Vermillion ST, Scardo JA, Newman RB, Chauhan SP. A randomized, double-blind trial of oral nifedipine and intravenous labetalol in hypertensive emergencies of pregnancy. Am J Obstet Gynecol. 1999;181:858-61.
20. Bashir S, Cheema AA, Mazhar R, Rehman A. The efficacy of hydralazine and nifedipine in the management of severe pre-eclampsia. Ann KEMU. 2013;19:164-8.
21. Sabir S, Yasmin S, Abbas G. Comparison of oral nifedipine with intravenous hydralazine for acute hypertensive emergencies of pregnancy. J Postgrad Med Inst. 2016;30:328-30.