

Vortioxetine-induced nausea and its treatment: a case report

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Vortioxetine is a multimodal antidepressant that binds with high affinity the serotonin transporter (SERT) > (serotonin receptor) 5-HT₃ > 5-HT_{1A} > 5-HT₇ > 5-HT_{1B} > 5-HT_{1D}. It acts by inhibiting the SERT, with antagonism activity on the 5-HT_{1D}, 5-HT₇ and 5-HT₃ receptors, partial agonism activity on the 5-HT_{1B} receptor, agonism activity at 5HT_{1A} receptor¹. Vortioxetine is a compound approved by the FDA for major depressive disorder. Its efficacy and tolerability are widely proven². Regarding tolerability, both in short and long-term studies, nausea was the most common treatment emergent adverse event (TEAE) and the primary TEAE that caused discontinuation after vortioxetine treatment²⁻⁴. Nausea is one of the most frequently reported adverse effects after SSRI and SNRI treatment. This can be attributed to their action on serotonin levels and on receptor 5-HT₃⁵. Nausea management includes: splitting daily dosage, taking medication after a meal, using drugs like 5-HT₂ antagonists, proton pump inhibitors, promethazine, prochlorperazine, or ondansetron⁶. It is well established how the antidepressant tolerability influences quality of life and adherence to pharmacological treatment⁷. In this study we describe a case of nausea induced by vortioxetine along with its following treatment in a 32-year-old Italian patient with a diagnosis of bipolar disorder type 2, most recent depressive episode. At the time of our evaluation the patient was treated with lurasidone 37 mg/day and lithium carbonate 600 mg/day. In the past, trials with SSRIs and SNRIs have been conducted with improvement of depressive symptoms but the onset of sexual dysfunction led to drug discontinuation. A trial with bupropion was reported to have induced the onset of anxious symptoms. A trial was then started with vortioxetine 10 mg, increased to 20 mg after 8 days, then nausea occurred. It was decided to introduce mirtazapine 15 mg in the evening. After 2 days of mirtazapine augmentation the patient reported improvement in the nausea that was maintained at follow up; in addition, 2 weeks later an improvement in mood, anxiety, sleep regularity was observed, as well as the absence of sexual dysfunctions. In our case report we used mirtazapine in augmentation to vortioxetine following a pharmacodynamic and clinical reasoning. Mirtazapine, thanks to its 5-HT₃ antagonism, has antiemetic properties already recognized in the literature⁸. Although the same 5-HT₃ antagonism is universally accepted for vortioxetine as well, a recent study has shown a different

behavior of vortioxetine on 5-HT₃ receptors than that hypothesized so far: it can have, in fact, a significative agonist activity. Quoting: “[...] the mechanism of vortioxetine differs from classical 5-HT_{3A} orthosteric ligands with inhibitory activity [...] vortioxetine binding induces a brief agonistic response followed by a rapid transition into a desensitized state from which vortioxetine has an extremely slow unbinding rate”⁹. Our case report suggests the possible role of mirtazapine against antidepressant-induced nausea. Further studies are needed to investigate how these data could be useful to explain and manipulate the clinical effects in terms of efficacy and tolerability.

Conflict of interests

The authors declare no conflict of interest.

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