

## Venlafaxine and reversible blepharodema

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The newer antidepressant venlafaxine is known to cause dilutional hyponatraemia, but to our knowledge no reports on localized oedemas in the absence of electrolyte disturbances are available. We present a case in which venlafaxine caused reversible blepharodema in an otherwise physically healthy patient.

Ms. M., a 25-yr-old women, suffered from schizo-affective disorder since being 23 years old. Upon administration of quetiapine, she completely recovered but relapsed twice due to medical non-compliance, resulting in the third hospitalization. Again, psychotic symptoms cleared upon prescription of 600 mg quetiapine; further, 45 mg mirtazapine was given. Quetiapine remained at a stable dose for 10 wk, mirtazapine for 2 wk; no side-effects were reported by the patient or observed by her physicians and no other medication was used. As she persistently complained about depressed mood, loss of motivation and drive, we additionally administered 75 mg of retarded venlafaxine in the morning. The next day, marked bilateral and symmetric blepharodema could be noted which did not ache on palpation, but caused discomfort on eye movements, generally worrying Ms. M. She had no relevant past medical history besides her psychiatric disorder, especially no occurrence of allergic sensitivity, and had never experienced localized oedema. No other oedemas were present, nor were other medical symptoms. Serum electrolytes were within the normal range. Believing that venlafaxine caused lid oedema, we discontinued venlafaxine after the second day; within 24 h, the symptom completely vanished.

Venlafaxine is known to produce hyponatraemia and the syndrome of inappropriate ADH secretion (SIADH; Schwartz–Bartter syndrome) as undesirable effects (Gupta et al., 1997; Masood et al., 1998; Ranieri et al., 1997; Wyeth-Pharma, 2000). This is probably due to an increase in vasopressin serum concentrations as a result of serotonin re-uptake inhibition (Masood et al., 1998) similar to selective serotonin re-uptake inhibitors (SSRIs) like fluvoxamine or sertraline, in which hyponatraemia is found in up to 0.5% in elderly

people (Kirby and Ames, 2001; Wilkinson et al., 1999). However, we are not aware of any report on localized oedemas associated either with venlafaxine or SSRIs. The underlying pathophysiological mechanism remains elusive and might include local electrolyte shifting, vasopressin-mediated fluid retention or (pseudo-) allergic reactions; nevertheless, no symptoms arguing for the latter were present in our patient. Both quetiapine and mirtazapine can cause facial oedema; however, our patient was on a stable dose of those drugs for several weeks and did not report any adverse effects. The development of abortive Serotonin syndrome, caused by the use of two serotonergic agents (mirtazapine and venlafaxine), represents another possible pathomechanism, especially as there are some, although not many, reports on Serotonin syndrome as an adverse effect of mirtazapine or venlafaxine treatment. However, the typical symptomatology of Serotonin syndrome involves fever, neuromuscular symptoms, and altered mental status, none of which were present in our patient. Furthermore, oedema is not a frequent symptom of Serotonin syndrome, so that we regard this diagnosis as unlikely. Nevertheless we cannot rule out the possibility that quetiapine or mirtazapine contributed to lid oedema in our case, though the close temporal coincidence between venlafaxine administration and oedema argues for a causal role of venlafaxine. In conclusion, as venlafaxine is currently widely applied, physicians should be aware of this harmless and reversible, but distressing, side-effect of this compound.

### References

- Gupta AK, Saravay SM (1997). Venlafaxine-induced hyponatremia. *Journal of Clinical Psychopharmacology* 17, 223–225.
- Kirby D, Ames D (2001). Hyponatraemia and selective serotonin re-uptake inhibitors in elderly patients. *International Journal of Geriatric Psychiatry* 16, 484–493.
- Masood GR, Karki SD, Patterson WR (1998). Hyponatremia with venlafaxine. *Annals of Pharmacotherapy* 32, 49–51.
- Ranieri P, Franzoni S, Rozzini R, Trabucchi M (1997). Venlafaxine-induced reset osmostat syndrome: case of a 79-year-old depressed woman. *Journal of Geriatric Psychiatry and Neurology* 10, 75–78.

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Wilkinson TJ, Begg EJ, Winter AC, Sainsbury R (1999).

Incidence and risk factors for hyponatraemia following treatment with fluoxetine or paroxetine in elderly people. *British Journal of Clinical Pharmacology* 47, 211–217.

Wyeth-Pharma GmbH, Münster, Germany (November 2000).

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