www.jmscr.igmpublication.org
Impact Factor 5.244
Index Copernicus Value: 5.88
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: http://dx.doi.org/10.18535/jmscr/v4i6.17

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Resistant Hypertension in Hemodialysis Patients

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Abstract

Objectives: *This study aimed to assess prevalence of resistant hypertension (RHT) in hemodialysis (HD) patients.*

Patients and Methods: *We conducted a cross sectional study on 135 HD patients. RHT was defined as failure to reach target blood pressure (BP) control (systolic BP <140 mmHg and diastolic BP < 90 mmHg) with maximal dose of 3 antihypertensive therapies (AHT) including diuretics in patients with good daily urine output (> 500 cc/day) or at least 2 L/session ultrafiltration volume in oliguric (<500-100 cc/day) or anuric patients (< 50 cc /day). Patients with post HD hypertension underwent 24h ambulatory monitor for their BP, which hourly measured their BP.*

Results: *In our study; 34 (25.2%) of patients were non hypertensives, 43 (31.8%) were controlled hypertensives, 58 (43.0%) were uncontrolled hypertensives. Uncontrolled hypertensives with inadequate AHT were 53 (39.2 %), where RHT patients were 5 (3.7%)of all study population.*

Conclusions: *We concluded that RHT had3.7% prevalence in HD patients.*

Keywords: *resistant hypertension, haemodialysis.*

Introduction

Hypertension is a major contributor toexcessive cardiovascular morbidity and mortality in in hemodialysis (HD) patients because it is a cause as well as a consequence ofchronic kidney disease (CKD) and end-stage renal disease (ESRD)[1]. Multiplemechanisms are likely involved in blood pressure dysregulation in HD patients and some of themhave resistant hypertension.RHT, defined as BP that remains above goal despite treatment with 3 different classes of AHTagents. One of the 3 agents should be a diuretic and all agents should be prescribed at optimal dose amounts orcontrolled hypertension with at least 4 drugs[2]. Aggressivecontrol of hypertension in dialysis ismandatory.Antihypertensive therapy (AHT) in HD patients was associated with a reduced risk of cardiovascular events, all-cause mortality, and

cardiovascular mortality[3]. HD provides better volume control inESRDpatients byachieving patient's dry weight. However, clearly defined guidelines are not available for hypertensive patients in the HD population and nearly 50-60% of HD patients continue to suffer fromHTN[4]despite multiplicity of AHT.RHT is estimated to affect 15% to 30% of patients with essential hypertension [5].The prevalence of RHT in dialysis patients is still unidentified. Our aim of this study was tostudy the prevalence of RHT in HD patients.

Patients and methods

We conductedacross sectional study, carried out on 135 patients who undergo regular HD in theDialysis Unit of Assiut University Hospital in 2015. Written consents were obtained from most of the participants; illiterate participants gave their consent by finger prints. The study was approved by the ethical committee of Facultyof Medicine in Assiut University. Blood pressurewas measured by well calibrated mercurial sphygmomanometers in 3 different haemodialysis sessions, half an hour before, one hour during and half an hour after cession.Recruited patients on AHT instructed to take their medications at night and to collect their urine output in sterile secured bottles. We used JNC 7 criteria for diagnosis of hypertension with systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg. Patients with post dialysis hypertension underwent 24h ambulatory monitor for their BP usingDel Mar Reynolds/England S.N; 00008970, which hourly measuredtheir BP. Maximal, minimal systolic and diastolic BPs were calculated. Night non dipper patients were identified. RHT was defined as failure to reach target BP control (systolic BP <140 mmHg and/or diastolic BP < 90 mmHg) with maximal dose of 3 medications including diuretics in patients with good daily urine output (> 500 cc/day) or at least 2 L/session ultrafiltration volume in oliguric (<500-100 cc/day) or anuric patients (< 50 cc /day).

Classification of patients

We classified our recruit according to their hypertension state into 3 groups; non hypertensives (*Non*HTN) with pre, intra and post dialysis BP <140 mmHg and diastolic BP < 90 mmHg) without AHT, controlled hypertensives (*C*HTN)with pre, intra and post dialysis BP <140 mmHg and diastolic BP < 90 mmHg) with AHT, and uncontrolled hypertensives groups (*UC*HTN)with pre, intra and post dialysis BP ≥140 mmHg and or diastolic BP ≥ 90 mmHg) with AHT. *UC*HTN was sub classified into *UC*HTN with inadequate AHT (less than 3 AHT) and RHTas previously defined.

Statistical analysis

The statistical analysis wasperformed using SPSS (version 16.0, SPSS Inc., Chicago, IL, USA). The Kolmogorov–Smirnov test will be used to test normally. The continuous variables were presented as the means ± SDand categorical variables were presented as percentages. Student *T* testwas used to compare between means of 2 continuous variables, ANOVA test was used to compare between means of > 2 continuous variables, and chi square testwas used to compare percentages and ratios. A p-value < 0.05 was considered statistically significant

Results

Basal characteristics

The studywas carried out on 135 regular HDpatients.34 (25.2%) of patients were *Non*HTN, 43 (31.8%) were *C*HTN, 58 (43.0%) were *UC*HTN (Figure 1). There were insignificant differences between groups as regard age, gender, BMI, apparent aetiology of ESRD and duration of dialysis (Table 1).

There were insignificant differences between *C*HTN and *UC*HTN groups in duration of hypertension. *C*HTN had significantly higher urine output than *UC*HTN.

Table (1): Demographic, Selected Clinical and Laboratory Characteristics of Patients

CHARACTERISTICS		*Non* HTN (n= 34)	CHTN (n= 43)	UCHTN (n= 58)	(P Value)
AGE(YEARS)		42.35 ± 15.46	43.60 ± 12.89	42.41 ± 13.55	*0.396*
MALEN (%)		20 (58.8%)	24 (55.8%)	24 (41.4%)	*0.187*
BMI	**Underweight** N (%)	6 (17.6%)	2 (4.7%)	3 (5.2%)	*0.064*
	Normal weight N (%)	18 (52.9%)	22 (51.2%)	30 (51.7%)	*0.988*
	Overweight N (%)	7 (20.6%)	9 (20.9%)	11 (19.0%)	*0.966*
	Obese N (%)	3 (8.8%)	10 (23.3%)	14 (24.1%)	*0.169*
Etiology	**Diabetes** N (%)	7 (20.6%)	13 (30.2%)	24 (41.4%)	*0.112*
	HypertensionN (%)	0 (0.0%)	6 (14.0%)	4 (6.9%)	*0.066*
	CIN N (%)	21 (61.8%)	18 (41.9%)	22 (37.9%)	*0.074*
	Others N (%)	6 (17.6%)	6 (14.0%)	8 (13.8%)	*0.865*
Duration of dialysis(YEARS)		5.81 ± 4.40	5.30 ± 4.09	4.10 ± 3.17	*0.087*
HB(g/dl)		10.5±2.39	11.0±3.15	10.1±2.22	*0.453*
Serum Ca(mg/dl)		8.1±2.08	8.6±2.13	8.3±1.52	*0.314*
Serum phosphate(mg/dl)		4.0±0.72	3.9±0.91	4.01±0.69	*0.608*
PD BUN(mg/dl)		55.30±5.30	53.9±7.2	55.0±0.02	*0.355*

NonHTN;non hypertensives, CHTN; controlled hypertensives, UCHTN; uncontrolled hypertensives,BMI: body mass index, ESRD: end stage renal disease, CIN: chronic interstitial nephritis, CIN included;chronic pyelonephritis, obstructive uropathy, analgesic nephropathy, reflux nephropathy, others included;ADPCKD, chronic GN, and SLE, PN BUN; post dialysis Blood Urea Nitrogen

There were insignificant differences between groups in rate and amount of ultrafiltration.*C*HTN had significantly lower BP measurements (pre, intra and post dialysis) and lower numbers of AHT than*UC*HTN group.

Uncontrolled hypertensives with inadequate AHT were 27 (46.6%) with only one AHT and 26 (44.8%) with two AHT, with a total of 53 (91.4 %) of UCHTN and 39.2 % of all study population. RHT patients were 5 (3.7%) of all study population (Figure 1).

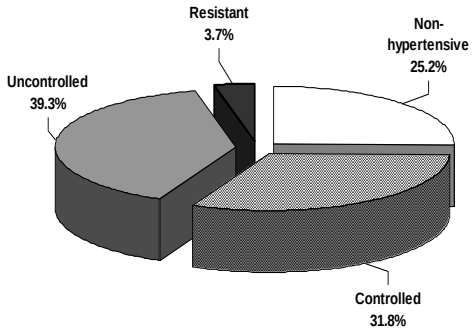

Figure 1: distribution of hypertensive state

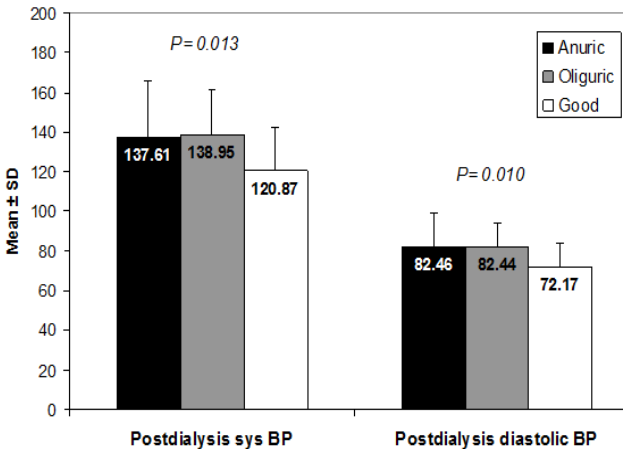

Figure 2:comparing post dialysis BP in urine output groups

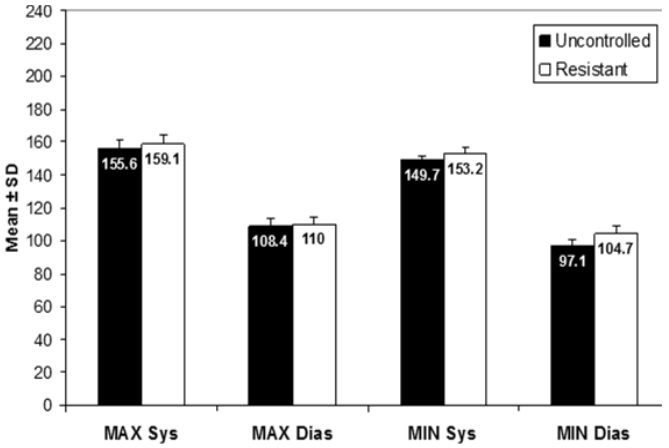

Figure 3: comparisons between BP in resistant hypertensives and other uncontrolled hypertensives

BP: blood pressure, MAX: maximum, Sys: systolic, MIN: minimal, Dias: diastolic

There were insignificant differences between uncontrolled hypertensives with inadequate AHTandRHT regarding; mean of maximal systolic pressure, mean of maximal diastolic pressure, mean of minimal systolic pressure, mean of minimal diastolic pressure (Figure3) and non-dipper state (Not shown).

Table (2): Hypertension duration, urine output,ultrafiltration characters and drug therapies

CHARACTERISTICS		CHTN (n= 34)	UCHTN (n= 58)	P-value
DURATION OF HTN (YEARS)		7.58 ± 5.62	7.38 ± 7.34	*0.881*
URINE OUTPUT	**Anuric**	19 (44.2%)	31 (53.4%)	
	Oliguric	12 (27.9%)	23 (39.7%)	*0.016*
	Good	12 (27.9%)	4 (6.9%)	
ULTRAFILTRATION		10 (23.3%)	21 (36.2%)	*0.163*
ULTRAFILTRATION VOLUME		3.00 ± 0.67	3.38 ± 0.92	*0.253*
PRE DIALYSIS	**Systolic BP** (mmhg)	125.58 ± 19.25	148.71 ± 25.44	*0.000*
	Diastolic BP (mmhg)	77.33 ± 18.72	85.86 ± 13.93	*0.010*
INTRA DIALYSIS	**Systolic BP** (mmhg)	121.40 ± 13.55	151.64 ± 20.42	*0.000*
	Diastolic BP (mmhg)	74.65 ± 17.91	88.79 ± 11.41	*0.000*
POST DIALYSIS	**Systolic BP**(mmhg)	116.28 ± 9.77	153.79 ± 19.52	*0.000*
	Diastolic BP (mmhg)	70.00 ± 8.73	90.26 ± 10.61	*0.000*
NUMBER OF DRUGS	**One Drug**	32 (74.4%)	27 (46.6%)	
	Two Drugs	8 (18.6%)	26 (44.8%)	*0.015*
	Three Drugs	3 (7.0%)	5 (8.6%)	

ANURIC: < 100 cc/day, OLIGURIC: 500 -100 cc/day and GOOD: > 500cc/day.

Urine output and post dialysis BP

By pooling both *C*HTN and *UC*HTN groups, there was a significant trend of post dialysis BP to be reduced as urine output increase (Figure 2).

Discussion

Our study groups were homogenous in age, gender, apparent aetiology of ESRD, duration of dialysisand duration of hypertensionwhich reduced confounding factors.Although rate and volumeof ultrafiltration had insignificant differences between*C*HTN and *UC*HTN, urine output was significantly higher in *C*HTN, which may emphasize the importance of residual renal function (RRF)inBP control.RRF has been found to be important in maintaining fluid balance of

HD patients. In the CANUSA Study, urine volume was a strong independent predictor of survival. Every 250 ml/min urine output was associated with a 36% reduction in overall mortality[6].Loss of RRF is independently associated with suboptimal blood pressure control, likely a result of chronic volume expansion[7].The severity of left ventricular hypertrophy (LVH), a strong independent predictor of mortality in dialysis patients, inversely correlates with the presence of RRF[8]. In addition, loss of RRF is associated with more severe anemia, hypoalbuminemia, and higher arterial pressure[9]. Patients on HD can preserve RRF and achieve better control of their BP by using synthetic membranes and ultrapure dialysis water, routine use of ACEIs and ARBs unless contraindicated, avoid use of non-steroidal anti-inflammatory drugs, oral phosphate solutions, and prolonged aminoglycoside antibiotics, intravenous contrast[10].

In our study survey;we found that inadequatecontrol of hypertensionhad a more significant prevalence in HD patients than RHT, where HD with inadequate AHT accounted for 53 (39.2%) of all study populations andRHT patients were 5 (3.7%)of all hemodialysis studypopulation. *Rahman et al*demonstrated that the prevalence of uncontrolled hypertension in HD patientswas 62%[11].

Interdialytic weight gain, as patient noncompliance with salt and fluid intake, was independent predictors of pre-dialysis systolic blood pressure[11].Other factors contributing to inadequate control of hypertension are:underlying secondary form of hypertension, patient noncompliance on AHT due to developments of side effects andinadequate ultrafiltration[1], inadequate prescription of medicationsdue to fear of intra-dialysis hypotension interfering with adequate ultrafiltration.

Additional strategies to reduce blood pressure should be implemented alongside the dialysis plan including; prolonged or increased frequency of HD, sympathetic denervation, bilateral nephrectomy [12].

Conclusion

We concluded that inadequatecontrol of hypertensionhad a more significant prevalence in HD patients than RHT, where *UC*HTN with inadequate AHT accounted by 53 (39.2%) of all study populations and RHT patients were 5 (3.7%) of all hemodialysis study population and 5 (8.6%) of *UC*HTN. Urine output was significantly higher in *C*HTN, which may emphasise the importance of RRF in BP control.

Study limitations

We recruited only Caucasian patients, which may limit extrapolation to other ethnic groups. Moreover, our results apply only to HDpatients under regular tertiary care. The small number of RHT made statistical difficulties to compare between them and*UC*HTN. We recommend the development of a well definite AHT protocols in managing hypertension in HD to aid in decreasing prevalence of uncontrolled hypertension.

Acknowledgements

The authors wish to acknowledgeDr. Abdel Mohsen Abdelhie, Mrs. Asmaa Abdellatif and Mr. Mohamoud in the dialysis unit for their contribution in gathering data and follow up of patients.

Conflict of interests

The authors declare that there was no conflict of interests as regard the publication of this paper.

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