Key Words: antidepressants, hyponatraemia, antiduresis, serotonin, elderly age-group

Escitalopram Induced SIADH in an Elderly Female: A Case Study

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ABSTRACT ~ *Hyponatraemia is a well-established and potentially, a life-threatening adverse effect of selective serotonin receptor uptake inhibitors (SSRI). However, its occurrence secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH) with escitalopram, has been reported extremely sporadically. The reporting of such rare, but life-threatening adverse effects of escitalopram assumes immense significance in light of the fact that SSRIs presently form the mainstay of treatment of depressive disorders. Here, we report a case where a 58 year old diabetic lady, when initiated on escitalopram for dysthymia developed severe hyponatraemia within 2 weeks. Further, we discuss other relevant cases that have been reported in the past with an eye on the management of SIADH and hyponatraemia.* Psychopharmacology Bulletin. *2017;47(4):64–67.*

Case History

A 58 year old lady, who was a known case of seronegative spondyloarthropathy, diabetes mellitus and dysthymia, was receiving a combination of oral prednisolone, hydroxychloroquine and methotrexate for her complaints of seronegative spondyloarthropathy. Further, to counter her dysthymia, she had been initiated on oral escitalopram two weeks prior to presenting in our hospital. Her blood sugar levels were being managed using a combination of fast and long acting insulin.

Symptomatology

The patient had to be hospitalized in our hospital with complaints of worsening lower back pain with a mild abdominal pain. Further, on obtaining a detailed history and after a thorough clinical examination, the mild abdominal pain was attributed to severe constipation.

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Diagnosis

The patient's initial work-up revealed her to be severely hyponatraemic with serum sodium level of 107 mmol/L. Her previous sodium levels, prior to initiating escitalopram, was normal (137.6 mmol/L). At this juncture, in view of a possibility of drug induced hyponatraemia, escitalopram was withheld. Further investigations revealed a high urinary sodium level (36 mmol/L), elevated urinary osmolality (291 mmol/kg) and reduced serum osmolarity (235 mmol/kg). The low serum urea (11.0 mg/dL), serum creatinine (0.4 mg/dL) and low uric acid (2.2 mg/dL) added weight to the suspicion that the lady in question had developed SIADH, possibly secondary to escitalopram. Additional laboratory investigations in the form of serum cortisol, thyroid hormones that were carried out to rule out any other causes of SIADH, revealed normal values.

Treatment

The lady was treated using high salt diet, fluid restriction and slow intravenous sodium chloride infusion. The lady's sodium levels prior to discharge was 134 mmol/L.

Discussion

Escitalopram, the pure S-enantiomer of its racemic derivative, i.e., citalopram belongs to the selective serotonin reuptake inhibitors (SSRI) class of anti-depressants. Ever since its introduction, it has rapidly become one of the therapeutic mainstays for the major depressive disorders and a spectrum of anxiety disorders.

Despite escitalopram being a relatively safe SSRI, there have been a few reports implicating it as the offending agent behind life-threatening hyponatraemia.[1–4] Our literature search revealed scant literature with regards to escitalopram induced hyponatraemia.[5] It has been conjectured that SSRIs could possibly increase the level of serotonin in the brain, which in turn via its activity over the 5-HT1 and 2 receptors could possibly increase the ADH secretion leading to hyponatraemia and thus painting a picture that resembles SIADH (Syndrome of inappropriate anti-diuretic hormone secretion).[6]

The median time duration required for the onset of hyponatraemia following SSRI usage has been pegged at 13 days.[7] However, hyponatraemia has been reported as late as 3 months after initiating patients on SSRI.[7] In addition, as evidenced by many previous reports, various patient attributes that may contribute to the possibility of developing hyponatraemia following escitalopram use have emerged

over the years.[3,5] Hence, such patients who are at-risk of developing hyponatraemia, could be monitored for lethargy, insomnia, irritability, confusion and other features indicative of hyponatraemia. If noted, then it should immediately raise a suspicion of SSRI induced hyponatraemia.[2] However, it is important to bear in mind that the absence of risk factors does not preclude the development of hyponatraemia in the patients receiving SSRIs. In light of the evidence provided by the various reports, the argument for conducting routine serum sodium levels prior to and after initiating escitalopram therapy is not bereft of scientific sense, at least during the initial stages. Moreover, before implicating the drug as the inciting factor for SIADH, one should search for clinical signs and symptoms that might give a clue to other causes of SIADH like cerebral and pulmonary tumors and infections, thyrotoxicosis as well.

As evidenced from previous reports, escitalopram induced hyponatraemia is a reversible electrolyte imbalance that gets corrected by withdrawal of the drug and by conservative management involving fluid restriction and oral and intravenous sodium supplementation.[2–4] Aggressive management was undertaken in only one such instance where the serum sodium levels had reduced drastically and the patient became symptomatic.[5] Despite having severe hyponatraemia, our patient did not exhibit the classical signs and symptoms associated with hyponatremia. Further, hyponatraemia combined with the deranged urinary osmolality, sodium levels and renal function tests supported the suspicion of SIADH in our patient.[8] A review of her medications revealed that her hyponatraemia could be drug induced, possibly escitalopram induced. Hence, escitalopram was withheld and she was managed conservatively with fluid restriction and oral as well as slow intravenous sodium supplementation. Aggressive measures were not adopted as she was not displaying any of the classical features of hyponatremia. In addition, correction of hyponatremia had to be carried out slowly exercising extreme caution so as to avoid the risk of developing central pontine myelinolysis due to rapid sodium correction. The Naranjo algorithm, on its application indicated that escitalopram may have 'probably' caused hyponatraemia due to SIADH.[9]

Further, re-initiation of escitalopram in patients who had earlier developed hyponatremia may be discouraged on ethical and medical grounds as substantiated by one case report where, a re-challenge with escitalopram led to recurrent hyponatraemia in an elderly lady with dementia with Lewy bodies.[4]

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