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Antidepressant induced recurrent hyponatremia: A case report

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[1]Hyponatremia is a known adverse effect of antidepressants. A review of the literature was performed in relation to one case treated in our hospital to identify risk factors and possible psychopharmacologic alternatives. A 57-year old woman with HIV and HCV suffered 4 episodes of severe hyponatremia within 5 months of treatment involving the following drugs: thiazide diuretic, venlafaxine, citalopram, olanzapine, haloperidol, enalapril and escitalopram. Risk of hyponatremia is higher in patients treated with antidepressants, especially selective serotonin reuptake inhibitors. Advance age, female gender, thiazidic diuretics, sodium levels in the lower limits and low weight increase the risk. All the SSRIs can produce hyponatremia. In most of the cases, this effect appears in the first month. It is not dose dependent and the patient recovers when treatment is interrupted. Early detection as well as the evaluation of concomitant risk factors in all patients starting antidepressant are important. It seems necessary to control ions periodically and to choose safe drugs.

Key words: Hyponatremia, Antidepressant SSRI, Diuretics, Antipsychotics, Enalapril

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Hiponatremia recurrente inducida por antidepresivos: a propósito de un caso

La hiponatremia es un efecto adverso conocido de los fármacos antidepresivos. A propósito de un caso tratado en nuestro hospital, se realizó revisión bibliográfica para identificar factores de riesgo y alternativas psicofarmacológicas. Mujer de 57 años de edad, VIH, VHC, que ha presentado 4 episodios de hiponatremia severa en 5 meses con los siguientes fármacos implicados: diurético tiazídico, venlafaxina, citalopram, olanzapina, haloperidol, enalapril y escitalopram. El riesgo de hiponatremia es mayor en pacientes tratados con antidepresivos, especialmente Inhibidores Selectivos de la Recaptación de Serotonina. Edad avanzada, sexo femenino, diuréticos tiazídicos, niveles de sodio en límite inferior y bajo peso aumentan el riesgo. Todos los ISRS pueden producir hiponatremia. El efecto aparece, en la mayoría de los casos, en el primer mes, no es dosis-dependiente y se recupera con la interrupción del tratamiento. La detección precoz es importante, así como evaluación de factores de riesgo concomitantes en todos los pacientes que vayan a iniciar tratamiento antidepresivo. Parece necesario controlar periódicamente iones y elegir fármacos seguros.

Palabras clave: Hiponatremia, Antidepresivos, ISRS, Diuréticos, Antipsicóticos, Enalapril

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INTRODUCTION

Hyponatremia is a side effect associated to different psychodrugs such as antipsychotics, mood stabilizers and antidepressants, especially selective serotonin reuptake inhibitors. This adverse effect is mediated by different mechanisms as the direct stimulation of the production of antidiuretic hormone (ADH) by SSRI and atypical antipsychotics, the direct effect on the renal tubular level with increase of reabsorption, sensitivity to the action of ADH and ADH release stimulation by prolonged blockage of the D2 receptors.[1,2]

Since its introduction, cases of hyponatremia due to the use of SSRI have been reported. Most are mild or asymptomatic, but there are also others that entail severe neurological symptoms or are even lethal. All the SSRIs may result in symptoms in equal proportion. However, this is also true of other psychopharmaceuticals such as tricyclic, dual, heterocyclic antidepressants, anti-seizure drugs and antipsychotics. Normally, hyponatremia secondary to SSRI treatment appears within the first weeks after its initiation with a mean appearance on day 13. It is "not dose-dependent" and the sodium levels normalize between 2 and 20 days after the drug is suspended.

The use of antidepressants, especially from the serotonergic group, together with age over 64 years and the presence of chronic conditions is a determining risk factor for hyponatremia, increasing the risk of synergic action of several of these factors.[3]

There are several retrospective and prospective studies, and clinical notes in relation to SSRI associated hyponatremia that determine the existence of risk factors favoring the appearance of hyponatremia secondary to the use of SSRI. These factors are elderly age, female gender, concomitant taking of diuretics, especially thiazidics, low body weight and low sodium plasma levels or levels in the low limit of normality prior to treatment. According to national and international pharmacovigilance committees, 1/3 of the reports of drug induced hyponatremia are severe, with the greatest frequency involving hydrochlorothiazide, carbamazepine, paroxetine, venlafaxine and sertraline.[4-11]

MEDICAL CHARACTERISTICS

A 53-year old woman was admitted due to precipitation within the context of a major depressive episode. She had presented several suicide gestures by venoclysis, drug overdose intake, intake of caustic agents and hanging in the last six months.

Medical backgrounds

Active smoker., Chronic bronchitis,. Stage C3 HIV with TARGA since 1996, geniotype 4 HCV. Several hospital admissions in recent months due to hyponatremia associated to SSRI antidepressants. First admission: 1 week of evolution of hyponatremia with hyperkalemia, euvolemic. Adrenal, renal, thyroid function normal. Vasopressin within range. Pre-treatment sodium 129 mEq/L. Treatment was initiated with delayed release venlafaxine 150 mg/d that was substituted by citalopram 20 mg/d after observing a decrease in sodium levels up to 127 mEq/L on the third day of treatment, in spite of which the decrease continued and sodium on admission was 115 mEq/L. On hospital discharge, treatment was initiated with agomelatine 25 mg/d. Clinical opinion: venlafaxine induced severe hyponatremia.

- Second admission: 4 months later. Hyponatremia (115 mEq/L) euvolemic. Receiving treatment with agomelatine 25mg/d and for the last 20 days amiloride/hydroclorotiazide 5/50 g 1c/d. Previous sodium normal. Symptoms of behavioral alterations with psychomotor agitation and maniform symptoms. Clinical opinion: thiazidic diuretic induced severe hyponatremia. Psychopharmacological treatment on discharge: clorazepate dipotassium 10mg: 3c/d, agomelatine 25 mg/d, olanzapine 5 mg/d.

- Third admission: 10 days later. Moderate hyponatremia (127 mEq/L). Without thiazidic or SSRI treatment. Under treatment with enalapril since last hospital admission. Improvement with hydric restriction. Previous treatment was maintained (clorazepate dipotassium, agomelatine, olanzapine). Clinical opinion: Moderate hyponatremia probably associated to angiotensin-converting enzyme (ACE) inhibitor and olanzapine.

- Psychiatric backgrounds: Alcohol and cannabis dependency in early total remission (6 months). Ex-intravenous drug abuser since 20 years ago. In follow-up by Mental Health with diagnosis of dysthymia and suspicion of cognitive impairment consistent with dementia-AIDS. Three siblings who died due to consumed suicide. In the current admission, under treatment with haloperidol 20 drops/d and clorazepate dipotassium 10 mg/d.

Current disease

Patient who was admitted due to precipitation within the context of persistent suicidal and depressive picture with predominance of low mood, feelings of despair, emptiness, lack of interest and anhedonia, pessimism and difficulty to cope with current adverse circumstances as well as hyporexia and nonspecific insomnia. Important and attention mnesic complaints

Course

An approach to the case was proposed with measures aimed at the prevention of the suicide (close supervision by health care staff, partial mechanical restraint and elimination of potentially harmful objects). In spite of the background of hyponatremia associated to different psychopharmaceuticals and diuretics, it was decided to initiate antidepressant treatment given the high suicidal risk and existing depressive picture. Escitalopram 10 mg/day was prescribed with seriated controls of ions at 48 hours, showing the following course:

- Na on admission: 136 mEq/L.
- Na at 48h of treatment initiation: 121 mEq/L. Suspension of escitalopram, the haloperidol dose was decreased to 10drops/d, hydric restriction, NaCL perfusion.
- Na on 5th day after interruption: improvement of sodium levels to 128 mEq/L. Hydric restriction and oral NaCl were maintained.

Treatment was continued, aimed at normalization of the plasma sodium levels, together with adjustment of risk factors for the development of hyponatremia: reducing haloperidol dose to the minimum effective, proposing pharmacological alternatives for treatment of the depressive picture, increasing baseline levels of sodium, etc.

DISCUSSION

The phenomenon of recurrent hyponatremia induced by the use of antidepressants has been described in the literature by some authors in subjects who were re-exposed to it as well as to different psychopharmaceuticals. Stovall[12] described the case of a 66-year old woman who presented hyponatremia with duloxetine and escitalopram; Arizon[13] that of an 87-year old woman treated with fluvoxamine and paroxetine, Raphael[14] that of a male who received sertraline and fluoxetine and recently, Puras[15] that of an 88-year old male under treatment with sertraline and thiazidics and then citalopram.

In our case, multiple factors converged for the presentation of the episodes of recurrent hyponatremia: use of antidepressants with risk profile (venlafaxine, citalopram, escitalopram), thiazidic diuretics, ACEIs, antipsychotics (olanzapine, haloperidol), low weight, female gender, previous sodium levels in the low limit (136 mEq/L) and concomitant multiple conditions (HIV, HCV, chronic bronchitis). It stands out that although the symptoms were observed in the first episodes between 13 and 20 days after initiation of the drugs, in the latter, it occurred at 48 hours, largely due to early detection by control of ions. On the management level, the case was a therapeutic challenge due to the need to initiate antidepressant treatment in a picture with a moderate depressive picture but with background of episodes of moderate and severe hyponatremia related to the use of psychopharmaceutics in the previous months. Although the blood sodium levels were seriated daily after the initiation of the drug, the choice of escitalopram is not postulated as the safest and best one. Our case also seems outstanding, compared to the rest of the cases of recurrent hyponatremia described in the literature, due to the lower duration of the inter-episode periods, with a time interval of 4 to 120 days, while in the other cases, they could be up to 20 months. We attribute this to the presence of multiple risk factors and greater biological vulnerability in our patient.

Given the wide use of SSRI and other psychopharmaceutics in the population, it is important to consider hyponatremia as a preventable and reversible adverse effect and to include the detection of subjects at high risk in order to establish safer drugs as well as early detection measures in the usual clinical practice.

In this sense, trazodone, bupropion, agomelatine and reboxetine are profiled as safe therapeutic options, given the limited notifications reported or in those which the concomitant use of other drugs could interfere.

CONFLICT OF INTERESTS

The authors deny the existence of conflict of interests.

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