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Case Series On Drug Induced Hyponatremia

Dr.Shiby Sara Shaji[1], Dr. Shone Padinjarethil George[1*], Dr. Chris Philip Mathew[2]
[1]Pharm D, [2]Associate Professor,
[1]Nazareth College of Pharmacy, Othera, Thiruvalla, Kerala, India
[2]Department of General Medicine, Believers Church Medical College Hospital, Thiruvalla, Kerala, India

***Corresponding Author:**
Dr. Shone Padinjarethil George
Pharm D, Nazareth College of Pharmacy, Othera, Thiruvalla, Kerala, India

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Abstract

Hyponatremia is an important electrolyte disorder that occurs when the serum sodium levels drop below 135 mmol/L, which might be either due to underlying pathophysiological conditions or drug-induced and is associated with increased morbidity and mortality. This case series focused on drug-induced hyponatremia and showed that geriatric age group and the female gender are more susceptible to develop hyponatremia, especially by antihypertensives. Knowledge regarding the risk factors and adequate monitoring of the serum sodium levels at regular intervals helps to reduce the incidence of drug-induced hyponatremia.

Keywords: Hyponatremia, Serum Sodium, Hypertension, Angiotensin Receptor Blocker, Diuretics, Angiotensin Converting Enzyme Inhibitor

Introduction

Hyponatremia is one of the most prevalent electrolyte imbalances, occurring when serum sodium levels are below 135 mmol/L. It may be caused due to defects in sodium metabolism or sodium transport across the membrane or an abnormality in intracellular sodium concentration.[1] The onset can be either acute or insidious. Usually the patient presents with symptoms of increased intracranial pressure such as headache, nausea, vomiting, altered level of consciousness, seizures, coma in severe cases. In order to provide the patient with right pharmacological therapy, it is crucial to categorise the type of true hyponatremia and to rule out pseudohyponatremia. In this case series we studied drug-induced hyponatremia and the risk factors contributing to the same.

Objective

Analysing drug-induced hyponatremia and the risk factors contributing to the same.

Methodology

In this study conducted at a tertiary care hospital in Kerala, a total of 50 cases diagnosed with drug-induced Hyponatremia were randomly selected and meticulously reviewed. Causality assessment was done using the WHO - UMC Causality Assessment Scale.[2] The risk factors contributing to the incidence of drug-induced hyponatremia were also assessed.

Results & Discussion

Hyponatremia, the most common electrolyte disorder, is characterised by serum sodium concentration <135 mmol//L. Based on serum sodium levels, it can be either mild, moderate or severe. Often it remains asymptomatic and is identified during routine laboratory investigations, but if the onset is acute and severe, then a life -threatening state may develop.[3] Hyponatremia can be either pseudo hyponatremia or true hyponatremia. Pseudo hyponatremia is seen in hyperglycemia, hyperproteinemia, hyperlipidemia. Based on the volume status, true hyponatremia is of 3 types:

Normovolemic Hyponatremia (SIADH, Hypothyroidism), Hypervolemic Hyponatremia (CCF, Cirrhosis) and Hypovolemic Hyponatremia (Vomiting, Diarrhoea, use of Diuretics). Rapid correction in case of chronic hyponatremia may lead to osmotic demyelination and is harmful.[4] Active treatment is required if the patient presents with altered sensorium, drowsiness, seizures, coma.

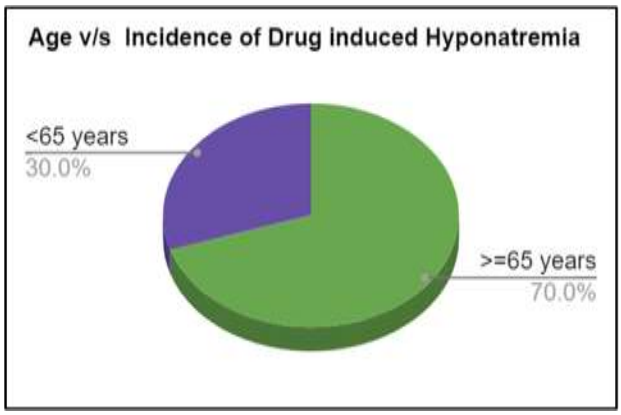
Table 1 - Severity of Hyponatremia based on Serum Sodium Levels.[5]

Severity	Serum Sodium Levels
Mild	130 -135 mmol/L
Moderate	125 -129 mmol/L
Severe	<125 mmol/L

Drugs such as AVP analogs, Diuretics, Antidepressants, Chemotherapeutic drugs are the common culprits in the development of hyponatremia.[4] In our study, we meticulously reviewed patients diagnosed with drug-induced hyponatremia and analysed the risk factors contributing to its development.

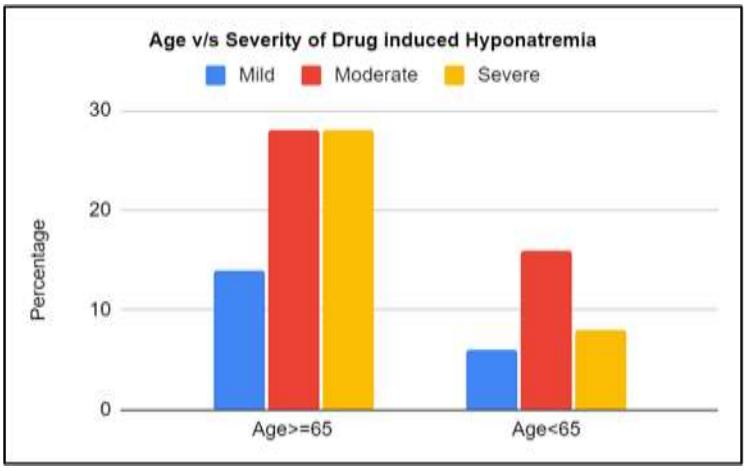
Figure 1 depicts that in our study, the incidence of drug-induced hyponatremia was higher among geriatrics (70%), which is in accordance with various studies substantiating poor prognosis of hyponatremia among elderly subjects. Age is a strong independent risk factor for the development of hyponatremia, which might be either due to impaired water excretory capacity because of age-related reduction in GFR, or due to frequent exposure to medications, and comorbidities may exacerbate the severity of the condition. Decrease in the intrarenal generation of prostaglandins also leads to impaired ability to excrete water in advanced age. SIADH, the most frequent syndrome seen among elderly due to high sensitivity to osmotic stimuli, is another contributing factor to hyponatremia.[6] Severe hyponatremia also developed in those aged above 65 years, as shown in Figure 2.

Figure 1



Volume 6, Issue 6; November-December 2023; Page No 336-340

Figure 2



According to our study, women are more predisposed to develop drug induced hyponatremia, as illustrated in Figure 3. Moderate to severe hyponatremia was also higher among them, as illustrated in Figure 4. They frequently suffer from pathological changes of sodium metabolism and have a higher risk of developing hyponatremia; they are more symptomatic at similar levels of hyponatremia when compared to men, and are consequently diagnosed more often than men.[7]

Figure 3

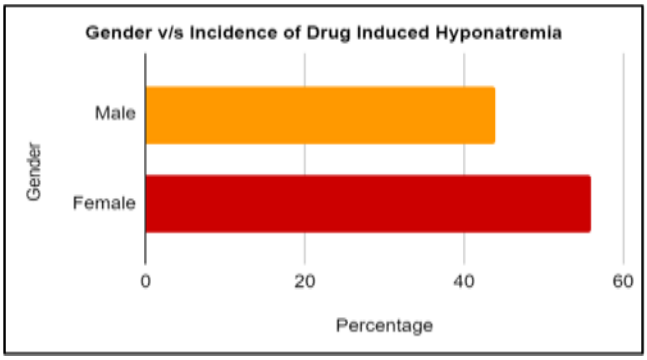
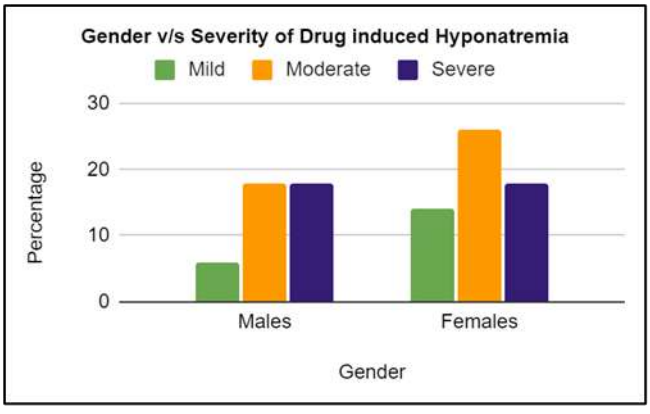


Figure 4



Volume 6, Issue 6; November-December 2023; Page No 336-340

According to our study the drugs responsible for hyponatremia were mainly antihypertensives which contributed to about 84 % of study subjects as depicted in Figure 5. Among them, 42.9% were caused by Angiotensin Receptor Blockers (ARBs), followed by Diuretics (33.3%), a combination of ARBs and Diuretics (19.0 %), and a combination of Calcium Channel Blockers (CCBs), ARBs, and Diuretics (4.8%) as illustrated in Figure 6. Since ARBs inhibits the vasoconstricting mechanism and aldosterone secreting effects of angiotensin II, it leads to reduced renal tubular sodium reabsorption and potassium secretion.[8] In our study, hyponatremia was also caused by antidepressants, anticonvulsants, tyrosine kinase inhibitors, alkylating agents, all of which accounts for 16% of total cases of hyponatremia.

Figure 5

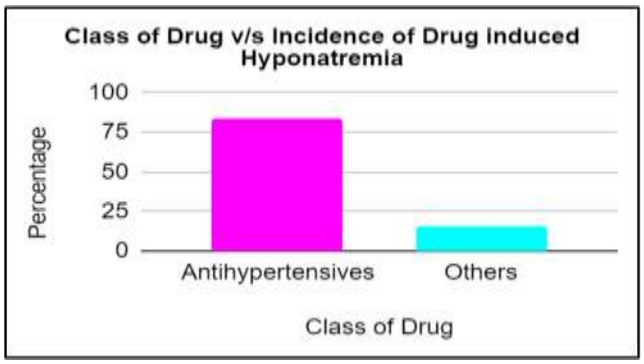
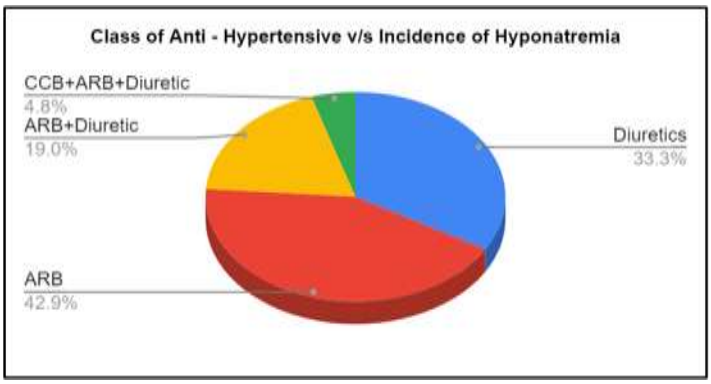
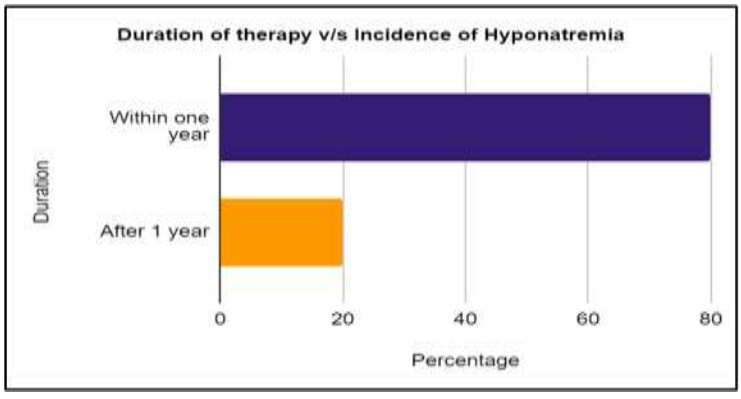


Figure 6



While assessing the duration of therapy and incidence, hyponatremia caused by drugs usually occurs within a few weeks of treatment, especially in those on diuretics. However, it was also observed after years of treatment especially when risk factors were present.[9] This same phenomenon was observed in our study, with 80 % of patients developing hyponatremia within 1 year, as pointed out in Figure 7.

Figure 7



Volume 6, Issue 6; November-December 2023; Page No 336-340

On causality assessment using the WHO-UMC Causality Assessment Scale, probable causal relationship with the prescribed drug was observed.

Hence from our study, it was observed that geriatrics, female patients, those on antihypertensives, especially on ARBs, are more susceptible to develop drug induced hyponatremia. There is an urgent need to improve awareness regarding drug induced hyponatremia and its consequences, especially in those who are at risk of developing the same. Adequate knowledge regarding the risk factors contributing to the development of hyponatremia and monitoring of serum sodium levels at regular intervals helps to reduce the incidence, thereby improving the quality of life of patients.[10]

Conclusion

Hyponatremia is a major electrolyte disorder associated with increased morbidity and mortality that can be caused by both disease conditions as well as prescription drugs. In this case series we analysed drug-induced hyponatremia and point out that the use of antihypertensives in advanced age, and the female gender are significant risk factors in the development of hyponatremia. Further, by using the WHO-UMC Causality Assessment Scale, probable causal relationship with prescribed drugs was observed. This study helps to reiterate that clinicians ought to be vigilant regarding the risk factors of drug-induced hyponatremia, and that monitoring of the serum sodium levels at timely intervals during therapy helps to cut down the incidence of drug-induced hyponatremia.

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Abbreviations

mmol/L- Millimoles Per Litre

WHO - World Health Organization

UMC - Uppsala Monitoring Center

AVP- Arginine Vasopressin

SIADH- Syndrome of Inappropriate Antidiuretic Hormone

CCF - Congestive Cardiac Failure

ARB- Angiotensin Receptor Blockers

CCB - Calcium Channel Blockers

GFR - Glomerular Filtration Rate

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Volume 6, Issue 6; November-December 2023; Page No 336-340