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Original Research Article

Comparative Study between Oral Labetalol Vs Oral Labetalol with Oral Frusemide in Control of Blood Pressure among Postpartum Mothers with Severe Pre-Eclampsia

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Conflict of interest: Nil

Abstract:

Background: About 10% of all pregnancies are still affected by pregnancy-related hypertension, which continues to be a serious public health concern. It ranks as the second most frequent global cause of maternal death. Both normotensive women and those who have had prior hypertension typically have a blood pressure peak three to six days after giving birth. Even without hypertension during pregnancy, about 5.7% of cases of preeclampsia or eclampsia may manifest de novo in the postpartum period (up to six weeks). There is mobilization of fluid from the extravascular spaces and interstitial areas to the intravascular space during the postpartum period, leading to hypertensive crisis and complications. Numerous strategies have been put forth to quicken postpartum mother recovery, but it is still unknown how beneficial they will be and what the best postpartum antihypertensive regimen should be. It has been suggested to employ furosemide for this purpose. This is a crucial justification for the use of furosemide therapy because, due to its mechanism of action, this loop diuretic can act on patients with fluid overload by removing intravascular fluid that has been mobilised during the postpartum period. This lowers blood volume, blood pressure, and the requirement for antihypertensive therapy.

Aims: The aim is to determine the effectiveness of a brief course of oral frusemide 40 mg OD in postpartum mothers with severe preeclampsia from postnatal day 1 to postnatal day 5

Objectives: (1) To assess if the brief course of oral frusemide. (2) Accelerates recovery. (3) Shortens duration of hospital stay by enhancing diuresis. (4) Reduces morbidity and mortality. (4) Reduces need for additional antihypertensive.

Methodology: (1) The study was a single blinded randomized control study. (2) Patients are randomized by simple randomization. (3) The study was conducted among postpartum mothers with severe preeclampsia who are already on treatment with oral labetalol, admitted and delivered in department of OG in GDMCH.

Results: (1) The data was collected from a total of 120 women who were equally divided into two groups, group A receiving labetalol and group B receiving labetalol and furosemide. (2) Almost half of them, 59 (49.17%) were between 28-37 weeks of gestation, 44 (36.67%) were found to be above 37 weeks of gestation and 17 (14.16%) were having less than 28 weeks of gestation. (3) Caesarean section was the most common mode of delivery observed in the study participants in 82 (68.3%). (4) About 13 (10.8%) study participants required additional antihypertensive drug (nifedipine) to lower their blood pressure among those receiving Tab. Labetalol alone. (5) There was a significant reduction in systolic blood pressure among those receiving Tab. Labetalol along with Tab. furosemide. (6) Complications were found to be significantly higher in group receiving Tab.Labetalol alone and all 5 cases of acute pulmonary edema were reported in the same.

Conclusion: These study results show that there is significant reduction in systolic blood pressure when postpartum mothers with severe Pre-Eclampsia were treated with Tab.Labetalol along with Tab.Furosemide. Complications were found to be significantly higher among those taking Tab.Labetalol alone and all 5 cases of acute pulmonary edema were reported among them. Additional anti-hypertensive drugs were required for blood pressure control only. These results indicate that furosemide when used along with labetalol can be used as an effective anti-hypertensive drug in postpartum period.

Keywords: Severe Pre-Eclampsia, Hypertension, Blood Pressure, Tab.Furosemide, Post-Partum Mothers.

Introduction

About 10% of all pregnancies are still affected by pregnancy-related hypertension, which continues to be a serious public health concern [1]. It ranks as the second most frequent global cause of maternal death [2]. More than 99% of maternal deaths attributed to hypertension occur in low-income nations globally, which is a reflection of both a greater incidence and inadequate prenatal care and treatment for obstetric emergencies [3].

Along with increased perinatal morbidity and mortality, [4] it is also a significant potentially life-threatening condition of life and a source of maternal near misses [5]. Additionally, it raises the risk of cardiovascular disease in affected women and has long-term side effects [6]. The risk factors and clinical manifestations of pre-eclampsia are given and pathogenesis of hypertensive disorders of pregnancy is illustrated.

Both normotensive women and those who have had prior hypertension typically have a blood pressure peak three to six days after giving birth. [7] Blood pressure may be raised by pain, medications (such as Nonsteroidal anti-inflammatory medicines [NSAIDs]), excessive fluid administration, or restoring vascular tone to levels seen before pregnancy [8] . Postpartum care for women with pre-existing hypertension or preeclampsia should be closely managed, and NSAIDs should not be used to treat discomfort. [9]

Even without hypertension during pregnancy, about 5.7% of cases of preeclampsia or eclampsia may manifest de novo in the postpartum period (up to six weeks) [10] . These women frequently exhibit visual alterations or new-onset severe headaches. It's vital to have a strong clinical index of suspicion (e.g., check blood pressure, perform urinalysis and consult obstetrics). Women with preeclampsia or eclampsia should be admitted to the hospital right away for monitoring, antihypertensive therapy, and magnesium sulphate treatment (often administered intravenously).

Management of preeclampsia begins with early diagnosis and intervention, focusing on prevention of seizures and adequate blood pressure control. Blood pressure control can be accomplished by utilizing drugs belonging to beta blocker class such as labetalol and calcium-channel blockers such as nifedipine. Fetal evaluation should also be done simultaneously which include ultrasonography of estimated fetal weight, amniotic fluid index, and antenatal testing, such as biophysical profiles and non-stress tests. Fetal status plays an important role in determining the mode of delivery in preeclampsia patients.

An outpatient oral medication regimen can be used to treat a postpartum hypertensive woman who is asymptomatic and has a blood pressure reading of less than 160/110 mm Hg. [7] Through the use of tests for the total blood count, levels of creatinine and liver enzymes, and urinalysis, all women with postpartum hypertension should be screened for HELLP (hemolysis, increased liver enzymes, low platelets) syndrome and other end-organ consequences.

Once blood pressure has been below 140/90 mm Hg for at least 48 hours, the drug dosage can be decreased. [9] The drugs commonly used in the treatment of hypertensive disorders of pregnancy.

Drug	Usual dosage	Maximum dosage
Nifedipine	20–30 mg daily	60 mg b.i.d.
Labetalol	100–200 mg b.i.d.	300 mg q.i.d.
Methyldopa	250–500 mg b.i.d.	500 mg q.i.d.
Enalapril	5–10 mg b.i.d.	10 mg b.i.d.

Liquid from the intravascular and interstitial areas is mobilised to extra vascular space during the postpartum period. 950 mEq of the total body sodium gained during pregnancy are also returned. Between three and five days after birth, there is an increase in sodium excretion in the urine. This may be related to an increase in atrial natriuretic peptide, which plays a role in natriuresis and inhibits aldosterone, angiotensin II, and vasopressin. Management of hypertensive disorders during pregnancy. Numerous strategies have been put forth to quicken postpartum mother recovery, but it is still unknown how beneficial they will be and what the best postpartum antihypertensive regimen should be. It has been suggested to employ furosemide for this purpose. In response to the mobilisation of interstitial and extravascular fluid into the intravascular space, the excess of total body water, and the insufficient secretion of sodium due to reduced renal function, patients with preeclampsia and eclampsia may experience persistent hypertension after delivery. This is a crucial justification for the use of furosemide therapy because, due to its mechanism of action, this loop diuretic can act on patients with fluid overload by

removing intravascular fluid that has been mobilised during the postpartum period.

This lowers blood volume, blood pressure, and the requirement for antihypertensive therapy. With the goal of maintaining low central venous pressure and pulmonary capillary wedge pressures, increasing colloid osmotic pressure, and halting the progression of pulmonary edema and congestive heart failure, this therapy makes sense when considering the pathophysiology of postpartum hypertension.

Postnatal furosemide may reduce the requirement for postnatal antihypertensive medication in the hospital for women with pre-eclampsia, but additional information on meaningful outcomes is required before this practise can be advised. Despite this, it is not yet fully understood how to treat postpartum hypertension optimally. Therefore, the purpose of the current study is to evaluate the efficacy of a brief course of oral furosemide in postpartum moms who have severe pre-eclampsia.

Aims: The aim is to determine the effectiveness of a brief course of oral frusemide 40 mg OD in postpartum mothers with severe preeclampsia from postnatal day 1 to postnatal day 5

Objectives:
To assess if the brief course of oral frusemide

- Accelerates recovery
- Shortens duration of hospital stay by enhancing diuresis
- Reduces morbidity and mortality
- Reduces need for additional antihypertensive

Methodology

Study Design

- The study was a single blinded randomized control study.
- Patients are randomized by simple randomization.

Study Population: The study was conducted among postpartum mothers with severe preeclampsia who are already on treatment with oral labetalol, admitted and delivered in department of OG in GDMCH.

Sample Size: 120 (60 in group A receiving oral labetalol alone, 60 in group B receiving oral labetalol with oral frusemide 40 mg OD from postnatal day 1 to postnatal day 5)

Duration of Study: One year (December 2022-December 2023)

Inclusion Criteria

- Antenatally admitted mothers with severe preeclampsia (blood pressure more than 160/100 mmHg) and on oral labetalol, was included in the study group after delivery at GDMCH
- Antenatally admitted mothers with BP > 140/90 mmHg on oral labetalol and with imminent symptoms – Headache, Vomiting , Blurring of vision, Epigastric pain was included in the study group after delivery at GDMCH
- Postpartum mothers with severe preeclampsia
- Urine output > 50ml/h severe
- Completion of magnesium sulphate regimen.

Exclusion Criteria

- Chronic hypertension
- Renal impairment
- Diabetes, sickle cell disease, rheumatologic disease , heart disease
- Hemodynamic instability
- Potassium < 3mEq/L

Results

120 study subjects participated in our study.

54.2% of the study population belonged to primi category and 45.8% were multigravida [Table-1]

Table 1: Parity of the Study Population

Parity	Frequency (N)	Percentage (%)
Primi	65	54.2
Multi	55	45.8

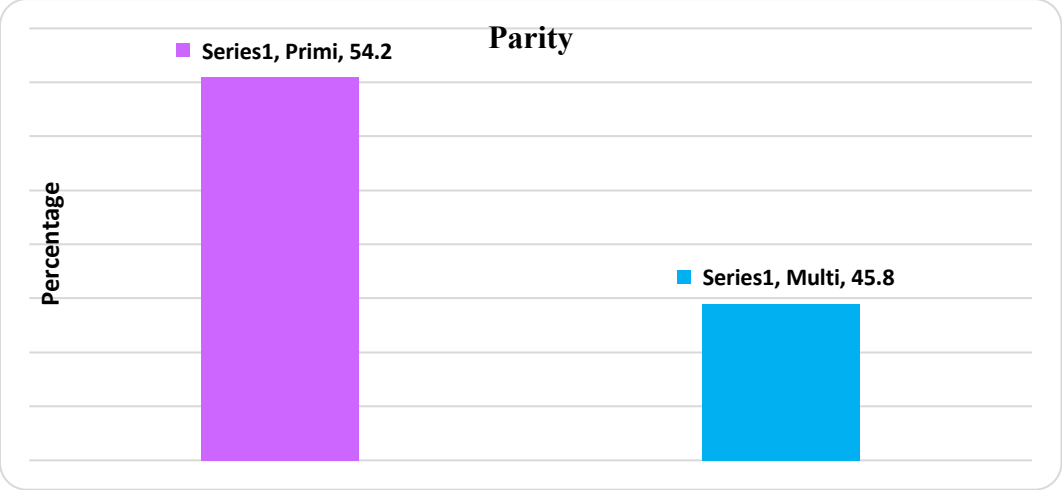

Figure 1: Parity of the Study Population

14.16% of the study participants had belonged to less than 28 weeks, 49.17% belonged to less than 37 weeks category and 36.67% belonged to 37 weeks and above category.[Table-2]

Table 2: Gestational Age

Gestational Age	Frequency (N)	Percentage (%)
Less than 28 Weeks	17	14.16
Less than 37 Weeks	59	49.17
37 Weeks and above	44	36.67

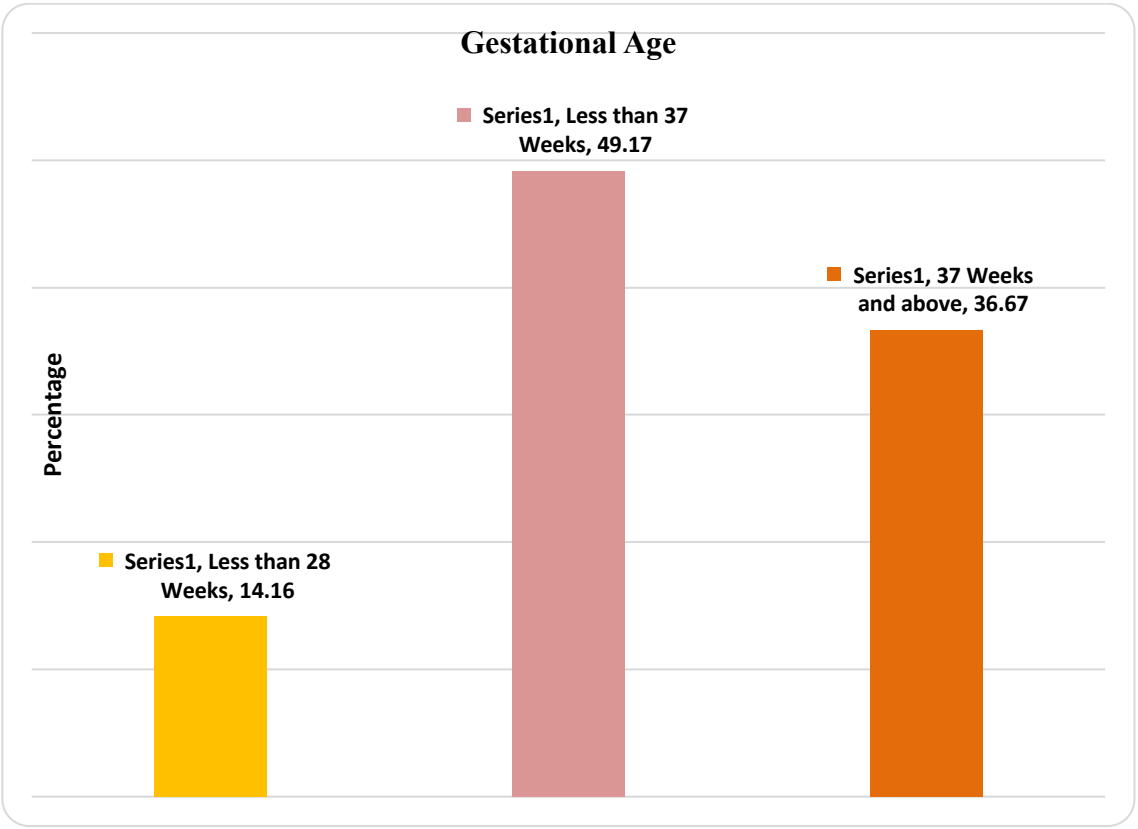

Figure 2: Gestational Age

90.8% did not have any complications,4.2% had acute pulmonary edema,1.7% were present each with PRES and Serous retinal detachment and 0.8% were seen with amarousis fugax and desaturation due to LRI.[TABLE-3].

Table 3: Complications

Complications	Frequency (N)	Percentage (%)
Acute Pulmonary Edema	5	4.2
PRES	2	1.7
Serous retinal detachment	2	1.7
Amarousis fugax	1	0.8
Desaturation due to LRI	1	0.8
Nil	109	90.8

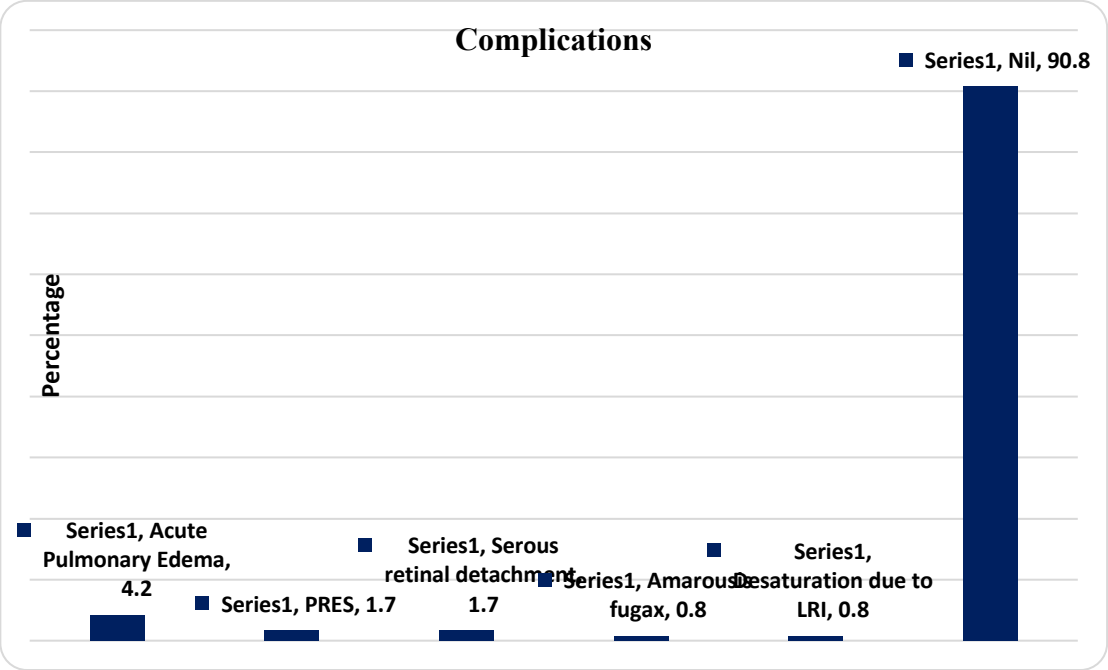

Figure 3: Complications

68.3% had LSCS, 16.6% had foley/gel induced expulsion of dead fetuses,12.6% had normal delivery and 0.8% had emergency hysterotomy,0.8% had outlet forceps delivery and 0.8% had vacuum delivery.[TABLE-4]

Table 4: Mode of Delivery

Mode of delivery	Frequency (N)	Percentage (%)
LSCS	82	68.3
Foley/Mifepristone/Misoprostol Induced Expulsion	20	16.6
LabourNaturale	15	12.6
Emergency Hysterotomy	1	0.8
Outlet Forceps	1	0.8
Vacuum Delivery	1	0.8

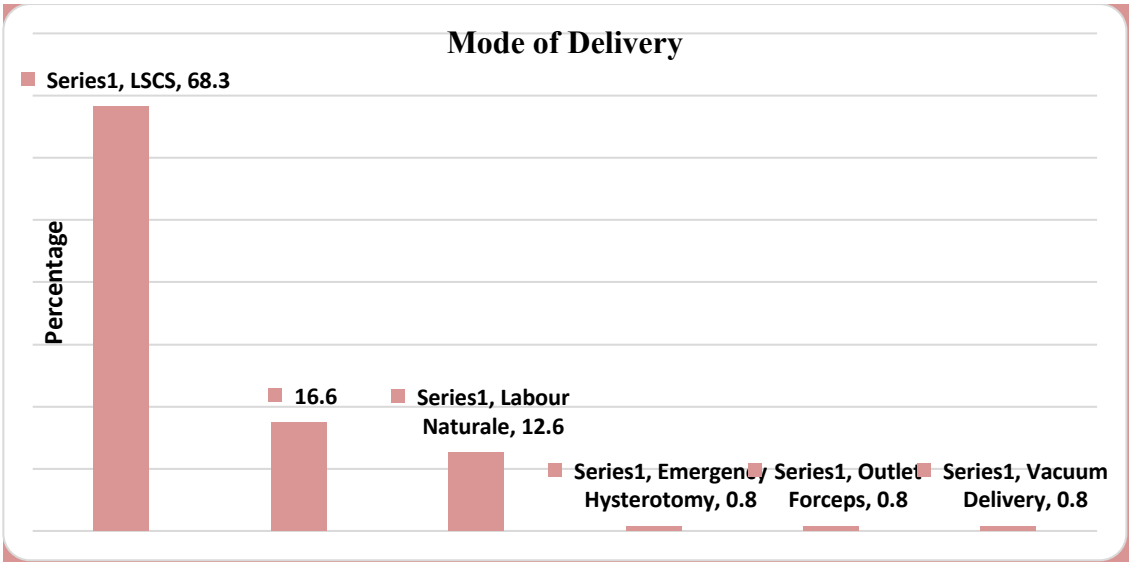

Figure 4: Mode of delivery

10.8% of the study population required nifedipine and others did not receive any additional anti hypertensives

Table 5: Additional Anti Hypertensives

Additional Anti-Hypertensive Required	Frequency (N)	Percentage (%)
Yes (Nifedipine)	13	10.8
No	107	89.2

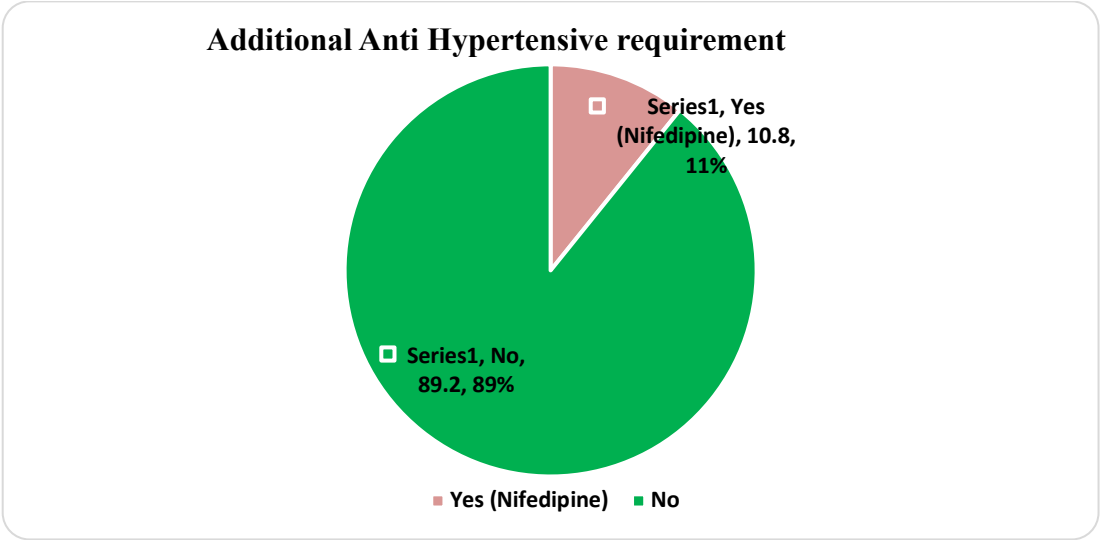

Figure 5: Additional Anti Hypertensives

There is significant difference in Pre and Post Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) among both the groups. Thus, medication in both the groups is effective in reducing the BP within their groups [Table-6]

Table 6: Effect of Blood Pressure among the Two Groups Using Paired 'T' Test

Group			Mean	Std. Deviation	p value
A (Labetalol)	Pair 1	Pre SBP	156.33	10.079	**<0.001**
		Post SBP	115.33	5.95	
	Pair 2	Pre DBP	103.83	6.662	**<0.001**
		Post DBP	76.50	5.15	
B (Labetalol And Furosemide)	Pair 1	Pre SBP	159.00	8.377	**<0.001**
		Post SBP	117.16	5.84	
	Pair 2	Pre DBP	105.00	7.011	**<0.001**
		Post DBP	77.66	4.26	

When comparing both groups the mean Post Systolic Blood Pressure in group B was lower than group A and it was statistically significant, whereas there was no significant difference in mean Post Diastolic Blood Pressure between the two groups[Table-7]

Table 7: Effect of Blood Pressure Between The Two Groups Using Independent Sample't' Test

Variable	Group	Mean	Std. Deviation	p value
Pre SBP	A	156.33	10.079	**0.059**
	B	159.00	8.377	
Pre DBP	A	103.83	6.662	0.176
	B	105.00	7.011	
Post SBP	A	115.3333	5.95653	**0.046**
	B	117.1667	5.84885	
Post DBP	A	76.5000	5.15028	**0.090**
	B	77.6667	4.26522	

The systolic BP variation between two groups wasfound to statistically significant at day 2, day 3, day 4, day 5 and also during discharges the mean systolic pressure was less indicating that group B had good blood pressure control and also the p value was <0.05 [Table-8]

Table 8: Comparison of Systolic Blood Pressure (Mm of Hg) Between Two Groups in the Study Population (Unpaired 'T' Test)

S. No	Time (in min)	Group A (N= 60) (Mean ±SD)	Group B (N=60) (Mean ±SD)	p value
1	At the time of admission	159.11 ± 9.634	160.45 ± 9.414	0.626
2	Day 1	140.11± 9.985	142.29 ± 9.456	0.628
3	Day 2	135.21 ± 9.542	134.91 ± 8.224	**0.024**
4	Day 3	130.86 ± 9.759	128.34 ± 9.732	**<0.001**
5	Day 4	124.71 ± 8.768	120.34 ± 5.789	**<0.001**
6	Day 5	120.11 ± 8.774	115.97 ± 8.736	**<0.001**
7	Day 14-Discharge	119.49 ± 9.522	120.80 ± 9.652	**0.047**

The diastolic BP variation between two groups was not statistically significant as the p value >0.05. [Table-9]

Table 9: Comparison of Diastolic Blood Pressure (Mm of Hg) Between Two Groups in the Study Population

S. No	Time (in min)	Group A (N= 35) (Mean ±SD)	Group B (N=35) (Mean ±SD)	p value
1	At the time of admission	106.54 ± 6.161	105.69 ± 7.125	0.942
2	Day 1	95.31 ± 4.040	90.26 ± 5.483	0.977
3	Day 2	88.58 ± 7.589	86.14 ± 8.456	0.885
4	Day 3	82.37 ± 7.621	80.26 ± 4.063	0.962
5	Day 4	80.14 ± 6.813	67.14 ± 7.026	0.845
6	Day 5	76.23 ± 6.634	73.91 ± 6.541	0.842
7	Day 14-Discharge	75.66 ± 8.640	74.03 ± 8.972	0.860

Among the study population,Group A 85% had no complications in the post natal period and 15% had complications like acute pulmonary edema, amarousis fugax, PRES, serous retinal detachment. Among Group B only 3.3% had complications like Desaturation due to LRI and Serous retinal detachment in the post natal period. There is statistically significant association between presence and absence of complication in mother with the group of who received drug labetalol alone having 15% of complication. [Table-10]

Table 10: Distribution of Complication in the Postnatal Period

		Complications		p value
		No	Yes	
Group	**A**	51 (85%)	9 (15%)	**0.027**
	B	58 (96.7%)	2 (3.3%)	

While majority of the complications were found in group A in the post natal period, Group B had just two complications. Incidence of acute pulmonary edema is higher followed by PRES. [Table-11]

Table 11: Distribution of Maternal Complications

			Complications					
			Acute Pulmonary edema	**Amarousis fugax**	**Desaturation due to LRI/ CPAP**	**Serous retinal Detachment**	**PRES**	**Nil**
Group	**A**	Count	5	1	0	1	2	51
		%	8.30%	1.70%	0.00%	1.70%	3.30%	85%
	B	Count	0	0	1	1	0	58
		%	0.00%	0.00%	1.70%	1.70%	0.00%	69.70%

Discussion

The study was conducted with the objectives of assessing the effectiveness of brief course of oral furosemide in postpartum mothers with severe pedal edema. The data was collected after getting approval from institutional ethical committee (IEC) and written informed consent from the study participants. The data was collected from a total of 120 women who were equally divided into two groups – A and B.

- Group A received labetalol and
- Group B received labetalol and furosemide

All the women who were approached agreed to take part in the study. There was no loss to follow up and the response rate was 100%.

Age and weight of the study participants: The mean (SD) age of the study participants was found to be 26.19 (5.15) years. In group A, the mean (SD) age was found to be 25.9 (5.41) years and in group B, the mean (SD) age was 26.48 (4.89) years. There were no differences in the mean age between the two groups with a P value of 0.269.

The mean (SD) weight of 60 study participants was found to be 70.08 (9.13) kg. In group A, the mean (SD) weight was found to be 68.12 (8.74) kg and in group B, the mean (SD) weight was 71.88 (9.55) kg. There were no differences in the mean weight between the two groups with a P value of 0.115. The baseline characters of age and weight were comparable in both groups A and B. This indicates that there will not be any effect modification because of these variables.

Parity and gestational age: Among 60 study participants, 65 (54.2%) were primi gravida and 55 (45.8%) were multi gravid. Almost half of them, 59 (49.17%) were between 28-37 weeks of gestation, 44 (36.67%) were found to be above 37 weeks of gestation and 17 (14.16%) were having less than 28 weeks of gestation. The mean (SD) gestational age in group A was 33.77 (5.44) weeks and in group B, it was 33.72 (4.99) weeks. There were no differences in gestational age between two groups.

Mode of delivery: Caesarean section was the most common mode of delivery observed in the study participants in 82 (68.3%) followed by gel induced expulsion in 20 (16.6%), normal vaginal delivery in 15 (12.6%), 1 emergency hysterotomy (0.8%), 1 outlet forceps (0.8%), 1 vacuum delivery (0.8%)

Effect on blood pressure among two groups: In group A, the mean (SD) systolic blood pressure (SBP) before and after treatment were 156.33 (10.07) mm Hg and 115.33 (5.95) mm Hg and their difference was found to be statistically significant with a P value of 0.001.

The mean (SD) diastolic blood pressure (DBP) before and after treatment were 103.83 (6.66) mm Hg and 76.50 (5.15) mm Hg and their difference was found to be statistically significant with a P value of 0.001.

In group B, the mean (SD) systolic blood pressure (SBP) before and after treatment were 159.01 (8.37) mm Hg and 117.16 (5.84) mm Hg and their difference was found to be statistically significant with a P value of 0.001. The mean (SD) diastolic blood pressure (DBP) before and after treatment were 105 (7.01) mm Hg and 77.66 (4.26) mm Hg and their difference was found to be statistically significant with a P value of 0.001.

These results show that the reduction in blood pressures in both groups A and B were equally effective. Perdigao JL et al also reported that the reduction in blood pressure, both systolic and diastolic to be greater in patients taking furosemide.

Effect of blood pressure between two groups: In group A, the mean (SD) SBP after treatment was found to be 117.17 (5.85) mm Hg and in group B, the mean (SD) SBP after treatment was found to be 115.33 (5.95) mm Hg. There was significant difference in the reduction of SBP with treatment with group A with a P value of 0.046.

In group A, the mean (SD) DBP after treatment was found to be 76.5 (5.15) mm Hg and in group B, the mean (SD) DBP after treatment was found to be 77.67 (4.26) mm Hg. There was no significant difference in the reduction of DBP with treatment either in group A or group B with a P value of 0.090.

Gracia PV et al had also reported significantly lower blood pressure in patients of preeclampsia who took furosemide treatment. The results of a study by Tamas P et al suggest that diuretics could be useful in the management of late-onset pre-eclampsia, indicating that an increase in water retention could

play a role in the development of late-onset pre-eclampsia.

Complications: Among 60 newborns in group A, death was observed in 9 (15%) and among 60 newborns in group B, death was observed in 15 (25%). There was higher prevalence of deaths in group B when compared to group A but the difference was not found to be significant with p value of 0.171.

About 2 (3.3%) patients in group B had some sort of complications while in group A, it was seen in 9 (15%) patients. Complications were found to be significantly higher in group A (LABETALOL ONLY GROUP) with a P value of 0.027. All 5 cases of acute pulmonary edema reported in the study were seen in group A.

This could be due to the fact that furosemide being a loop diuretic reduces blood volume thereby preventing pulmonary edema in group B (Labetalol and Furosemide group). Similar results were also found in studies done by Stamilio DM et al and Bruce KH et al .However, in a meta-analysis conducted by Collins et al, no significant differences in neonatal outcomes were observed in furosemide treatment group. This could be due to differences in population characteristics or presence of any confounding factors.

Given the significant maternal morbidity and mortality associated with postpartum hypertension, it is critical to find ways to improve blood pressure control and optimize maternal outcomes.

We found that in women who took postpartum furosemide, there was a decrease in the risk of persistent hypertension postpartum and leads to a faster resolution of postpartum hypertension most profoundly in women without severe disease. This has important maternal health implications in decreasing the burden of disease related to hypertensive disorders of pregnancy.

Summary

1. The study was conducted with the objectives of assessing the effectiveness of brief course of oral furosemide in postpartum mothers with severe pedal edema.
2. The data was collected from a total of 120 women who were equally divided into two groups, group A receiving labetalol and group B receiving labetalol and furosemide.
3. The mean (SD) age of the study participants was found to be 26.19 (5.15) years. In group A, the mean (SD) age was found to be 25.9 (5.41) years and in group B, the mean (SD) age was 26.48 (4.89) years.
4. The mean (SD) weight of 60 study participants was found to be 70.08 (9.13) kg. In group A, the mean (SD) weight was found to be 68.12 (8.74) kg and in group B, the mean (SD) weight was 71.88 (9.55) kg.
5. Among 60 study participants, 65 (54.2%) were primi gravida and 55 (45.8%) were multi gravid.
6. Almost half of them, 59 (49.17%) were between 28-37 weeks of gestation, 44 (36.67%) were found to be above 37 weeks of gestation and 17 (14.16%) were having less than 28 weeks of gestation.
7. Caesarean section was the most common mode of delivery observed in the study participants in 82 (68.3%).
8. About 13 (10.8%) study participants required additional anti-hypertensive drug (nifedipine) to lower their blood pressure and all belonged to group A.
9. These study results show that the change in blood pressures before and after treatment in both groups A and B were significant.
10. There was a significant reduction in systolic blood pressure in group B when compared to group A.
11. Complications were found to be significantly higher in group A (P value 0.027) and all 5 cases of acute pulmonary edema were reported in group A.

Conclusion

These study results show that the change in blood pressures before and after treatment in both groups A and B were significant. There was a significant reduction in systolic blood pressure in group B when compared to group A.

Complications were found to be significantly higher in group A and all 5 cases of acute pulmonary edema were reported in group A. Additional anti-hypertensive drugs were required for blood pressure control only in group A. These results indicate that furosemide when used along with labetalol can be used as an effective anti-hypertensive drug in postpartum period.

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