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Indapamide Induced SIADH with Hypokalaemia: A Case Report.

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ABSTRACT

Hyponatremia and hypokalemia is very common among elderly and hospital bound patients. Etiology includes physiological changes, disease per se and also drugs. Elderly patients with hyponatremia usually have features typical of Syndrome of inappropriate antidiuretic hormone (SIADH). Signs and symptoms depend on the degree of hyponatremia and also on the rate at which patients develop it. Many drugs produce SIADH which includes vasopressin, NSAIDs, antipsychotics, antidepressants and thiazide and thiazide like diuretics. We report a case of Indapamide induced SIADH and hypokalemia in a 80 year old male who is a known hypertensive. Increasing use of Indapamide will put patients in a risk of hyponatremia as well as hypokalemia .Changes in the mental status and complaints of weakness and fatigue, in elderly patients taking Indapamide should prompt the clinician to measure serum sodium concentration as well as the potassium concentration for adverse drug reactions.

Keywords: Hyponatremia, Hypokalemia, Syndrome of inappropriate antidiuretic hormone (SIADH), Diuretics

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INTRODUCTION

Hyponatremia and hypokalemia is very common among elderly and hospital bound patients. Etiology includes physiological changes, disease per se and also drugs. Elderly patients with hyponatremia usually have features typical of SIADH. Signs and symptoms depend on the degree of hyponatremia and also on the rate at which patients develop it. Many drugs produce SIADH which includes Vasopressin, NSAIDs, antipsychotics, antidepressants and Thiazide and thiazide like diuretics. Old age is also one of the main risk factor. Drug induced SIADH usually resolves after stopping the offending agent. Hypokalemia in geriatric population is mainly because of diuretics. Decreased potassium intake, concurrent diseases and other medications are also contributing factors. We report a case of Indapamide induced SIADH and hypokalemia in a 80 year old male who is a known hypertensive.

CASE HISTORY

A 80 year old male patient came with complaints of altered sensorium, pain abdomen, dyspnea and fever since two days . He also complains of myalgia, arthralgia and increased frequency of micturition. On examination, his vitals were normal with blood pressure of 180/100 mm of Hg. He had grade 3 dyspnea. Other system examination was normal. Patient is a known case of hypertension for many years and was on multiple medications which includes Amlodipine, diltiazem, Indapamide, nitroglycerine and moxonidine. Laboratory investigations **(TABLE 1)** pointed towards hyponatremia with coexisting hypokalemia. Serum osmolality was 236mosmol/kg and urine osmolality was 546 mosmol/kg with urine sodium excretion of 88mmol/L. It confirmed the diagnosis of SIADH. Indapamide was suspected to be the reason for these adverse effects and drug was discontinued. Patient was changed to olmesartan once daily and other medications were continued. IV fluid correction with 1.6 % NaCl was given at a rate of 20ml/hr for correction of hyponatremia and syrup KMAC 15 ml four times daily was given to correct hypokalemia. The condition of the patient improved and his sodium levels came back to normal and also his potassium levels. Patient was discharged with Telmisartan 40 mg once daily along with amlodipine, nitroglycerine and moxonidine. Review after 2 weeks patient was completely normal with good blood pressure control.

TABLE 1 : LABORATORY INVESTIGATIONS

DATE	13/12/2015	15/12/2015	16/12/2015	17/12/2015	18/12/2015	20/12/2015	2/03/2015
UREA (mg/dl)	19	33	-	-	-	15	24
CREATINE (mg/dl)	0.7	0.9	-	-	-	0.7	0.8
SODIUM (mmol/L)	112	120	123	129	127	137	141
POTASSIUM (mmol/L)	3.3	3.5	3.2	3.2	3.8	4.1	4.4

DISCUSSION

Hyponatremia (defined as a serum sodium level <134mmol/L) is a common electrolyte abnormality seen in clinical practice associated with morbidity and mortality[1]. Drugs are the main culprits causing electrolyte disturbances and a meticulous drug history is essential in case of electrolyte abnormalities. Hyponatremia is one of the most commonest drug induced electrolyte abnormality. Diuretics heads the list as one of the leading cause of hyponatremia, with an incidence of 11% in a case series of 114 geriatric patients [2]. Interestingly diuretics are the most common cause of community- developed hyponatremia[3]. Diuretic-induced hyponatremia is caused almost exclusively by thiazide or thiazide-like agents[4].

Hypokalemia is defined as a serum potassium concentration of less than 3.5 mEq/L. This is also among the most commonly encountered electrolyte abnormalities in clinical practice. Hypokalemia is caused due to total-body potassium deficit, or shift of potassium into intracellular compartment[5]. Medication-induced hypokalemia is very common in old age[6] . Diuretic play a major role in causing hypokalemia in the elderly. Low dietary potassium intake, decreased renal reserve, concurrent disease (e.g., congestive heart failure, renal failure), concomitant therapies (e.g., glucocorticoids), and use of high-dose, long-acting thiazide diuretics are major factors that contribute to diuretic-induced hypokalemia in the elderly.

Indapamide is a thiazide-like diuretic which is used to treat hypertension and edema . It reduces blood pressure via two major proposed mechanisms, vascular smooth muscles relaxation and diuresis. Hypokalemia is the most frequently observed electrolyte imbalance. However, the incidence of severe hypokalemia is rare. It is to be noted that hyponatremia also follows Indapamide administration, as well as the combination of hydrochlorothiazide and amiloride. Despite many studies the pathophysiological mechanisms underlying diuretic-induced hyponatremia are unclear. Main mechanisms causing hyponatremia are excess renal loss of potassium plus sodium compared with water losses due to excess diuretic induced electrolyte loss and excess ADH induced water retention, coexistent hypokalemia leading to a trans cellular cation exchange in which potassium leaves the intracellular compartment to replenish the extracellular stores, whereas sodium moves intracellularly to preserve electro neutrality, by diminishing sodium chloride reabsorption in the renal tubules due to direct inhibition of urinary dilution , stimulation of thirst, by depleting magnesium stores and excessive ADH secretion[7]. Proposed mechanism by which Indapamide causes hypokalemia is by acting directly in the cortical diluting segment of the distal convoluted tubule it causes increases in renin–angiotensin– aldosterone system and thereby there is an increase in sodium delivery to the renal distal tubules. This leads to a dose-related decreased serum potassium concentrations due to increase in potassium excretion [8].

In our case, patient was elderly and was a known hypertensive on Indapamide and other medications. He came with complaints suggesting hyponatremia and hypokalemia. Laboratory investigations confirmed the diagnosis of SIADH along with hypokalemia. Indapamide was suspected and drug was stopped. Hyponatremia was corrected with 1.6 % sodium chloride and hypokalemia was corrected using KMAC syrup. Patient was put on olmisartan once daily dosing . Electrolyte levels returned to normal in one week and his blood pressure was also under control. Patient was discharged and was asked to review after two weeks. Causality assessment was done as per Naranjo's scaling [9] and severity and preventability assessment was also done as per Hartwig's[10] and Thornton's scale [10] respectively . Results are tabulated as follows in **table 2.** A probable causal relationship was established and adverse reactions were found to be of level 4 severity and probably preventable .

TABLE 2: ADVERSE DRUG MONITORING

ADVERSE REACTION	NARANJO'S SCALING (CAUSALITY)	HARTWIG'S SCALING (SEVERITY)	THORNTON'S SCALING (PREVENTIBILITY)
HYPONATREMIA	PROBABLE	LEVEL 4 SEVERITY	PROBABLY PREVENTABLE
HYPOKALEMIA	PROBABLE	LEVEL FOUR SEVERITY	PROBABLY PREVENTABLE

CONCLUSION

Increasing use of Indapamide will put patients in a risk of hyponatremia. Changes in the mental status, in elderly patients taking Indapamide should prompt the clinician to measure serum sodium concentration. The analysis of this case prompts a new hypothesis to determine ADH levels in patients receiving Indapamide coming with complaints of hyponatremia. The hypothesis related to the possibility of hyponatremia being caused by Indapamide can be overlooked and possibility of Indapamide induced hyponatremia due to exacerbation of SIADH by Indapamide can be thought about . Monitoring of Serum potassium concentration of patients under Indapamide therapy is mandatory as diuretic induced hypokalemia is very common among geriatric group.

REFERENCES

[1] Anderson RJ, Chung HM, Kluge R, Schrier RW: Hyponatremia: A prospective analysis of its epidemiology and the pathogenetic role of vasopressin. Ann Intern Med 102:164-168, 1985.
[2] Spital A. Diuretic-induced hyponatremia. Am J Nephrol 19:447-452, 1999.
[3] Liamis G, Christidis D, Alexandridis G, Bairaktari E, Madias N, Elisaf M: Uric acid homeostasis in the evaluation of diuretic-induced hyponatremia. J Investig Med 55:36-44, 2007.
[4] Friedman E, Shadel M, Halkin H, Farfel Z: Thiazideinduced hyponatremia. Reproducibility by single dose rechallenged and an analysis of pathogenesis. Ann Intern Med 110:24-30, 1989.
[5] Gennari FJ. Hypokalemia. N Engl J Med. 1998;339(7):451–458.

[6] Flamenbaum W. Diuretic use in the elderly: potential for diuretic-induced hypokalemia. Am J Cardiol. 1986;57(2):38A–43A
[7] Abramow M, Cogan E: Clinical aspects and pathophysiology of diuretic-induced hyponatremia. Adv Nephrol Necker Hosp 13:1-28, 1984
[8] Chaffman M, Heel RC, Brogden RN, Speight TM, Avery GS. Indapamide. A review of its pharmacodynamic properties and therapeutic efficacy in hypertension. Drugs. 1984;28:189–235
[9] Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, RobertsEA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-45.
[10] Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm 1992;49:2229- 32