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Original Research Article

Effect of diuretics on sodium, potassium and chloride levels- a cross sectional study

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ABSTRACT

Background: Diuretics are one of the widely used class of drugs used in various cardiovascular and other disorders. However, they can cause various metabolic adverse effects, electrolyte imbalance being among important changes.
Methods: A cross sectional study was conducted in which patients diagnosed with hypertension for at least one month were included. Over a period of 6 months patients were enrolled irrespective of whether they were taking diuretics or not. Demographic details, drug therapy and electrolyte levels were recorded in a proforma. Data was analyzed for difference in serum electrolyte levels between diuretic and nondiuretic groups as well as between different diuretic groups.
Results: Out of total 177 participants, 71 were on diuretic therapy. There was significant difference in mean serum sodium (S. Na), potassium (S. K) and chlorine (S. Cl) levels between diuretic and nondiuretic groups ($P<0.05$). Hyponatremia, hypokalemia and hyperkalemia were observed. Thiazide diuretic group showed significantly greater hyponatremia compared to other diuretics ($P=0.028$). Hyperkalemia was observed in participants receiving K sparing diuretic or combination of loop and K sparing diuretics. Old age and number of comorbidities showed negative association with S. Na. Females had significantly more hyponatremia than male participants.
Conclusions: The study confirms that diuretics cause various abnormalities in electrolytes namely Na and K levels. Old age, comorbidities and female sex are risk factors for hyponatremia.

Keywords: Diuretics, Electrolytes, Metabolic side effects, Potassium, Sodium

INTRODUCTION

Diuretics are among the most commonly used therapeutic agents in clinical practice. Thiazide-type diuretics are useful first-line agents in the treatment of hypertension because they have been proven to reduce cardiovascular mortality and morbidity in systolic and diastolic forms of hypertension and at low cost while loop diuretics are used for conditions of clinically significant fluid overload like heart failure, significant fluid retention with vasodilator drugs, or with advanced renal failure and can be combined with thiazide-type diuretics.[1,2] Potassium retaining diuretics are useful in combination with loop or thiazides to reduce potassium loss. Spironolactone is used in combination with other drugs for treatment of hypertension and heart failure.[3]

Diuretics act by diminishing sodium reabsorption at different sites of action of nephron leading to a variety of fluid and electrolyte complications. Most common electrolytes affected are sodium (Na) and potassium (K). Common abnormalities include hyponatremia, hypokalemia, and hyperkalemia. They can occur with thiazides, loop diuretics and potassium retaining diuretics.

Loop diuretics and thiazides can produce hypokalemic, hypochloremic, metabolic alkalosis that responds to potassium chloride replacement. Hyperkalemia is an important complication of the potassium-sparing agents, especially in patients with an underlying tendency for hyperkalemia.[4-6]

Thiazide-induced hypokalemia is associated with increased blood glucose, and treatment of thiazide-induced hypokalemia may reverse glucose intolerance and possibly prevent diabetes.[4]

Thiazide use has been shown to be a clear risk factor for hyponatremia and hypokalemia. The effect is dose-dependent and highly variable depending on the individual drug. Syncope and falls seem to be causally related to thiazide use.[7] Less hypokalemia due to loop diuretics may be due to shorter half-life of loop diuretics and the ability of loop diuretics to inhibit calcium absorption in the loop of Henle. The increase in calcium delivery to the lumen of the distal nephron inhibits Na reabsorption and diminishes K secretion.[6]

Potassium-sparing diuretics such as spironolactone, amiloride, and triamterene have the potential to cause hyperkalemia. Hyperkalemia is associated with an increased risk of death, and this is partly explicable by hyperkalemia-induced cardiac arrhythmia. In addition to its well-established effects on cardiac excitability, hyperkalemia could also contribute to peripheral neuropathy and cause renal tubular acidosis.[8]

From India, a few studies have reported diuretics induced electrolyte abnormalities.[4] Hence this cross-sectional study was undertaken with objective of finding electrolyte changes, limited to Na, K and Cl in patients on diuretic therapy as compared to patients not on diuretic therapy.

METHODS

Study setting

The study included outpatient department of a tertiary care hospital in Ahmedabad city in Gujarat state of India.

Study design

It was a cross sectional study of patients with hypertension attending outpatient departments of general medicine and cardiology.

The study was approved by institutional ethics committee of Jivraj Mehata Smarak Health Foundation. Patients of both sexes, age 18 years and above, diagnosed with hypertension at least for last one month and on treatment for the same were included. They were explained about the study and those who consented were included. Data was collected from June 2017 to December 2017. Data was collected on a proforma which included demographic details, duration of disease, co- morbidities and drug therapy details. Those who had records of electrolyte levels measured recently were noted while those not having were advised to get electrolytes test done in hospital laboratory. The electrolytes measured included S. Na, S. K, and S. Cl.

Data was analysed using statistical package for the social sciences (SPSS) version 20. Continuous data was expressed as mean±standard deviation (SD). Z test was used for comparing two groups. Analysis of variance (ANOVA) with posthoc Tukey test was used for comparing more than 2 groups. $P<0.05$ was considered statistically significant

RESULTS

Total 177 patients participated with 107 (60%) males. Seventy-one (40%) participants were on diuretics while 106 were not taking any diuretic. There was no significant difference in age between diuretic and nondiuretic group. All 177 were hypertensive with 102 having no comorbidity. Important comorbidity was coronary artery disease in 61 participants (34.5%). Comparison of serum electrolytes shows statistically significant difference between diuretic group and nondiuretic group (Table 1).

Hyponatremia (S. Na <135 mMol) was observed in 33.8% (24/71) on diuretic therapy, significantly higher compared to 17% (18/106) in patients not taking any diuretic ($P<0.05$). Hypokalemia (S. K <3.6 mmol) was present in 19% (14/71) and 1.8% (2/106) patients of diuretic and nondiuretic group respectively which is significantly higher ($P<0.05$). Hyperkalemia (S. K >5.5 mMol) was found in 7% of diuretic group compared to 0% in nondiuretic group.

Out of 24 participants with hyponatremia, 16 were asymptomatic, 14 complained of weakness, vertigo-5 and headache-1. While among patients with hypokalemia, 4 were asymptomatic, and 10 had weakness or nausea.

Out of 71 participants of diuretic group, 33 were on thiazide/thiazide like diuretics while 19 on fixed dose combination of loop + K sparing diuretic, 8 on loop and 11 on potassium sparing diuretics. Comparison of serum electrolytes shows statistically significant difference in S. Sodium between these groups. $F=3.25$, $p=0.028$) S. K levels showed no statistically difference ($F=1.1044$, $p=0.354$) thiazide group showing lower levels than group on other diuretics. There was no significant difference for S. Cl levels (Table 2).

In the diuretic group, S. Na levels exhibited significant negative correlation with number of comorbidities ($rs=-0.32753$, $p=0.00682$ while there was positive association with S. K levels ($rs=0.40081$, $p=0.00078$). There was negative but nonsignificant correlation with age for S. Na (($r=-0.0461$, $p=0.703259$). S. Na showed significantly higher levels in males than in females ($p<0.05$).

Table 1: Characteristics of study population (N=177).

Characteristic	Diuretic group (71)	Non-diuretic group (106)	P value
Mean age±SD	61.563±11.316	60.144±10.742	0.406
Range	28-91	29-85	
Sex			
No. male	40	67	0.236
No. female	31	39	
Morbidity			
Hypertension	71	106	
Comorbidity			
CAD	24	37	
DM	04	02	
Others	04	01	
None	39	63	
S. Na - meq/l (mean±SD)	134.083±5.110	136.182±3.345	0.002
S. K - meq/l (mean±SD)	4.33±0.848	4.337±0.426	<0.05
S. Cl -meq/l (mean±SD)	98.2±16.7	101.2±4.7	<0.05

Table 2: Comparison of participants with electrolyte abnormalities between diuretic and nondiuretic groups (N=177).

Characteristic (no.) (meq/l)	Diuretic group (N=71)	Non-diuretic group (N=106)	P value
S. Na ≤134	24	18	<0.02
S. K ≤ 3.5	14	2	<0.0001
S. Cl ≤98	14	20	0.987

Table 3: Comparison of mean electrolyte values in patients receiving different diuretics (N=71).

Characteristic	Thiazide (N=33)	Loop (N=10)	Loop + K sparing (N=18)	K sparing (N=10)	#F value
S. Na	136.23±4.66	133.44±3.79	132.97±4.70	131.56±5.55	*3.25314
S. K	4.26±0.54	4.64±0.79	4.57±1.30	4.74±0.69	1.10439

#F value as measured by ANOVA, *p<0.05

DISCUSSION

Sodium, potassium, and chloride are the significant electrolytes along with magnesium, calcium, phosphate, and bicarbonates. Among the electrolyte disorders, hyponatremia is the most frequent. Hyponatremia is diagnosed when the serum sodium level is less than 135 mmol/l. Hyponatremia has neurological manifestations. Patients may present with headaches, confusion, nausea, delirium. Older age, female, low body mass and low sodium diet has been shown to be important risk factors.[9]

In our study hyponatremia was observed in significantly higher frequency (in diuretic group compared to the nondiuretic group. Also, hyponatremia was more frequent than hypokalemia in diuretic group. Most participants with hyponatremia were asymptomatic (16/24) while other complained of weakness, headache and/or vertigo. Similar observation has been made in previous studies.[6] Previous studies have reported hyponatremia between 13 and 22%.[6,10] However these studies were related to thiazide related electrolyte disorders. Indian study from North India reported 27%.[11] While other Indian studies have reported between 5.2-28.8%.[12,13]

Potassium disorders are related to cardiac arrhythmias. Hypokalemia occurs when serum potassium levels under 3.6 mmol/l—weakness, fatigue, and muscle twitching present in hypokalemia.[6] In our study hypokalemia was significantly higher in diuretic group than non-diuretic group. Weakness was complained by 10 out of 14 patients with hypokalemia. Previous studies report 7. 2% incidence of hypokalemia. Diuretic induced hypokalemia has been shown to be dose dependent.[9,14]

Hyperkalemia occurs when the serum potassium levels are above 5.5 mmol/l, hyperkalemia was observed in 5/71 (7%) in diuretic group and they were either on K sparing diuretic alone or in combination with loop diuretics. Hyperkalemia is one of the important adverse effects of K sparing diuretics and is dose dependent. Moreover, loop diuretics are also considered one of the risk factors for hyperkalemia. Age, concomitant medications like beta blockers, angiotensin converting enzyme (ACE) inhibitors are also other important risk factors.[15]

Comparison between different diuretics showed that thiazides caused significantly greater hyponatremia than the other groups of diuretics. There was no significant

difference for S. K and S. Cl levels between different diuretics. Thiazides and thiazide-related agents are implicated most often. However, loop diuretics, K sparing diuretics and combinations of diuretics also may also be responsible. A review suggested that 73% of cases of hyponatremia were associated with use of thiazide-related agents, 6% with furosemide and only 1% with spironolactone.[16] Thus, thiazides and related-agents are >10-fold more likely than loop diuretics to produce hyponatraemia.[17] Older age, female gender, low body mass and concomitant medications have been among important risk factors for hyponatremia.[18] Old age and higher dose of thiazides has also been associated with greater hypokalemia.[4,16] This study also showed negative correlation of S. Na with age and number of comorbidities. Female participants had significantly lower S. Na levels than male participants.

Limitations of this study are cross sectional design, small sample size, and a single health care centre. However, the strength is comparison with a control nondiuretic group and also between different diuretics.

CONCLUSION

The study confirms that use of diuretics can cause electrolyte disorders related to sodium, potassium and chloride. Hyponatremia is more frequent with thiazide diuretics than the other groups. Old age, female sex and comorbidities have important influence on electrolyte disturbances caused by diuretics. It is important to measure serum electrolytes of patients on diuretic therapy at regular intervals.

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