SSRI-Induced Hyponatremia

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Introduction

Hyponatremia is a potentially life-threatening condition and medication causes of hyponatremia should be considered whenever present in a patient's regimen. [1-6]. Having a sound understanding of the most common offending agents is important in order to recognize and adequately manage patients presenting with this electrolyte disturbance. Many psychiatric medications including antidepressants, antipsychotics, and mood stabilizers have the potential to cause hyponatremia [1,2,7-26].

Many psychotropic medication causes of hyponatremia are thought to involve the syndrome of inappropriate antidiuresis (SIAD) [2, 7-14, 26]. Increased total body water and dysregulation of antidiuretic hormone (ADH) levels or activity lead to the syndrome of inappropriate antidiuresis (SIAD) [1]. Here we report a case of SIAD secondary to use of the SSRI citalopram in an elderly female patient.

Methods

The CL Psychiatry team at a Michigan hospital reviewed the patient's records, interviewed the patient, and discussed the case as a group. One of the 4th year medical students on the team was selected to conduct a PubMed literature review of the topic and present to the team and then to the current CMU Psychiatry Residents.

The presentation was formatted into a case report and then later into an abstract and poster.

Purpose

To promote increased knowledge on the topic and better care for patients like ours, we conducted a PubMed review of SIAD and psychotropic causes of hyponatremia and compiled our findings for easier access by clinicians.

Case

Our patient had a history of COPD, hypothyroidism, and hypertension and originally presented to the emergency department from home with AMS secondary to a UTI in July of 2020. She was discharged home with a 6-day course of cephalexin but was also noted to be anxious during her visit and was given lorazepam 1mg BID as needed while in the hospital.

On follow up with her PCP four days later, lorazepam was discontinued, and she was prescribed citalopram 10mg PO daily for anxiety. Two days after starting citalopram, she had acutely worsening AMS and presented to the ER with a sodium of 114 mEq/L.

Her other home medications included: Amlodipine 2.5 mg PO daily, Cephalexin 500 mg PO Q8hrs (7-day course started 5 days prior to presentation in the ER), Levothyroxine 75 mcg PO QAM, Lisinopril 10 mg PO daily, Lorazepam 1 mg BID PRN, Omega-3, Turmeric, Probiotics, Glucosamine-Chondroitin, Guar gum.

The patient was admitted to the medical floor and SIAD (previously called SIADH) secondary to citalopram was diagnosed and managed with fluid restriction and demeclocycline (not FDA-approved for this use). Psychiatry was consulted for medication recommendations to treat her anxiety, but the patient did not complain of any symptoms that would benefit sufficiently to justify antidepressant therapy given her recent adverse reaction and the fact that her anxiety was primarily situational and absent when she was out of the hospital without altered mental status.

SIAD

Diagnostic criteria:

- plasma osmolality <275 mOsm/kg H2O,
- urinary osmolality >100 mOsm/kg H2O,
- urine sodium >30 mEq/L, with normal sodium and water intake, and exclusion of other causes of euvolemic hyponatremia [24].

Risk factors:

- old age, natriuretic polypharmacy,
- body weight <60kg, female sex, and
- low sodium at baseline [2, 14].
- Dose-dependent risk of SIAD with SSRIs [8, 20, 23].

Discussion

ADH retains free water in response to plasma hyperosmolality, hypovolemia, or hypotension [1,27]. In SIAD, free water is retained without these triggers and ECF increases leading to inhibition of aldosterone secretion and elevated ANP which maintains euvolemia via more natriuresis and further renin-angiotensin inhibition, worsening overall hyponatremia [1, 28]. Overall incidence of 0.5%, rises to ~ 12-33% in elderly patients [2, 7-14, 17-24, 26].

Median onset of 13 days after starting an SSRI, can be as soon as 3 days, earliest seen with citalopram is 4 days [11, 20-22]. No described differential risk of SIAD within SSRI class. Relevant non-pharmacologic causes of SIAD include psychogenic polydipsia, neoplasm, and ICP [1, 6, 29, 30].

ICP secondary to our patient's meningioma was discussed but deemed less likely given her good response after holding citalopram. Treatment involved water restriction and diuresis [7].

Medication options include demeclocycline thought to downregulate aquaporin-2 gene transcription (would more likely treat SSRI-induced SIAD) and tolvaptan thought to block ADH V2 receptors [7, 12, 14, 33, 34].

Rapid correction can lead to osmotic demyelination syndrome and central pontine myelinolysis, seizures, parkinsonian movement disorders, or locked-in syndrome [35]. Risk factors for this include serum Na <105 mEq/L [35].

Conclusion

Although generally considered safe medications, SSRIs do have the potential to cause severe side effects with potentially dangerous consequences. The occurrence of such side effects appears to be rare with an overall reported occurrence of about 0.5% of patients treated, but this adverse effect is far more common in elderly patients [2, 7-14, 17-24, 26].

Hyponatremia appears to be a side effect typically seen within the first month of SSRI treatment with a median time of onset of 13 days after initiation [18]. There are reports as early as three days after beginning these medications however, as well as cases well after the first month [11, 22]. Additionally, there does appear to be a dose-dependent effect for this adverse event in some cases [8, 20, 23]. Although generally comparatively safe medications, caution should be taken for the use of SSRIs, especially in elderly patients with risk factors for hyponatremia.

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