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ORIGINAL ARTICLE.

Role of Fractional Sodium Excretion in patients with Refractory Hypertension

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ABSTRACT

Background: Although numerous trials establish reliable profit of dietary sodium (Na+) restriction on blood pressure (BP) control in persons with hypertension, few studies tested the role of fractional sodium excretion "FENa" (a surrogate measure of dietary salt intake) as a predictor of hypertension resistance. We aimed to study the correlation between urinary sodium excretion (UNA) and refractory hypertension (RfHTN).

Methods: This study prospectively included 170 hypertensive patients from Zagazig University Hospitals, and police hospitals. Participants were categorized into two groups; group A (AG): 85 patients with controlled BP and group B (BG): 85 patients with uncontrolled BP. Ambulatory blood pressure (ABPM) measurements were used to assess BP and 24-h urine collection was used to estimate FENa level.

Results: The present study showed statistically significant relationship between FENa and BP. FENa results came out with statistically significant differences between two groups; median value is 1.07±0.31% in AG and med ian value is 1.25±0.65% within BG (P- value<0.020). Patients with estimated 24UNA≥200mEq/day showed higher BP readings (mean SBP was 142.67±4.37mmHg) in comparison to those with 24UNA<200mEq/day (128.87±9.68mmHg). In patients with 24UNA≥200mEq/day; (83.3%) were non dippers, (16.7%) were dippers in comparison to those with 24UNA<200mEq/day non dippers were (60.4%), dippers (39.6%).

Conclusion: Nutritional education aiming for reduction of habitual salt consumption is expected to be effective for achieving adequate BP target in hypertensive patients.

Keywords: FENa, ABPM, RfHTN

INTRODUCTION

Uncontrolled hypertension remains the most single causative factor for 70% of all neurological disasters and 50% of cardiac emergencies [1]. Hypertension diagnosis should not be dependent on a single blood pressure (BP) measurement. By providing numerous automated BP readings, ambulatory blood pressure monitoring (ABPM) became the gold standard for diagnosis and follow up BP [2].

Refractory hypertension (RfHTN) is considered phenotype of antihypertensive medication failure in which BP stays uncontrolled on maximal or near-maximal treatment [3]. Numerous trials established reliable profit of dietary sodium (Na+) restriction on BP control in patients with hypertension. Excessive dietary Na+ reduction (50 mEq/d) for one week to high dietary Na+ intake (250 mEq/d) encourage a substantial reduction in BP, dipping 24-hour ABPM by 20.1/9.8 mmHg [3].

This study aimed to to correlate between urinary sodium excretion (UNA) and refractory hypertension (RfHTN).

METHODS

This study prospectively included 170 hypertensive patients from Zagazig University and Police hospitals at the time from March 2015 to December 2020. Written consent of acceptance of

sharing in the study was taken from all patients. The study was approved by the research ethical committee of Faculty of Medicine, Zagazig University Hospitals, and Police Hospital. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Exclusion criteria were those with secondary hypertension (Renal disorders - Endocrine syndromes - Scleroderma - Cancers - Coarcation of the aorta), recent history of stroke, liver disease, obstructive sleep apnea, heart failure, urinary tract infection, pre-renal azotemia, and sepsis. Participants were categorized into two groups; Group A (AG): 85 patients with controlled BP and Group B (BG): 85 patients with uncontrolled BP. All patients were subjected to full history taking, clinical examination, office BP measurement, laboratory investigations (complete blood count - kidney function – serum electrolytes - lipid profile - blood sugar) and echocardiography. ABPM assessment was performed by (CONTEC medical systems ABPM 50, care health, made in Germany) with diagnostic criteria for hypertension; office BP ≥140 ≥90 mmHg and ABPM readings: Daytime ≥135 ≥85 mmHg - Night-time ≥120 ≥70 mmHg - 24 hour (mean) ≥130 ≥80 mmHg [4]. Fractional excretion of sodium (FENa) was estimated by 24-h urine sample collection and normal level of FENa is 1-3%, below 1% is considered low FENa, above 3% is considered high and below 0.2% is considered as diuretic resistance [5].

STATISTICAL ANALYSIS

Data were collected, revised, coded, and entered to the Statistical Package for Social Sciences (IBM SPSS) version 20 and Qualitative data were presented as number and percentages while quantitative data were presented as mean, standard deviations and ranges. The comparison between two groups with qualitative data was done by using Chi –square test. The comparison between two independent groups with quantitative data and parametric distribution was done by using independent t-test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the P value was considered significant as the following: P>0.05: Non-significant - P<0.05: Significant - P<0.01: Highly significant.

RESULTS

Average age of the enrolled patients was (46.75±7.58) years, there was no statistically significant difference in demographic data between two groups except in age (Table 1). Statistically significant difference was found between AG and BG regarding dipping pattern (Table 2). FENa results came out with statistically significant differences between two groups; median value was 1.07±0.31% in AG and median value was 1.25±0.65% in BG (Table 3). Patients with estimated 24UNA≥200mEq/day showed higher BP readings in comparison to those with 24UNA<200mEq/day. Regarding dipping pattern, 83.3% of patients with 24UNA≥200mEq/day were non dippers in comparison to 60.4% in those with 24UNA<200mEq/day (Table 4). Also in the study, 100% of patients with UNA≥200mEq per day showed RfHTN (Table 5).

Table 1: Demographic Data

		AG	BG	P-value
		No=85	No=85	
Age (years)	Mean ± SD	44.93±7.14	48.58±7.60	0.002
	Range	20–62	37–69	
Gender	Female	40 (47.1%)	33 (38.8%)	0.278
	Male	45 (52.9%)	52 (61.2%)	
BMI (Kg/m2)	Mean ± SD	28.29±2.25	28.75±2.32	0.192
	Range	25–33	25–34	
Smoking	No	60 (70.6%)	58 (68.2%)	0.739
	Yes	25 (29.4%)	27 (31.8%)	
HTN Family H/O	No	48 (56.5%)	43 (50.6%)	0.442

		AG	BG	P-value
		No=85	No=85	
DM	Yes	37 (43.5%)	42 (49.4%)	0.496
	No	63 (74.1%)	59 (69.4%)	
	Yes	22 (25.9%)	26 (30.6%)	

P-value>0.05 - Non significant; P-value<0.05- Significant; P-value<0.01- Highly significant BMI; body mass index – HTN; hypertension – H/O; History - DM; Diabetes mellitus

Table 2: BP findings

BP Data		AG	BG	P-value
		No=85	No=85	
Office SBP (mmHg)	Mean ± SD	141.82±12.63	147.18±12.33	0.006
	Range	120–180	125–175	
Mean 24H SBP (mmHg)	Mean ± SD	121.25±6.10	137.46±5.10	0.000
	Range	107–129	126–150	
Mean 24H DBP (mmHg)	Mean ± SD	70.93±5.14	81.86±7.87	0.000
	Range	53–79	68–99	
Dipping	Non dipper	35 (41.2%)	69 (81.2%)	0.000
	Dipper	50 (58.8%)	16 (18.8%)	

BP; blood pressure- SBP; systolic BP- DBP; diastolic BP

Table 3: Sodium excretion data

UNA Data		AG	BG	P-value
		No=85	No=85	
FENa (%)	Mean ± SD	1.07±0.31	1.25±0.65	0.020
	Range	0.5–2	0.5–3.7	
UNA (mmoL/d)	< 200	85 (100.0%)	79 (92.9%)	0.013
	> 200	0 (0.0%)	6 (7.1%)	

FENa; fractional sodium excretion – UNA; urinary sodium

Table 4: Relation of UNA level with BP parameters

BP Data		UNA (mmoL/d)		P-value
		<200	>200	
		No=164	No=6	
Office SBP (mmHg)	Mean ± SD	143.81±12.35	163.33±8.16	0.000
	Range	120–180	155–175	
Mean 24H SBP (mmHg)	Mean ± SD	128.87±9.68	142.67±4.37	0.001
	Range	107–148	138–150	
Mean 24H DBP (mmHg)	Mean ± SD	75.98±8.26	87.83±10.55	0.001
	Range	53–99	75–99	
Dipper	Non dipper	99 (60.4%)	5 (83.3%)	0.257
	Dipper	65 (39.6%)	1 (16.7%)	

BP; blood pressure- SBP; systolic BP- DBP; diastolic BP- UNA; urinary sodium

Table 5: Relation of UNA with hypertension treatment

Hypertension treatment		UNA (mmoL/d)		P-value
		<200	>200	
		No=164	No=6	
ACEi/ ARBS	No	57 (34.8%)	0 (0.0%)	0.077
	Yes	107 (65.2%)	6 (100.0%)	
Calcium channel blockers	No	119 (72.6%)	0 (0.0%)	0.000
	Yes	45 (27.4%)	6 (100.0%)	
Diuretics	No	95 (57.9%)	0 (0.0%)	0.005
	Yes	69 (42.1%)	6 (100.0%)	
Triple therapy	No	154 (93.9%)	0 (0.0%)	0.000
	Yes	10 (6.1%)	6 (100.0%)	

UNA; urinary sodium- ACEi; angiotensin converting enzyme inhibitors- ARBS; angiotensin receptor blockers.

DISCUSSION

This study showed statistically significant relationship between 24UNA and BP. These findings relatively coincided with findings of Barbato et al., [6] who found that FENa was higher in patients with resistant hypertension. FENa was a further independent predictor of RH (FENa raising the risk of RH by 1.3 times). Also, Koo et al., [7] detected an association between salt intake and the diastolic BP. Koo observed an association between salt intake estimated by 24UNA and the target of BP (130/80,140/90mmHg). When 24UNA was over 80mEq/L; the odds of BP over 130/90mmHg was 2.4 times in patients with chronic kidney disease (CKD), for that reason; Koo suggested that patients with CKD should limit their daily salt intake below 2.5gm to assume target BP. In same manner Cook et al., [8] examined the relationship between Na+ intake and long-term mortality. Among 3126 participants; 251 deaths occurred in patients with low Na+ consumption in comparison to 272 in higher Na+ consumption group. Same as our results Nakano et al., [9] documented that 3-month intensive salt restriction education resulted in in lowering ABPM levels (4.5-1.3mmHg in uncontrolled group compared with the controlled group 2.8-1.3 mmHg). Yang et al., [10] also observed the effects of low Na+ salt intake on the BP. By observing 126 patients; SBP of the low salt group was statistically lower in comparison to the normal salt group after 6 months of intervention, also Na+ intake decreased by 55.0mmol/24h in the ISH low salt group, and the SBP decreased by 10.18mmHg. In Concordance to our results; Van Der Stouwe et al., [11] found a weak but statistically significant relationship between 24UNA and BP, suggesting that reductions in salt consumption led to little BP changeability, For 1 gm addition of UNA; tiny but considerable SBP elevation of 0.33%.

But findings were in contrast to data published by Asfar et al., [12] who evaluated different BP patterns and found no difference between hypertension subtypes, dipping patterns and 24UNA, this disagreement was due to most of the enrolled patients were relatively well controlled and that patient's population was relatively obese. Also Welsh et al., [13] demonstrated a lack of straightforward linear relationships between high Na+ intake and increased risk of mortality of CVD, Alternatively, lower Na+ intake may risk via activation of the renin-angiotensin- aldosterone system to maintain Na+ and water homeostasis exposing the cardiovascular system to the deleterious effects of aldosterone. And this discordance was probably due to the individuals recruited were volunteers and, therefore, may not be representative of older or more comorbid populations, also estimating UNA from a single urine sample may be inaccurate.

CONCLUSION

ABPM remains advantageous, superior, and also is considered the gold standard for demonstrating different hypertension subtypes. FENa could be considered a further dependent predictor of refractory hypertension; 24UNA was significantly associated with BP elevation. Based on previous results; our study emphasizing the importance of nutritional education aiming for reduction of habitual salt consumption is expected to

be an effective measure for achieving adequate BP target in hypertensive patients.

Conflict of Interest: Nothing to declare.

Financial Disclosures: Nothing to declare.

REFERENCES

1- **Poulter NR, Lackland DT.** May measurement month: a global blood pressure screening campaign. Lancet. 2017; 389(10080), pp.1678-80.

2- **Tully PJ, Yano Y, Launer LJ, Kario K, Nagai M, Mooijaart SP, et al.** Association between blood pressure variability and cerebral small vessel disease: a systematic review and meta-analysis. J Am Heart Assoc. 2020; 9(1), p.e013841.

3- **Acelajado MC, Hughes ZH, Oparil S, Calhoun DA.** Treatment of resistant and refractory hypertension. Circ Res. 2019; 124(7), pp.1061-70.

4- **Jennings GL.** Relieving the pressure: new Australian hypertension guideline. Med J Aust. 2016; 205(2), pp.63-4.

5- **Enany B, Sabt S, Roshdy K.** Fractional sodium excretion and its relation to in-hospital morbidity and mortality in patients admitted with decompensated heart failure. Am J Cardiol. 2013; 111(7), p.61B.

6- **Barbato A, Galletti F, Iacone R, Cappuccio FP, Rossi G, Ippolito R, et al.** Predictors of resistant hypertension in an unselected sample of an adult male population in Italy. Intern Emerg Med. 2012; 7(4), pp.343-51.

7- **Koo HS, Kim YC, Ahn SY, Oh SW, Kim S, Chin HJ.** Analysis of correlation between 24-hour urinary sodium and the degree of blood pressure control in patients with chronic kidney disease and non-chronic kidney disease. J Korean Med Sci. 2014; 29(Suppl 2), p.S117.

8- **Cook NR, Appel LJ, Whelton PK.** Sodium intake and all-cause mortality over 20 years in the trials of hypertension prevention. J Am Coll Cardiol. 2016; 68(15), pp.1609-17.

9- **Nakano M, Eguchi K, Sato T, Onoguchi A, Hoshide S, Kario K.** Effect of intensive salt restriction education on clinic, home, and ambulatory blood pressure levels in treated hypertensive patients during a 3-month education period. J Clin Hypertens. 2016; 18(5), pp.385-92.

10- **Yang GH, Zhou X, Ji WJ, Liu JX, Sun J, Shi R, et al.** Effects of a low salt diet on isolated systolic hypertension: A community-based population study. Med. 2018; 97(14).

11- **Van Der Stouwe JG, Carmeli C, Aeschbacher S, Schoen T, Krisai P, Wenger G, et al.** Association of 24-hour blood pressure with urinary sodium excretion in healthy adults. Am J Hypertens. 2018; 31(7), pp.784-91.

12- **Afsar B, Elsurer R, Kirkpantur A, Kanbay M.** Urinary sodium excretion and ambulatory blood pressure findings in patients with hypertension. J Clin Hypertens. 2015; 17(3), pp.200-6.

13- **Welsh CE, Welsh P, Jhund P, Delles C, Celis-Morales C, Lewsey JD, et al.** Urinary sodium excretion, blood pressure, and risk of future cardiovascular disease and mortality in subjects without prior cardiovascular disease. Hypertension. 2019; 73(6), pp.1202-9.

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