

Research Article



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EVALUATING THE ASSOCIATION BETWEEN THIAZIDE TREATMENT AND SYNCOPE OR FALLS IN INDIAN HYPERTENSIVE PATIENTS WHO WERE HOSPITALIZED

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ABSTRACT

Background: In addition to increasing the risk of falls and syncope, thiazides are frequently used to treat hypertension.

Aim: This study sought to determine if thiazide medication was associated with syncope or falls in hospitalized hypertensive Indian patients.

Methods: This study evaluated 472 people who were on thiazides for hypertension and who came to the Institute throughout the study period, as well as 472 control participants who were not taking thiazides. The demographic information, clinical information, test results, and outcomes of each participant were collected and evaluated from the Institute's prior records. The incidence of syncope or a fall incident was the primary outcome evaluated. Additionally, the relationship between syncope/fall risk and other variables was evaluated.

Results: The study's findings revealed that, with a p-value of less than 0.05, the prevalence of metabolic alkalosis, chronic renal disease, acute kidney damage, hypercalcemia, hypokalaemia, and hyponatremia was greater in thiazide-using participants than in control subjects. Additionally, thiazide-using participants had a considerably greater prevalence of syncope and falls than controls ($p=0.002$). Additionally, participants with lower eGFR, acute renal damage, metabolic alkalosis, hypokalaemia, hyponatremia, longer thiazide duration, congestive heart failure, and age had a higher risk of syncope/fall.

Conclusion: Syncope, which is primarily caused by renal impairment and electrolyte imbalances, is linked to the use of thiazide diuretics in individuals with hypertension. These results focus on vital role of individualized treatment and careful monitoring approaches for prescription of thiazide diuretics in subjects having hypertension.

Keywords: Electrolyte disturbances, falls, hypertension, renal impairment, syncope, thiazide diuretics

INTRODUCTION

In India as well as many other countries, hypertension is one of the most prevalent chronic illnesses. In these patients, thiazide diuretics are frequently recommended either by itself or in combination with other antihypertensive medications.¹

Even while thiazide diuretics are generally well-tolerated and effective medications, they can have a number of negative side effects, including decreased renal function, metabolic problems, and electrolyte imbalances. In patients who are older and have concomitant conditions, they can cause syncope and falls. The most likely reason for elevated risk has been linked to a number of electrolyte abnormalities, such as metabolic alkalosis, hypercalcemia, hypokalaemia, hyponatremia, and acute kidney injury (AKI). The use of thiazide diuretics increases the risk of syncope and falls in the general population, albeit this risk is higher in seniors.²

Given their possible concurrent use of other medications and underlying conditions, the data from the existing literature show limited evidence in addressing the association in hypertensive subjects, especially those who typically have unique clinical profiles and can be especially vulnerable to the adverse events of using thiazide diuretics.³

It will be easier to make clinical decisions about how to reduce adverse events in these people if the precise association between fall risk and syncope and thiazide diuretic usage is known. Healthcare professionals may concentrate on more thorough follow-up, customized preventative measures, and alternative therapy for improved patient safety and quality of care by identifying the demographic and risk factors for susceptible people.⁴

This study sought to determine the relationship between thiazide diuretic usage and the incidence of syncope and falls in hypertensive adults. The study also evaluated the potential modulation of syncope and fall risk in these participants by clinical variables, clinical impairment, and electrolyte imbalances.

MATERIALS AND METHODS

The current retrospective study sought to determine how the usage of thiazide diuretics related to the incidence of syncope and falls in hypertensive adults. Additionally, the study evaluated whether clinical characteristics, decreased renal function, and electrolyte imbalances may influence these participants' risk of syncope and falls. Participants in the research were from the Institute's Department of Medicine. Prior to research participation, all participants and school officials provided written and verbal informed consent.

The current investigation evaluated 472 participants who were taking thiazides and had hypertension when they first arrived at the institute throughout the study period, as well as 472 control subjects who were not taking thiazides. Participants who were 18 years of age or older who were prescribed thiazide diuretics to treat hypertension met the study's inclusion requirements. The subjects were identified using the Institute's prior medical data and records. The study's exclusion criteria included participants who were lost to follow-up and had inadequate medical records and data.

The institute's electronic medical record system made all of the data available to competent experts. Information was gathered on age, gender, duration of thiazide use (often 12.5 mg daily), and concurrent medication use (e.g., angiotensin-converting enzyme, ACE), comorbidity duration, beta-blockers, calcium channel blockers, inhibitors/angiotensin receptor blockers (ARBs), body mass index (BMI), and thiazide dosage range (12.5 mg to 100 mg/day).

Study participants' laboratory results were evaluated for the existence of electrolyte abnormalities (hyponatremia, hypokalaemia, hypercalcemia, and metabolic alkalosis), creatinine levels, serum electrolyte levels (sodium, potassium, and calcium), and estimated glomerular filtration rate [eGFR]. To calculate eGFR (estimated glomerular filtration rate), a reference equation was utilized.⁵ When syncope or fall episodes occurred during the trial, that was the main outcome evaluated and fall incidents that occurred during the study, as determined by the prior institutional data.

The definition of hyponatremia was 10.2 mg/dl of sodium in the serum. The Kidney Disease Improving Global Outcomes (KDIGO) recommendations were used to identify acute kidney injury (AKI) and chronic kidney disease (CKD). A blood bicarbonate level more than 28 mmol/l was considered metabolic alkalosis.⁶⁻⁸

ANOVA, the chi-square test, the student's t-test, Fisher's exact test, the Mann Whitney U test, and SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk, NY, USA) were used to statistically evaluate the collected data. When the p-value was less than 0.05, the significance threshold was taken into account.

RESULTS

The goal of the current retrospective study was to evaluate the relationship between thiazide diuretic usage and the incidence of syncope and falls in hypertensive adults. The study also evaluated the potential modulation of syncope and fall risk in these participants by clinical variables, electrolyte imbalances, and decreased renal function. With $p=0.544$, the mean age of the research participants in the thiazide and non-thiazide groups was statistically not significant. Gender, mean duration of hypertension, mean BMI, congestive heart failure, and duration of diabetes mellitus all showed similar non-significant differences (p -values of 1, 0.166, 0.634, 0.206, 0.672, and 0.334, respectively). The usage of beta blockers, ACE inhibitors, and calcium channel blockers did not differ significantly from the use of other drugs ($p=0.544$, 0.624, and 0.572, respectively). Subjects on thiazides experienced significantly longer durations of congestive heart failure, as well as falls and syncope occurrences (p -values of 0.04 and 0.002, respectively) (Table 1).

Metabolic alkalosis and hypercalcemia were found to be significantly more common in study participants taking thiazide diuretics, with $p<0.001$ and 0.006, respectively, in terms of the severity and prevalence of electrolyte disturbance. Moderate and severe hypokalaemia were comparable in persons taking and not taking thiazides ($p=0.81$ and 0.2, respectively), with mild hypokalaemia being significantly greater in those taking thiazides ($p=0.02$). Additionally, thiazide-using patients had substantially greater hyponatremia ($p=0.04$) (Table 2).

According to the study's findings, evaluating risk variables associated with syncope or falls in hypertensive patients, There were 33.2% (n=194) syncope/fall occurrences in participants older than 65 and 13.9% (n=50) in subjects younger than 65. 38.2% (n=68) of the participants with AKI reported experiencing syncope or a fall episode. According to Table 3, syncope/fall events were observed in 33.3% (n=94) of the subjects with metabolic alkalosis, 40.9% (n=60) of the subjects with hypokalaemia, 35.7% (n=72) of the subjects with hyponatremia, and 37.9% (n=88) of the subjects with congestive heart failure.

When the risk of syncope/fall events and the duration of thiazide use were compared, 32.2% (n=152) of the subjects on thiazides experienced syncope/fall events, while 19.5% (n=92/472), 27.5% (n=44/160), 33.3% (n=52/156), and 35.9% (n=56/156) of the subjects with durations of no use, <12 months, 12-24 months, and >24 months, respectively, experienced syncope/fall events (Table 4).

DISCUSSION

The current study evaluated 472 people who were using thiazides for hypertension and who came to the Institute throughout the designated study period, as well as 472 control participants who were not on thiazides. With $p=0.544$, the mean age of the research participants in the thiazide and non-thiazide groups was statistically not significant. Gender, mean duration of hypertension, mean BMI, congestive heart failure, and duration of diabetes mellitus all showed similar non-significant differences (p-values of 1, 0.166, 0.634, 0.206, 0.672, and 0.334, respectively). The usage of beta blockers, ACE inhibitors, and calcium channel blockers did not differ significantly from the use of other drugs ($p=0.544$, 0.624, and 0.572, respectively). The duration of congestive heart failure and the incidence of falls and syncope were significantly greater in thiazide-using patients (p-values of 0.04 and 0.002, respectively).

These statistics were similar to those from earlier studies by Charkos TG et al. (2019) and Abubakar AA et al. (2021), in which the authors evaluated participants with comparisons to the current study's demographics and illness data. The findings of the study demonstrated that the prevalence and severity of electrolyte disruption were considerably greater in study participants taking thiazide diuretics, with $p<0.001$ and 0.006 for metabolic alkalosis and hypercalcemia, respectively. There was a significant increase in mild hypokalaemia in those using thiazides ($p=0.02$), while moderate and severe hypokalaemia were comparable in those taking and not taking thiazides ($p=0.81$ and 0.2, respectively).

Additionally, individuals on thiazides had substantially greater levels of hyponatremia ($p=0.04$). The findings of the present study were in line with those of Bai X et al. (2011) in 2023 and Ostermann ME et al. (2012) in 2003, where the authors observed similar levels of electrolyte disruption severity and prevalence in study participants using thiazide diuretics.

When risk variables associated with syncope/fall events were evaluated in hypertensive participants, it was shown that 13.9% (n=50) of the subjects had syncope/fall events when they were younger than 65, and 33.2% (n=194) when they were older than 65. Syncope/fall episodes were recorded in 38.2% (n=68) of the AKI individuals. Among individuals with metabolic alkalosis, 33.3% (n=94) experienced syncope or fall episodes. 40.9% (n=60) of patients with hypokalaemia and 35.7% (n=72) of subjects with hyponatremia reported experiencing syncope or falling, and in subjects with congestive heart failure in 37.9% (n=88) study subjects respectively. These results were consistent with the findings of the 2009 study by Moranne O et al.¹³ and the 2017 study by Kuo SCH et al.¹⁴, where the authors reported similar results to the presnet study for the assessment of risk variables associated with syncope/fall episodes in participants with hypertension.

The study's findings also demonstrated that when comparing the risk of syncope/fall events to the length of thiazide use, 32.2% (n=152) of the subjects on thiazides experienced syncope/fall events, while 19.5% (n=92/472), 27.5% (n=44/160), 33.3% (n=52/156), and 35.9% (n=56/156) of the subjects with durations of no use, <12 months, 12-24 months, and >24 months, respectively, experienced syncope/fall events.

These findings were in line with those of Arampatzis S et al. (2015) and Burst V et al. (2017), who found a similar correlation between the length of thiazide usage and the risk of syncope/fall episodes in their investigations.

CONCLUSION

Notwithstanding its limitations, the current study comes to the conclusion that the use of thiazide diuretics in hypertensive people is linked to syncope, which is primarily caused by electrolyte imbalances and renal impairment. These findings highlight how important customized care and close observation are when prescribing thiazide diuretics to hypertensive patients.

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Characteristics	On thiazides	Not on thiazides	p-value
Mean age (years)	68.2±9.4	67.6±10.0	0.544
Gender (male)	236 (50)	236 (50)	1
Thiazide use duration (months)	22.6±15.0	-	-
Mean hypertension duration (years)	9.4±6.2	8.6±5.4	0.166
Diabetes mellitus n (%)	188 (39.8)	178 (37.7)	0.634
Mean BMI (kg/m ²)	29.0±5.0	28.4±4.6	0.206
Congestive heart failure duration (years)	5.2±3.0	4.6±2.6	0.04
Congestive heart failure n (%)	112 (23.7)	120 (25.4)	0.672
Diabetes mellitus duration (years)	7.0±4.4	6.6±4.0	0.334
Use of other medicines			
Calcium channel blockers	150 (31.8)	138 (19.5)	0.544
Beta blockers	178 (37.7)	168 (35.6)	0.624
ACE inhibitors/ARBs	268 (56.8)	256 (54.2)	0.572
Events for syncope/falls	152 (32.2)	92 (19.5)	0.002

Table 1: Clinical and demographic characteristics in two groups of study subjects

Characteristics	On thiazides	Not on thiazides	p-value
Metabolic alkalosis	178 (37.7)	104 (22)	<0.001
Hypercalcemia	74 (15.7)	34 (7.2)	0.006
Hypokalemia	104 (22)	64 (13.6)	

Mild (3-3.5mmol/l)	64 (61.5)	32 (50)	0.02
Moderate (2.5-2.9 mmol/l)	24 (23.1)	22 (34.4)	0.81
Severe (<2.5 mmol/l)	16 (15.4)	10 (15.6)	0.2
Hyponatremia	114 (24.1)	62 (13.1)	0.04
Mild (130-134 mmol/l)	70 (61.4)	40 (64.5)	0.01
Moderate (125-129 mmol/l)	38 (33.3)	16 (25.8)	0.02
Severe (<125 mmol/l)	6 (5.3)	6 (9.7)	1

Table 2: Severity and prevalence of electrolyte disturbance in study subjects on thiazide diuretics

Parameters	Syncope/fall events	
	Number (n)	Percentage (%)
Age (years)		
<65	50/360	13.9
>65	194/584	33.2
Acute kidney injury		
No	176/766	23
Yes	68/178	38.2
Metabolic alkalosis		
No	150/662	22.7
Yes	94/282	33.3
hypokalemia		
No	184/776	23.7
Yes	60/168	40.9
Hyponatremia		
No	172/768	22.4
Yes	72/176	35.7
Congestive heart failure		
No	156/712	21.9
Yes	88/232	37.9

Table 3: Assessment of risk factors linked with syncope/fall events in subjects with hypertension

Parameters	Syncope/fall events	
	Number (n)	Percentage (%)
Thiazide use		
No	92/472	19.5
Yes	152/472	32.2
Thiazide use duration		
No use	92/472	19.5
<12 months	44/160	27.5
12-24 months	52/156	33.3
>24 months	56/156	35.9

Table 4: Association in risk of syncope/fall events and thiazide use duration