Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies

Journal home page: www.jamdsr.com doi: 10.21276/jamdsr

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805 SJIF (Impact factor) 2017= 6.261; Index Copernicus value 2016 = 76.77

Original Article

Prevalence of Thiazide- Induced Hyponatremia

Vikram Sharma[1], Anil Gupta[2]

[1]Associate Professor, [2]Professor & HOD Department of Medicine, ASCOMS Hospital, Sidhra, Jammu, India

***ABSTRACT*:**

Background: Hyponatremia is an occasional but potentially fatal complication of diuretic therapy. Severe thiazide-induced hyponatremia causes debilitating symptoms such as confusion, falls and seizures, and can sometimes be fatal. **Aim of the study:** To evaluate prevalence of thiazide- induced hyponatremia. **Materials and methods:** The study was conducted in the Department of General Medicine of the ASCOMS Hospital. The study was conducted from June 2015 from June 2017. We reviewed the medical records of the department for the study period to identify patients reporting with thiazide induced hyponatremia. A series of questions (queries) was designed to extract the following data – the date, dose and name of any thiazide prescribed within the given time frame and the date and results of electrolyte tests. The timing of the sodium concentration measurements in relation to the thiazide prescriptions were investigated. **Results:** A total of 707 patients were identified. The number of male patients was 329. The highest prevalence of patients with thiazide induced hyponatremia was seen in age group 70-79 years followed by age group 60-69 years. Least prevalence was seen in age group 19-29 years. **Conclusion:** We conclude that thiazide induced hyponatremia is common in patients reporting to department of general medicine. Elderly patients are at particular risk of hyponatremia.

Key words: Thiazide, hyponatremia, blood pressure, sodium

Received: 18 January 2018 Revised: 16 February 2018 Accepted: 27 February 2018

Corresponding Author: Dr. Anil Gupta, Professor & HOD Department of Medicine, ASCOMS Hospital, Sidhra, Jammu, India

This article may be cited as: Sharma V, Gupta A. Prevalence of Thiazide- Induced Hyponatremia. J Adv Med Dent Scie Res 2018;6(4):59-61.

INTRODUCTION:

Thiazide diuretics include all diuretics believed to have a primary action to inhibit NaCl reabsorption in the distal convoluted tubule and have been used in the management of hypertension for over 50 years.[1, 2] These agents decrease blood pressure (BP) when administered as monotherapy, enhance the efficacy of other antihypertensive agents, and reduce hypertension-related morbidity and mortality. However, the use of thiazide diuretics is often limited by concerns about some metabolic change, e.g., hyponatremia, hypokalemia and insulin resistance.[3, 4]Hyponatremia is an occasional but potentially fatal complication of diuretic therapy. Severe thiazide-induced hyponatremia causes debilitating symptoms such as confusion, falls and seizures, and can sometimes be fatal. Thiazide-induced hyponatremia necessitating hospital admission is common enough to suggest that current monitoring regimens are suboptima. Importantly, the mechanism of thiazide-induced hyponatremia is also poorly understood.[5] Mean serum sodium concentration in the total treated population is virtually unchanged by thiazide therapy, implying that thiazide-induced hyponatremia occurs in a susceptible subgroup. However, this subgroup cannot be prospectively identified at present and so thiazide-induced hyponatremia is largely unpredictable at the point of thiazide initiation.[6] Hence, the present study is planned to evaluate prevalence of thiazide- induced hyponatremia.

MATERIALS AND METHODS:

The study was conducted in the Department of General Medicine of the ASCOMS Hospital. The ethical clearance for the study was obtained from the ethical board of the institute prior to commencement of the study. The study was conducted from June 2015 from June 2017. We reviewed the medical records of the department for the study period to identify patients reporting with thiazide induced hyponatremia. A series of questions (queries) was designed to extract the following data – the date, dose and name of any thiazide prescribed within the given time frame and the date and results of electrolyte tests. The timing of

the sodium concentration measurements in relation to the thiazide prescriptions were investigated.

The statistical analysis of the data was done using SPSS version 20.0 for windows. The Student's t-test and Chi-square test were used to check the significance of the data. The p-value less than 0.05 was predetermined as statistically significant.

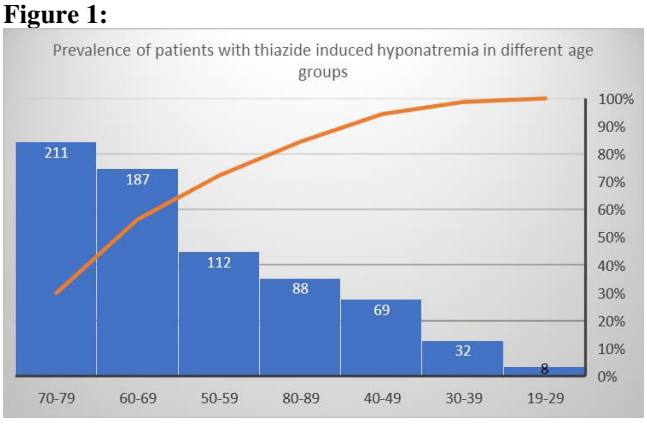
RESULTS:

A total of 707 patients were identified. The number of male patients was 329. Table 1 shows prevalence of patients with thiazide induced hyponatremia in different age groups. The highest prevalence of patients with thiazide induced hyponatremia was seen in age group 70-79 years (n=211), followed by age group 60-69 years (n=187). Least prevalence was seen in age group 19-29 years (n=8). Highest frequency of male patients was seen in age group 70-79 years. Mean Na^+ level in age group 19-29 years was 128 $mmol^{-1}$, in age group 30-39 years was 122 $mmol^{-1}$, in age group 40-49 years was 129 $mmol^{-1}$, in age group 50-59 years was 131 $mmol^{-1}$, in age group 60-69 years was 132 $mmol^{-1}$, in age group 70-79 years was 126 $mmol^{-1}$ and in age group 80-89 years was 129 $mmol^{-1}$. The results were found to be statistically non-significant. [Fig 1]

Table 1: Prevalence of patients with thiazide induced hyponatremia in different age groups

Age (years)	No. of patients (n)	No. of male patients	Mean Na+ level ($mmol^{-1}$) at admission
19-29	8	3	128
30-39	32	12	122
40-49	69	23	129
50-59	112	48	131
60-69	187	92	132
70-79	211	118	126
80-89	88	33	129
Total	**707**	**329**	**130**

Figure 1:



DISCUSSION:

In the present, study we identified 707 patients with thiazide induced hyponatremia. We observed that the highest prevalence of patients with thiazide induced hyponatremia was seen in age group 70-79 years, followed by age group 60-69 years. But the results were statistically non-significant. The results were compared with previous studies and results were consistent with previous studies.Chow KM et al examined whether a subgroup of patients is particularly susceptible to this complication. They defined and recruited cases of symptomatic hyponatremia that necessitated hospitalization from January 1996 to April 2002. Controls were selected from 8420 patients being prescribed thiazides and seen at the same institution during that period of time. There were 223 cases and 216 controls, with a median 115 days thiazide use. Cases were older than controls (76 +/- 9 vs. 66 +/- 13 years) and lighter (52.3 +/- 10.3 vs. 63.4 +/- 3 kg). By univariate analysis, serum potassium level, use of indapamide, elderly home institutionalization and physical immobility were risk factors for thiazide-induced hyponatremia, but gender, duration of thiazide use, concomitant therapy with loop diuretics, angiotensin-converting enzyme inhibitors or non-steroidal anti-inflammatory drugs, and renal function were not. By stepwise logistic regression analysis, patient age, body weight and serum potassium were the only independent predictive factors. Each 10-year increment of age was associated with a two-fold increase in risk. For a 5 kg increment in mass, there was a 27% decrease in odds ratio. One SD increase in serum potassium was associated with a 63% decrease in risk. They concluded that hyponatremia is a common problem after thiazide therapy. Extra caution and close monitoring are warranted when prescribing thiazides for elderly patients with low body mass. Friedman E et al determined whether a single-dose of thiazide administered to patients with previous thiazide-induced hyponatremia will cause hyponatremia and, if so, to analyze its pathogenesis. It was a prospective controlled study comparing patients with previous thiazide-induced hyponatremia with two control groups. Eleven patients with thiazide-induced (Kaluril [hydrochlorothiazide, 50 mg; amiloride, 5 mg]) hyponatremia of less than 130 mmol/L at least 1 week before the study. Two groups of controls: 10 young healthy volunteers and 11 elderly hypertensive patients previously treated uneventfully with thiazide. Blood pressure, pulse rate, body weight, serum urea, creatinine, sodium, potassium, magnesium, osmolality, plasma antidiuretic hormone, renin, aldosterone and also urinary sodium, potassium, osmolality, and cyclic adenosine monophosphate (cAMP) were measured before and 6 to 8, 12, and 24 hours after drug administration. Within 6 to 8 hours serum sodium decreased in patients, young controls, and elderly controls by 5.5 +/- 1.1 (mean +/- SE), 1.2 +/- 0.4, and 1.8 +/- 0.9 mmol/L, respectively. Serum osmolality decreased in patients, young controls, and elderly controls by 14.9 +/- 2.6, 2.8 +/- 1.6, and 6.6 +/- 1.5 mmol/kg, respectively. All patients and only one control subject reached osmolality of less than 280 mmol/kg. At 6 to 8 hours all patients gained weight (0.85 +/- 0.13 kg) whereas young and elderly controls lost weight (0.47 +/- 0.23 and

0.45 +/- 0.2 kg, respectively). Patients' responses to the drug did not differ from both control groups regarding sodium and potassium urinary excretion, osmolar and free water clearance, and antidiuretic hormone blood levels. Water restriction in one patient attenuated serum sodium reduction. They concluded that use of a single-dose of a thiazide diuretic may predict the development of hyponatremia. Increased body weight apparently due to polydipsia may play a major role in the pathogenesis of thiazide-induced hyponatremia.[7, 8]

Sharabi Y et al performed study to characterise hypertensive patients at increased risk to develop hyponatraemia. They reviewed charts of hypertensive patients hospitalised in Chaim Sheba Medical Center for hyponatraemia from 1990 to 1997. Patients with other causes of hyponatraemia were excluded. The General Practice Maccabi database was used to estimate age and sex distribution of patients prescribed diuretics for hypertension. They identified 180 hypertensive patients (149 F, 31 M; mean age 76.4 +/- 9.2 years) hospitalised because of hyponatraemia. Across all age groups, odds ratio (OR) to develop hyponatraemia was three times higher for women vs men. One hundred and sixty-two patients (90%) were older than 65 years. Patients of both sexes older than 65 years were 10 times (and if they were older than 75 years 16 times) more likely to develop hyponatraemia than those younger than 65 years. Most patients (74.5%) used a thiazide-based diuretic; only 10% used a low dose (<25 mg/day). In 37% of patients diuretics were used for more than 1 year before hyponatraemia developed. Diuretic-induced hyponatraemia may be insidious and appear even after prolonged diuretics use. Elderly women seem to be at particularly high risk. In this population diuretic use should be associated with close monitoring of sodium and potassium levels. Clayton JA et al estimated the frequency of hyponatraemia and hypokalaemia amongst patients taking a thiazide diuretic in primary care. A computerized search of the electronic prescribing and laboratory records of six UK general practices was performed. Of the 32 218 adult patients identified, 3773 had received at least one prescription for a thiazide between the years 1990 and 2002. Detailed prescribing data were available for 2942 patients of whom 951 (32.3%) had a recorded check of their electrolytes. One hundred and ninety-six (20.6%) had a sodium and/or potassium concentration below the normal range. The sodium distribution had a negative skew (-1.8) and in 130 (13.7%) patients was within the hyponatraemic range. Hypokalaemia was less common, occurring in 79 (8.5%) patients.

Hyponatraemia was significantly associated with increased age; the odds ratio for developing hyponatraemia in patients over 70 years was 3.87 compared with those of < or = 70 years. Hypokalaemia was significantly associated with increased thiazide dose. They concluded that prescription of a thiazide diuretic in primary care is associated with a high frequency of hyponatraemia and hypokalaemia. Thiazides should be prescribed at low dose and the risk of hyponatraemia, especially in the elderly, should be considered and monitored for when prescribing these agents.[9, 10]

CONCLUSION:

Within the limitations of the study, we conclude that thiazide induced hyponatremia is common in patients reporting to department of general medicine. Elderly patients are at particular risk of hyponatremia.

REFERENCES:

1. Moser M, Macaulay AI. Chlorothiazide as an adjunct in the treatment of essential hypertension. Am J Cardiol. 1959;3:214–219.
2. Mann SJ. The silent epidemic of thiazide-induced hyponatremia. J ClinHypertens (Greenwich) 2008;10:477–484.
3. Glover M, Mercier Zuber A, O'Shaughnessy KM. Hypertension, dietary salt intake, and the role of the thiazide-sensitive sodium chloride transporter NCCT. Cardiovasc Ther. 2011;29(1):68–76.
4. Freis ED, Wanko A, Wilson IM, Parrish AE. Treatment of essential hypertension with chlorothiazide (diuril): Its use alone and combined with other antihypertensive agents. J Am Med Assoc. 1958;166(2):137–140. doi: 10.1001/jama.1958.02990020025004.
5. Fichman MP, Vorherr H, Kleeman CR, et al. Diuretic-induced hyponatremia. Ann Intern Med. 1971;75:853–863.
6. Cohen DL, Townsend RR. Hyponatremia and thiazides. J ClinHypertens (Greenwich) 2012;14:653.
7. Chow KM, Szeto CC, Wong TY, et al. Risk factors for thiazide-induced hyponatraemia. QJM. 2003;96:911–917.
8. Friedman E, Shadel M, Halkin H, Farfel Z. Thiazide-induced hyponatremia. Reproducibility by single dose rechallenge and an analysis of pathogenesis. Ann Intern Med. 1989 Jan 1;110(1):24-30.
9. Sharabi Y, Illan R, Kamari Y, Cohen H, Nadler M, Messerli FH, Grossman E. Diuretic induced hyponatraemia in elderly hypertensive women. J Hum Hypertens. 2002 Sep;16(9):631-5.
10. Clayton JA, Rodgers S, Blakey J, Avery A, Hall IP. Thiazide diuretic prescription and electrolyte abnormalities in primary care. Br J ClinPharmacol. 2006 Jan;61(1):87-95.

Source of support: Nil **Conflict of interest:** None declared