appeared when the diuretic was withheld. The treatment strategy was then changed to taper the dosage of amusulpride from 800 to 400 mg per day and to stop using the diuretic. Within one week with this strategy, the bilateral pedal edema resolved entirely. The patient's psychiatric condition remained stable on this dosage of amisulpride.

In our case, treatment of amisulpride alone or an adverse interaction between amisulpride and lorazepam may be responsible for the patient's bilateral pedal edema. The latter is less likely because amisulpride and lorazepam have not been reported to have significant pharmacokinetic interaction. In addition, amisulpride appeared to be associated with the patient's pedal edema in a dose-related fashion since the pedal edema disappeared after prescribing a lower dosage of amisulpride. The finding of elevated IgE with normal values of C3 and C4 was similar to a previous report regarding risperidone-associated allergic reaction [4]. In that report, the authors suggested that the allergic reaction in their case might be type I or type IV allergic reaction since IgE level was elevated and C3/C4 levels were within normal limits. It suggests that the pathogenesis of pedal edema in both cases might be caused by a similar mechanism. However, the pathophysiological mechanism of amisulpride-associated pedal edema is still not clear as of edema associated with other new antipsychotic agents. It is subject to further clinical investigation and research concerning this issue.

References

[1] Christensen RC. Olanzapine-associated bilateral pedal edema. J Clin Psychiatry 2003;84(8):972.

[2] Coulouvrat C, Dondey-Nouvel L. Safety of amisulpride (Solian): a review of 11 clinical studies. Int Clin Psychopharmacol 1999;14(4): 209–18.

[3] Ravasia S. Risperidone-induced edema. Can J Psychiatry 2001;46(5): 453–4.

[4] Terao T, Kojima H, Eto A. Risperidone and allergic reactions. J Clin Psychiatry 1998;59(2):82–3.

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Received 8 March 2004; accepted 12 May 2004

Available online 08 October 2004

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doi:10.1016/j.eurpsy.2004.07.003

Antidepressant-associated mania with escitalopram

1. To the editor

Escitalopram, the single isomer of citalopram recently commercially available in Europe, is a potent serotonin transporter (SERT) antagonist and possesses the greatest SERT selectivity [4]. Although the treatment with the SSRI citalopram has a reduced emergence of antidepressant associated mania (AAM) in patients with unipolar depression we describe the case of AAM in a patient undergoing escitalopram therapy [1,2].

Mr. H. a 33-year-old Caucasian male inpatient, heavy smoker (>20 cigarettes/d), with a body mass index of 24.36, was diagnosed for the first time in 1992 as suffering from unipolar depressive disorder in comorbidity with a narcissistic personality disorder according to ICD-10. He was rehospitalized for the 3rd time after experiencing his 5th severe depressive episode manifested by sleep disturbances, depressed mood, decreased interest and by suicidal ideations. Based on previous experiences of treatment resistance to citalopram, the new compound escitalopram was started tapering the dosage from 20 to 40 mg/d reaching a steady state plasma concentration of 60 ng/ml (corresponding to 40–80 mg/d of citalopram) [5]. For sleep induction lorazepam 2 mg was given. Ten days following this treatment regimen within 2 days the patient suddenly developed severe insomnia, racing thoughts, talkativeness, elevated mood, psychomotor restlessness, aggressive and uncontrolled behaviour with sexual desinhibition toward other inpatients. Carbamazepine at 600 mg/d combined with risperidone 2 mg/d was prescribed. Escitalopram was tapered off within 10 days and just 15 days after its discontinuation the manic episode resolved. It is noteworthy that in a previous treatment trial with ECT during his 4th depressive episode (diagnosed as therapy refractory) the patient manifested a delirium with euphoria accompanied by confusion and memory disturbances and thus discernable from a switch to hypomania [3]. This presumed delirious state subsided after discontinuation ECT and prescribing the mood stabilizer valproic acid the patient recovered as described in the index episode.

This case suggests that (1) escitalopram has the potency to induce a AAM in patients affected by unipolar depression rather than citalopram, (2) the previously observed delirium with euphoria retrospectively was an ECT emergent mania indicating the difficulty to distinguish between these two conditions and (3) the prescription of escitalopram may require particular monitoring in patients suffering from bipolar disorders since these patients are most likely to exhibit hypomanic or manic reactions.

References

[1] Barak Y, Kimhi R, Weizman R. Is electivity for serotonin uptake associated with a reduced emergence of manic episodes in depressed patients? Int Clin Psychopharmacol 2000;15(1):53–6.

[2] Bryois C, Ferrero F. Mania induced by citalopram. Arch Gen Psychiatry 1994;51(8):664–5.
[3] Devanand DP, Sackeim HA, Decina P, Prudic J. The development of mania and organic euphoria during ECT. J Clin Psychiatry 1988; 49(2):69–71.
[4] Owens MJ, Knight DL, Nemeroff CB. Second-generation SSRIs: human monoamine transporter binding profile of escitalopram and R-fluoxetine. Biol Psychiatry 2001;50(5):345–50.
[5] Rochat B, Amey M, Baumann P. Analysis of enantiomers of citalopram and its demethylated metabolites in plasma of depressive patients using chiral reverse-phase liquid chromatography. Ther Drug Monit 1995;17(3):273–9.

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Received 17 May 2004; accepted 7 June 2004

Available online 08 October 2004

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doi:10.1016/j.eurpsy.2004.06.032

Serotonin syndrome due to association of venlafaxine, maprotiline and reboxetine

Venlafaxine is a powerful antidepressant from the age of selective serotonin reuptake post-inhibitors, with a dual serotonergic (5HT) and noradrenergic (NA) action. It has been associated to serotonin syndrome (SS) in some isolated cases, when introduced immediately after abrupt discontinuation of fenelzine [2] or fluoxetine [1] or even when administered alone at low doses [3]. However, we did not know the association of SS with maprotiline or reboxetine when administered separately or combined with venlafaxine. We next present a case of this triple combination with a resultant SS.

1. Case

A 50-year-old man, with antecedents of hepatopathy and alcohol dependence. He was receiving ambulatory treatment with venlafaxine 300 mg/d, ludiomil 150 mg/d, reboxetine 8 mg/d, vitamin B complex and intramuscular *S*-adenosilmetionine. He was admitted in our Psychiatry Unit after having gone to the hospital emergency service with a clinic of negativism and perplexity, which was evaluated as a somatic syndrome, a complication of the depressive disorder for which he had been receiving treatment, of several days of progressive evolution. The psychopathological exploration revealed a confusion state, semi perplexity, oppositionist negativism, and semi stuporous mutism. In the physical exploration, there was non-parkinsonic generalized rigidity, alternating with psychomotor agitation, tremor in superior extremities, profuse diaphoresis, hyperreflexia with very elevated symmetrical osteotendinous reflexes, with flexor cutaneous. The blood pressure oscillated between 140/105 and 125/80 mmHg. The axilar temperature was 37.4 °C. Cardiac and respiratory frequency with light alterations. Analysis: leukocytosis of 16.900 with neutrophilia (70%), CK = 964 U/l, and thyroid hormones with TSH = 4.58 μUl/ml and T4L = 1.22 ng/dl, with no more interesting findings. Negative determination of drug abuse in urine. Negative serologies. Thorax X-ray: elevation of right diaphragm; ECG and cranial magnetic resonance with no findings. As he manifested serotonergic clinic, all the previous psychopharmacological treatment was retired, introducing endovenous fluid therapy and diazepam in slow perfusion. The syndrome resolved within the following days, with a complete recovery and no sequels.

2. Our comment

An antidepressant therapeutic strategy with a clear serotonergic and noradrenergic enhancement was chosen. Venlafaxine is a relatively weak inhibitor of CYP2D6 isoenzime, but reboxetine inhibits it more, so there is also pharmacokinetic interaction. From the pharmacodynamic perspective, the 5HT neuron postsynaptic action through somatodendritic alpha 1 receptors is excitatory and makes NA act as an accelerator that stimulates 5HT liberation. Enhancing venlafaxine also inhibits dopamine reuptake, contributing to the confussional syndrome presented by the patient.

Despite its importance, SS is not properly taken into account many times and not recognizing it on time can potentially be very serious.

References

[1] Bhatara VS, Magnus RD, Paul KL, Preskorn SH. Serotonin syndrome induced by venlafaxine and fluoxetine: a case study in polypharmacy and potential pharmacodynamic and pharmacokinetic mechanisms. Ann Pharmacother 1998;32:432–6.
[2] Diamond S, Pepper BJ, Diamond ML, Freitag FG, Urban GJ, Erdemoglu AK. Serotonin syndrome induced by transitioning from phenelzine to venlafaxine: four patient reports. Neurology 1998;5: 274–6.