

its predictive capacity in prospective studies such as those currently underway in our research group.

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Safety in the use of antidepressants: Vortioxetine-induce hyponatremia in a case report[☆]

Seguridad en el uso de antidepresivos: hiponatremia inducida con vortioxetina a propósito de un caso

Dear Editor,

Hyponatremia, defined as a level of sodium in the serum below 135 mmol/l, is in practice the most common hydro-electric disorder. It is a known side effect of antidepressants, antipsychotics and mood stabilisers.¹ The mechanism may be mediated by stimulation of the production of antidiuretic hormone by serotonergic actions or dopaminergic blocking, which may be aggravated by polydipsia or xerostomia. It may manifest with general symptoms (nausea, fatigue, cramps and headache) or severe neuropsychiatric symptoms of cerebral oedema (confusion, agitation, altered gait, lethargy, convulsions and coma). Even mild forms are associated with increased morbimortality.²

The frequency with which hyponatremia is induced by antidepressants varies from 0.06% to 70%, and it has the



following risk factors: a history of hyponatremia, advanced age, female sex, low weight, cirrhosis, heart or kidney failure and the use of diuretics, ACE inhibitors or laxatives. The risk seems to be greater with ISRS and venlafaxine than it is with mirtazapine and some tricyclics.¹ The risk cannot be established in other groups due to the lack of epidemiological data. This is striking, given that monitoring is extremely simple (biochemistry with ions) and that it is found in the recommendations of guides and agreements on monitoring the physical health of patients with depression.³ However, the outstanding finding is that it is hard for the recommendations contained in guides to be put into practice in the absence of resources and strategies aimed at implementing them.⁴

In connection with this risk, in our hospital we witnessed a fatal case of hyponatremia associated with the use of vortioxetine. A 72-year-old woman was evaluated in March 2016 in the Mental Health department due to low mood, loss of interest, anhedonia, tiredness, lack of concentration and reduced activity, with a history of recurring depressive disorder from the age of 55 years old and several previous hospitalisations due to severe hyponatremia associated with several psychopharmaceuticals (fluoxetine, amitriptyline, mirtazapine and asenapine) without SIADH being proven. The current treatment was maprotiline 75 mg/d, with which she had not suffered any severe new hyponatremia in the past year. In the current episode vortioxetine was proposed as the treatment, in a crossed change strategy, with a 5 mg dose of vortioxetine and a reduced dose of maprotiline (37.5 mg/d) and, after 4 weeks, 10 mg/d vortioxetine had to be maintained. Nevertheless, 26 days afterwards she was admitted to the ICU from the Emergency Department after suffering a convulsion. In spite of recovering sodium values

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to 131 mmol/l, after 13 days of admission she presented a fall in the level of consciousness (Glasgow Coma Scale = 3), and a thromboembolic cerebrovascular accident was suggested as a complication of a flutter suffered in the first days. In spite of resuscitation manoeuvres, and after suffering asystole and dying breathing, the patient died within a few minutes.

This case underlines the importance of the prevention, detection and treatment of the side effects of antidepressants. In spite of the fact that treatment with antidepressants may be associated with a lower risk of hospital admission in elderly patients,⁵ unsuitable monitoring may increase the risk of complications and morbimortality. More specifically, hyponatremia may arise with any antidepressant, independently of the group it belongs to.¹ Vortioxetine, a new multimodal antidepressant, is considered to be a safe treatment for depression, including patients above the age of 65 years old, although the associated frequency of induced hyponatremia is unknown due to its recent commercialisation. Only one case of hyponatremia at below 110 mmol/l⁶ has been reported in a premarketing study, and this may be due to the serotonergic actions of vortioxetine. While the technical data sheet of the FDA includes this effect,⁷ the one by the Spanish agency (AEMPS) only shows this as a class effect, stating that "with the use of antidepressants with a serotonergic effect [...] rare cases of hyponatremia have been notified."⁸ The accessibility of all of the data obtained in trials as well as recently has been remarked on in this journal,⁹ as it would favour not only transparency but also scientific knowledge and clinical safety. Finally, in this patient, who was at higher risk due to her age and history of hyponatremia, closer monitoring of serum electrolytes could have prevented or detected the hyponatremia, which usually arises quickly in the first weeks of treatment.¹⁰

Due to all of the above considerations, the authors believe that the safe monitoring of patients treated with antidepressants requires, on the one hand, the availability of complete and reliable information on molecule study data, and on the other hand, knowledge and application of the current clinical guides. Most particularly in patients with hyponatremia risk factors careful measurement of serum electrolytes may be recommendable in the first weeks after commencing to take a new antidepressant.

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Conflict of interests

José María Pelayo-Terán received payment for a conference during the year 2016 from the Lundbeck company (which

commercialises vortioxetine in Spain). The authors have no conflict of interests to declare in connection with the data published in this paper.

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