



COMPARISON OF FREQUENCY OF ORTHOSTATIC HYPOTENSION IN HYPERTENSIVE DIALYSIS PATIENTS ON COMBINATION OF ANTIHYPERTENSIVE THERAPY WITH AND WITHOUT PRAZOSIN

General Medicine

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ABSTRACT

Introduction: Orthostatic hypotension (OH) is sudden decrease in systolic blood pressure >20mmHg or diastolic BP>10mmHg within 3 minutes on standing. Prazosin is one of the frequently used antihypertensive in chronic renal failure and dialysis patients, which is also known to cause postural hypotension. The present study was undertaken to assess the frequency of orthostatic hypotension in hypertensive dialysis patients who were on combination of antihypertensives with and without prazosin. **Methodology:** Hypertensive patients undergoing hemodialysis were divided into 2 groups: Group 1: patients on antihypertensives with prazosin; Group 2: Patients on antihypertensives without prazosin. Blood pressure of the study patients were measured 10 minutes before dialysis in both supine and within 3 minutes of standing. In postdialysis period, 10 minutes after completion of hemodialysis, blood pressure was measured like predialysis sessions. Documentation of usage of concurrent medications, comorbidities was done. **Statistical Analysis:** Considering power of 90% and alpha error of 1%, the sample size required for present study was estimated to be minimum of 44 in each group. However, it was decided to include in 50 in each group. **Results:** The frequency of both systolic and diastolic OH was observed more in group 2 than group 1 with increased frequency OH in postdialysis sessions. Occurrence of OH was more among elderly patients, using multiple antihypertensive agents with multiple comorbidities

KEYWORDS

Orthostatic hypotension; prazosin; antihypertensive; chronic dialysis; blood pressure.

INTRODUCTION

Orthostatic hypotension (OH) is defined as reduction in systolic blood pressure by 20 mmHg and diastolic blood pressure of 10 mmHg within 3 minutes of standing from lying down position. There is pooling of blood to the lower extremities on sudden standing resulting in decreased venous return to heart and brain leading to syncope, falls, etc. Some of the causes for orthostatic hypotension are blood loss, dehydration, systemic alterations, medications like alpha blockers, diuretics, anti-parkinsonism drugs, etc. Orthostatic hypotension should be detected earlier as it is predictive of future overall mortality.¹ Orthostatic hypotension has shown to increase the risk of chronic kidney disease in middle aged individuals and it is commonly seen in elderly age group.

Hypertension is highly prevalent condition and is an independent risk factor for various diseases like chronic kidney disease, stroke, dementia, metabolic syndrome, etc. It is one of the main cause for end stage kidney disease.² Up to 90% of renal dialysis patients will be on antihypertensive medications like diuretics, angiotensin converting enzyme inhibitors, vasodilators, alpha blockers as a monotherapy or with the combinations.³

One of most commonly used antihypertensive for adequate control of blood pressure (BP) is prazosin, an alpha blocker known to be renoprotective as it is minimally excreted through kidney.⁴ But, prazosin when added to antihypertensive regimen can cause postural blood pressure changes. It is potentiated by plasma volume depletion, absence of peripheral vasoconstriction.⁵

There are very few studies done in Indian population determining the effect of prazosin on blood pressure in hypertensive dialysis patients. Hence, the present study was undertaken to compare the frequency of orthostatic hypotension with and without prazosin in hypertensive dialysis patients who are on antihypertensive therapy and also to assess the effects of prazosin on blood pressure variability occurring during dialysis.

METHODOLOGY

- **Study Design:** A hospital based observational study
- **Study Period:** One year
- **Study Population:** Hypertensive patients undergoing hemodialysis on outpatient basis in a tertiary care hospital
- **Informed Consent:** Taken from study patients
- **Ethics Committee Approval:** Approved by Institutional Ethics committee (Reg no: ECR/215/Inst/Ker/2013)

Method Of Collection Of Data:

This is an observational study conducted to compare the frequency of orthostatic hypotension among hypertensive dialysis patients who were on antihypertensives with / without prazosin.

Hemodialysis patients who were on antihypertensives attending dialysis unit aged >18 years were selected. Baseline characteristics of the patients such as age, gender, vitals, duration of hemodialysis, comorbidities like diabetes and its complications, concomitant medications for comorbidities, duration of hypertension, antihypertensive medications being used were recorded in a predesigned proforma for all the patients who were enrolled in the study.

Patients were divided into two groups based on the treatment they were receiving:

- Group 1: Patients on antihypertensives with prazosin
- Group 2: Patients on antihypertensives without prazosin

In the present study, reduction of >10 mmHg in both systolic and diastolic blood pressure on sudden standing (<3 minutes) from supine position was considered as orthostatic hypotension.

Blood pressure of the study patients were measured 10 minutes before dialysis in both supine and within 3 minutes of standing by using sphygmomanometer and readings were noted. During hemodialysis, blood pressure was measured every 30 minutes throughout the dialysis, 5 readings of blood pressure was obtained after measuring BP every 30 minutes during intradialytic session (Duration of hemodialysis - 2.5 to 3 hours). Average of intradialytic blood pressure was calculated.

In postdialysis period, 10 minutes after completion of hemodialysis, blood pressure was measured in both supine and standing position like predialysis sessions. Average of three readings of blood pressure in both predialysis and post dialysis sessions were calculated which were taken for one week (three dialysis sessions / week).

In a study conducted by Bailey RR et al, use of prazosin in the treatment of patient with hypertension and renal function impairment, it was found that the drug was effective in 29 patients i.e., 29/38 (76%) and postural hypotension was present in 10/38 (26.3%) patients.¹⁴ Assuming that, in the other group receiving diuretic and beta blocker, the effectiveness will be around 40% and postural hypotension of 20% and considering power of 90% and alpha error of 1%, the sample size

required for present study was estimated to be minimum of 44 in each group. However, it was decided to include in 50 in each group.

Statistical Analysis:

All quantitative variables like age, blood pressure was presented using descriptive statistics like mean, median, range and standard deviation. All qualitative variables like gender, comorbidities and concurrent medications were presented using frequencies and percentages. Pre and post dialysis blood pressure values were compared in both the groups and tested for statistical significance using paired t-test/wilcoxon's signed rank test. Between the groups, comparison of blood pressure values was carried out using independent t-test/Mann Whitney 'U' test.

RESULTS & DISCUSSION:

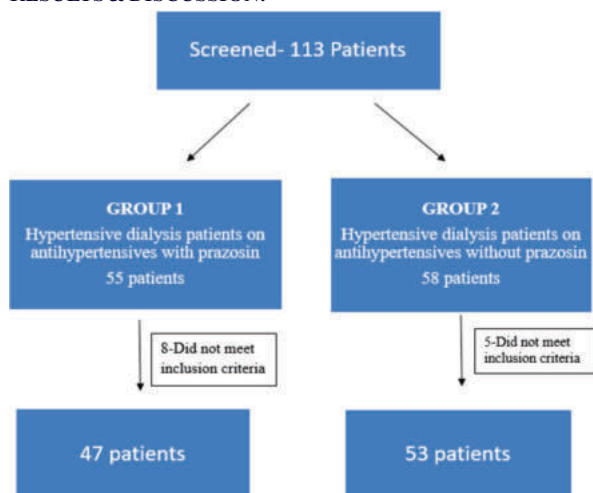


Figure 1: Patient Flow Chart

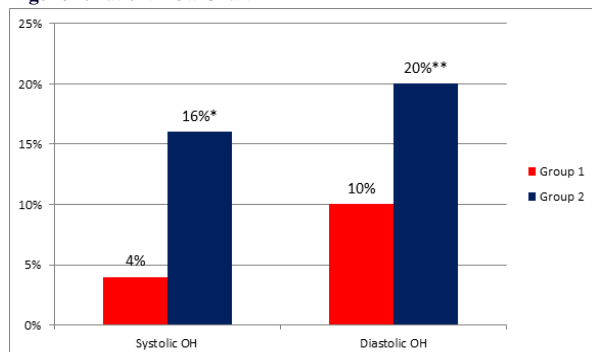


Figure 2: Overall occurrence of orthostatic hypotension among hypertensive dialysis patients

Statistical method: Independent t-test

*p- value: 0.002- statistically significant difference present in systolic OH between 2 groups

**p value: 0.000- statistically significant difference present in diastolic OH between 2 groups

Table 1: Baseline Characteristics Of Study Patients

Sl no	Characteristics	Group 1 (n=47)	Group 2 (n=53)	P value
1	Age in years Mean (SD)	59 (9.8)	44 (10.3)	0.004*
	Minimum age (yrs)	34	21	
	Maximum age (yrs)	78	93	
2	Gender			0.002*
	Male (n=70)	36	34	
	Female (n=30)	11	19	
3	BMI(Kg/m ²) Mean(SD)	26.7(4.8)	25.3(5.6)	0.125
4	Predialysis BP values			
	Systolic BP(mmHg) Mean (SD)	147.5 (5.8)	142.8 (5.1)	0.89
	Diastolic BP(mmHg) Mean (SD)	82.8 (7.8)	79.6 (8.2)	0.323

5	Diabetes mellitus (n=69)	34	35	0.12
6	Diabetic complications N (%) \$	13 (27)	12 (22)	0.154
7	Duration of hypertension in years Mean (SD)	7 (6.8)	8 (4.9)	0.23
8	Duration of hemodialysis in years Mean (SD)	2 (1.2)	2.8 (1.4)	0.182
9	Concomitant medications n (%)			
	Antidiabetics	34 (72)	35 (66)	
	Hypolipidemics	16 (34)	22 (41)	
	Erythropoietin	20 (42)	19 (35)	
	Phosphate binders	32 (68)	36 (76)	

*P value<0.005 is statistically significant, \$Diabetes complications – Peripheral neuropathy, self reported physician diagnosed leg ulcers & retinopathy.

Table 2: Frequency Of Orthostatic Hypotension In Patients Below And Above 50 Years Of Age

Age group < 50 years n=34				Age group > 50 years n=66			
Group 1 (n=14)		Group 2 (n=20)		Group 1 (n=33)		Group 2 (n=33)	
Systoli c OH	Diastol ic OH	Systoli c OH	Diastol ic OH	Systoli c OH	Diastol ic OH	Systoli c OH	Diastol ic OH
0	7%	4%	10%	9%	26%	10%	27%

Table 3: Frequency Of Orthostatic Hypotension In Male And Female Patients

Male N=70				Female n=30			
Group 1 (n=34)		Group 2 (n=36)		Group 1 (n=13)		Group 2 (n=17)	
Systoli c OH	Diastol ic OH	Systoli c OH	Diastol ic OH	Systoli c OH	Diastol ic OH	Systoli c OH	Diastol ic OH
5%	6%	15%	16%	9%	8%	15%	21%

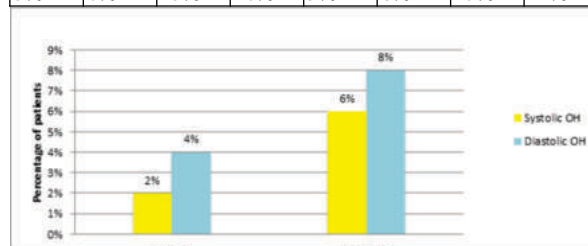


Figure 3: Percentage of patients having systolic & diastolic orthostatic hypotension during predialysis (average of 3 dialysis sessions)

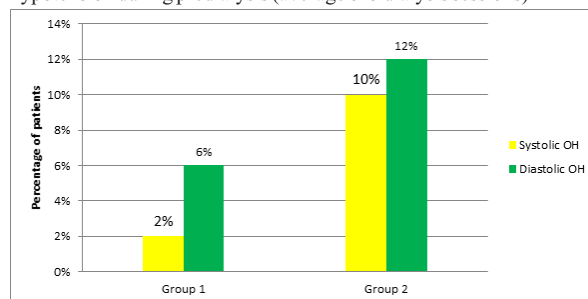


Figure 4: Percentage Of Patients Having Systolic Orthostatic Hypotension During Postdialysis Session (average of 3 dialysis sessions)

Table 5 : Occurrence Of Orthostatic Hypotension In Patients Having Only Hypertension As A Risk Factor

Hypertension (n=42)				Hypertension with comorbidities(n=58)			
Group 1 (n=16)		Group 2 (n=26)		Group 1 (n=31)		Group 2 (n=27)	
Systoli c OH	Diastol ic OH	Systoli c OH	Diastol ic OH	Systoli c OH	Diastol ic OH	Systoli c OH	Diastol ic OH
2%	4%	5%	6%	4%	4%	10%	15%

In the present study, a total of 113 hypertensive dialysis patients who were on antihypertensives and on dialysis for more than 6 months, were screened and divided into 2 groups based on their antihypertensive treatment as **Group 1**(On antihypertensives with

prazosin) with 55 patients and **Group 2** (On antihypertensives without prazosin) with 58 patients. Among them, 8 patients in group 1 and 5 in group 2 were excluded as they did not meet the inclusion criteria. Finally, there were 47 patients in group 1 and 53 in group 2 as shown in figure 1.

Table 6 : Occurrence Of Orthostatic Hypotension With Number Of Antihypertensives Being Used Among Study Patients

Number Of Antihypertensives Being Used	Systolic OH	Diastolic OH
One (n=9)	3%	5%
Two(n=79)	7%	11%
Three(n=12)	10%	14%

Baseline characteristics of the study patients were compared between the groups as shown in table 1. In this study, there was a statistically significant difference in age and gender variables observed, which may be due to more number of male patients and many were in >50 years age group. Other baseline parameters were comparable between the groups.

Orthostatic hypotension is defined as decrease in systolic and diastolic blood pressure in both supine and standing position is greater than 20/10 mmHg.¹ But, the present study considers the patients experiencing >10mmHg reduction of both systolic and diastolic BP on sudden standing (<3min) from supine position as significant as there were less number of patients who had >10mmHg reduction in blood pressure on postural change. As orthostatic hypotension is more reproducible in the morning and for logistic reasons, detailed assessment was done on patients undergoing hemodialysis on daytime shifts.² Alpha-1-adrenergic blocker (prazosin) is an effective antihypertensive agent in the patients on hemodialysis but it's use alone to control hypertension in the patients on hemodialysis increases the risk of orthostatic hypotension and intradialytic hypotension.³

In the present study, overall frequency of systolic and diastolic orthostatic hypotension was more in group 2 (16% and 20%) than in group 1 (4% and 10%) respectively. Diastolic OH was observed more than systolic OH as shown in figure 2. This is in contrast to study conducted by Kamaruzzaman S et al where there was more frequency of systolic OH than diastolic OH.⁴

Overall occurrence of orthostatic hypotension was more in age group >50 years in group 2 when compared to group 1 as shown in table 2. This is similar to study by Roberts R et al, where there was a high incidence of OH in elderly age group (38%). This may be due to blunting of baroreflex mechanisms, co-morbidities and various medications used in elderly people.⁵

Occurrence of orthostatic hypotension was more in females than males and in group 2 when compared to group 1 as shown in table 3. This is similar to the study done by Abdel-Rahman EM et al, where there was a high incidence of OH in females (47%). The reason may be due to less number of female participants in both the studies and women are more susceptible for orthostatic changes in BP due to more active parasympathetic system and high estrogen levels.⁶

In the present study, during predialysis and postdialysis session, orthostatic hypotension was observed more in group 2 than in group 1 as shown in figure 2. Blood pressure changes when compared with study done by Curtis JR et al, where there was a significant orthostatic hypotension observed in both systolic and diastolic blood pressures on addition of small doses of prazosin to the antihypertensive regimen in renal impairment patients. Diastolic OH was more observed which may be attributed to vasodilatation caused by prazosin and volume depletion after dialysis.⁷

During intradialysis period, most of the patients had intradialytic decrease in blood pressure, which was seen in all the patients in group 1 and 95% of patients in the group 2. This is similar to study by Pavan M et al where there was high incidence of intradialytic hypotension than hypertension. Decrease in BP may be due to antihypertensives being used and change in the dialysis solution composition (the type of buffer used, water quality, electrolyte composition).⁸

The frequency of OH in patients having only hypertension and hypertension with other comorbidities as risk factors was more in group 2 than group 1 as shown in table 5. Overall occurrence of OH

was seen more with hypertension with other comorbidities than hypertension alone which is similar to the study done by Kamaruzzaman S et al where OH was more prevalent in patients with multiple comorbidities (32%) than one risk factor (16%). Multiple comorbidities are independent determinants of OH. Pathophysiological changes such as sympathetic failure, atherosclerosis with diabetes, age related autonomic diseases can contribute to occurrence of OH.⁴ Numerous studies have demonstrated the increased risk of OH with increasing burden of antihypertensive agents as these drugs individually has propensity to cause OH.^{9,10,11}

Intradialytic weight loss of more >2.5Kg was considered as significant weight loss. In the present study, 11 patients had significant weight loss. Weight loss may be due to removal of excess fluid and electrolytes during dialysis session.⁴¹ Patients with <2.5kg interdialytic weight gain >2.5kg were 17. This is in contrast to study done by Ipema KJ et al⁴⁰ where most of the patients had >2.5kg weight gain. Interdialytic weight gain of >2.5kg will usually be associated with higher predialysis BP, greater intradialytic reduction in blood pressure and increased mortality. It is also an indicator of nutritional status of the patient.^{12,13}

Fatigue was the most common patient reported symptom followed by dizziness, increased thirst and cramps in both the groups during interdialytic period. This may be due to electrolyte changes during inter and intradialysis period.¹³

CONCLUSION

There was increased frequency of orthostatic hypotension among Group 2 (Patients on antihypertensives without prazosin) when compared to Group 1 (Patients on antihypertensives with prazosin). Occurrence of OH was more in the age group >50 years and in female patients.

Occurrence of OH was more in patients using multiple antihypertensives than single agent and in patients having hypertension with other comorbidities than hypertension alone.

Orthostatic hypotension is a major problem in elderly subjects having comorbidities, using multiple antihypertensives. Hemodialysis is also an independent determinant of OH. Though OH due to antihypertensives is evident, drugs used in hemodialysis patients can be continued as they are renoprotective and delays the consequences of hypertension.

As the sample size of the study is small and there are many confounding factors like comorbidities, multiple medications and hemodialysis itself which are likely to cause OH, large randomized control trials are required to minimize confounding factors and attribute OH to the specific causative agent.

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Conflict Of Interest: None

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