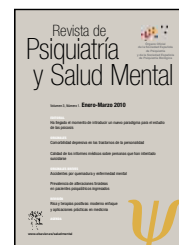


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## SCIENTIFIC LETTER

### Venlafaxine and inappropriate antidiuretic hormone excretion

### Venlafaxina y secreción inadecuada de hormona antidiurética

*To the Editor:*

Venlafaxine is a potent serotonin-norepinephrine reuptake inhibitor and a weak dopamine reuptake inhibitor. Its primary indication is the prevention and treatment of depressive disorders.<sup>1</sup>

The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is defined as the sustained release of arginine vasopressin (ADH) in the absence of the usual stimuli, especially hyperosmolality and hypovolemia. To arrive at this diagnosis by exclusion, conditions that feature effectual volume reduction (cardiac insufficiency, cirrhosis with ascites, hypovolemia, etc.) must first be ruled out, and normal renal, suprarenal, and thyroid function must be demonstrated.<sup>2</sup> It is characterized by hyponatremia, plasma hypoosmolality, inappropriately elevated urine osmolality, and natriuresis usually above 40 mmol/L. Common causes are tumours—small cell cancers of the lung, in particular—and drugs,<sup>3</sup> among which the serotonin reuptake inhibitors are prominent. The mechanism by which they produce this condition varies.<sup>4,5</sup> A direct effect on renal tubular cells, the role of serotonin in vasopressin synthesis, increased ADH production by the hypothalamus, and an increased effect of vasopressin all have been described.

We present the case of a woman who developed severe hyponatremia while under treatment with venlafaxine.

70-year-old woman with history of arterial hypertension and depressive syndrome. She had been under treatment for the previous 2 months with venlafaxine 75 mg/day and enalapril 20 mg/day. She presented with symptoms of epigastric discomfort, nausea, somnolence, and dizziness of several days' duration.

Physical examination revealed only obesity (Body Mass Index 32 kg/m<sup>2</sup>) and bradypsychia. There was no edema or signs of dehydration.

Basic laboratory parameters were all normal, except for plasma sodium (Na) of 111 mmol/L, plasma osmolality of 231 mOsm/kg, urine Na of 38 mmol/L, and urine osmolality of 330 mOsm/kg (normal value 300-900 mOsm/kg). Baseline cortisol and thyrotropin were normal.

In view of the initial suspicion of a venlafaxine-induced SIADH, the drug was discontinued and fluid restriction with normal saline IV was ordered. The patient progressed favourably, and when discharged 5 days later, she was asymptomatic with a plasma Na of 136 mmol/L. Thirty days later, under treatment with enalapril, her plasma Na remained normal.

Among the adverse effects reported on the technical data sheet for venlafaxine is the rare chance (>0.1% and <1% of hyponatremia.<sup>1</sup> In a prospective study, Roxanas et al<sup>6</sup> found that 10 out of 58 patients over 65 years of age (17.2%) developed hyponatremia within a few days of starting venlafaxine therapy. As was seen in our case, there is a higher incidence of this syndrome in elderly patients and in females. Likewise, concomitant diuretic therapy presents an added risk factor.<sup>7</sup> It is estimated that hyponatremia appears at about 1-2 weeks, although cases in 1 to 360 days have been described.<sup>8</sup>

Our patient was taking enalapril concurrently which, although very rarely, has been noted to be involved in this adverse reaction.<sup>9</sup> However, 1 month from discharge (with venlafaxine suspended and taking enalapril), the patient's plasma sodium was normal.

In conclusion, we feel it is important to stress that SIADH associated with serotonergic antidepressants is common and potentially serious.<sup>10</sup> Because the symptoms of this condition lack specificity, they may be confusing and cause the physician to interpret them as further symptoms of the depression. Therefore, we believe that the patient's neurological status and sodium levels should be closely monitored, especially in the first 15-30 days of treatment—most especially if the patient is a female who is elderly or has other risk factors, such as the concomitant use of diuretics, low weight, and hypothyroidism.

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