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Title: Nausea in an antidepressant with 5HT-3 Antagonism

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Introduction: About 17.3 million adults in the US have suffered from a major depressive episode in 2017 (1). The main stays to treat depression are with SSRIs and SNRIs which are used to increase the amount of serotonin within the synaptic cleft. GI disturbances are commonly seen in patients on SSRIs and according to a study: 17% to 26% of patients had experienced nausea or stomach upset while on SSRIs (8). Nausea and vomiting has been known to cause treatment discontinuation of SSRIs (2). The highest rate of GI side effects has been associated with the SSRI fluvoxamine, however, newer antidepressants such as Vortioxetine have also been frequently reported with GI side effects like nausea (2). Most side effects of SSRIs occur due to the extensive number of serotonin receptors in the body, especially in the gut. Typically, many side effects of SSRIs resolve within a few days to weeks.

Case Presentation: Patient is a 44-year-old Caucasian female with a history of hypertension, obesity, and migraines. Psychiatric history includes depression which was diagnosed when she was in college. Her symptoms of depression include apathy, hypersomnia, feelings of guilt, self-isolation when depressed and endorses passive suicidal ideation without plan. She has tried multiple different anti-depressants, but mostly stayed on Escitalopram (Lexapro) and Citalopram (Celexa) for the past 20-25 years due to fewer side effects compared to other medications. A few months ago, she was switched to the newer anti-depressant Vortioxetine (Trintellix)10mg. She noted decreased depressive symptoms with the medication, however she had severe nausea and vomiting for which she had to start taking Ondansetron (Zofran). Afterwards, she noted no problems and felt that her mood was amazing with the new regimen. Five months after starting Vortioxetine, she had to be hospitalized for some surgical complications and during her hospital stay, she was given Vortioxetine without Ondansetron and it resulted in her feeling nauseous again. After receiving Ondansetron, the nausea resolved.

Discussion: The mechanism of action of Vortioxetine includes serotonin transporter (SERT) blockade, agonism of 5HT-1A and 5HT-1B receptors, and antagonism of 5HT-1D, 5HT-7 and 5HT-3 receptors all of which increase the amount of serotonin within the synaptic cleft. 5-HT3 antagonists like Ondansetron are known to be potent anti-emetics. However, blockade of 5-HT3 receptors on interneurons in the brain can increase serotonin, dopamine, norepinephrine, acetylcholine, and histamine (5). Vortioxetine is known to cause downstream effects on these neurotransmitters, as well as glutamate and GABA. 5-HT3 antagonists decrease afferent visceral and chemoreceptor trigger zone stimulation of the medullary vomiting center by decreasing the action of serotonin (6). Other known treatments for nausea include antihistamines, anticholinergics, and dopamine antagonists (6). Nausea from Vortioxetine could be due to its effect on interneurons in the brain or from downstream changes in other neurotransmitters associated with nausea and vomiting. These mechanisms may overshadow any hypothetical anti-nausea effect from antagonism of 5HT-3.

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