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18-Year-old who attempted suicide by ingesting 300 mg of vortioxetine: A case report

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1. Introduction

Vortioxetine is a novel antidepressant and atypical antipsychotic that does not fit in to the established classes of Selective Serotonin Release Inhibitors (SSRIs), tricyclic antidepressants, nor monoamine oxidase inhibition. It belongs to the "N06AX Other, Antidepressants" class (WHOCC - ATC/DDD Index. 2021). Vortioxetine was approved by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) in 2013 for treatment of Major Depressive Disorder(MDD) (DB09068.pdf 2021) (Anonymous 2018). The recommended initial dose is 10 mg daily and can be increased to 20 mg per day according to tolerability (DB09068.pdf 2021). Generally, vortioxetine is considered a safe drug with most common attributed side effects including nausea, constipation dizziness and vomiting, it also causes no major changes in laboratory values, weight, electrocardiogram (ECG), or vital signs parameters (Boulenger et al., 2014).

Data concerning toxicity from vortioxetine is scarce in the literature. In premarketing clinical trials, overdose ranging from 40 mg to 75 mg showed an increased association with nausea, dizziness, diarrhea, abdominal discomfort, generalized pruritus, somnolence, and flushing (PubChem 2021). Furthermore, the latter has no antidote (DB09068.pdf 2021). To date, there is only one case report on its toxicity (Mazza et al., 2018). We will be reporting a case by which an 18-year-old patient diagnosed with MDD attempted suicide by ingesting 300 mg of vortioxetine.

2. Case presentation

The patient was an adolescent female, with a history of cholecystectomy, iron deficiency on iron supplementation, and MDD on vortioxetine 15 mg daily since 2019. Patient hasn't been compliant to her medication until COVID 19 lockdown in Lebanon that occurred in January 2021 where she was having worsening in depression symptoms and thus started taking vortioxetine regularly. She hadn't sought medical attention until she arrived at our Emergency Department (ED) for vomiting, abdominal pain, and drowsiness after taking 30 tablets of vortioxetine10 mg (total of 300 mg) 3 h prior to presentation in a suicidal attempt as reported by her mother. In the ED, she was hemodynamically stable (Heart rate 66 beat/min, blood pressure 93/54, Respiratory rate 21, Oxygen saturation 97% on room air) and had Glasgow Coma Score of 15. On physical exam, she was drowsy, responded briskly to voice stimulation, coherent and was able to maintain conversation and follow commands. She had no focal neurologic deficit with cranial nerves being intact and had no signs or symptoms of serotonin syndrome. All other physical exam showed no abnormal findings. Nasogastric tube was inserted, charcoal 50 gs given once, and since vortioxetine is a new drug with unknown toxicity profile and unclear pharmacokinetics with toxicity, the ED team elected to do gastric lavage. She was also given esomeprazole 40 mg intravenously (IV) once, metoclopramide 10 mg IV once, and ondansetron 8 mg IV once. Corrected QT on ECG was 431 milliseconds, and all labs including complete blood count and differential,

Abbreviations: FDA, Food and Drug Administration; MDD, Major Depressive Disorder; ECG, Electrocardiogram; ED, Emergency Department; EMA, European Medicines Agency; IV, Intravenous.

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Table 1
Labs upon admission, 12 h later, and 24 h later.

CBC & DIFFERENTIAL (Blood)	Ref Range	Units	Upon Admission	12 hrs later	24 hrs later
CBC & DIFFERENTIAL			OK		
CORRECTED WBC	4–10	$x10^3/\mu L$	5.26		
RBC	4.2 - 5.4	x10/μL	4.21		
HGB	12–16	g/dL	14.1		
HCT	34–47	%	39.3		
PLT	150 - 400	$x10^3/\mu L$	194		
%NEUT	40 - 74	%	60.6		
%LYMPH	19 - 48	%	25.2		
%MONO	3.4 - 9	%	10.2		
%EOS	0 - 7	%	1.4		
%BASO	0 - 1.5	%	0.6		
%LUC	0 - 4	%	2.0		
Chemistry	**Ref Range**	**Units**			
SODIUM	136–145	mEq/L	140	138	141
POTASSIUM	3.5 - 5.1	mEq/L	4.4	4.0	4.4
CHLORIDE	98 - 107	mEq/L	106	107	108
CO2	22 - 29	mEq/L	23	21	24
UREA	< 50	mg/dL	16	11	
CREATININE	0.51 - 0.95	mg/dL	0.71	0.66	
GGT	< 40	U/L	15		
ALKALINE PHOSPHATASE	35–105	U/L	58		
SGPT	< 34	U/L	13		
SGOT	< 33	U/L	16		
CPK	26 –140	U/L	63		
DIRECT BILIRUBIN	0 - 0.3	mg/dL	0.3		
INDIRECT BILIRUBIN	0.2–1	mg/dL	0.7		
CKMB	< 2.88	ng/mL	1		
TROPONIN T	< 14	ng/L	3		
C REACTIVE PROTEIN (CRP)	< 0.5	mg/dL	0.1		
PROTHROMBIN TIME (%)	70 - 100	%	89.0		
PT PATIENT		*sec*	14.4		
PT CONTROL		*sec*	13.4		
INR	1 - 1.3		1.08		
Partial Thromboplastin Time (PTT)			OK		
PTT CONTROL		*sec*	31		
PTT PATIENT	< 36	*sec*	31		

biochemistry, liver function tests, cardiac enzymes, and partial thrombin and prothrombin times were also within normal ranges (Table 1).

Patient was admitted to the Intensive Care Unit (ICU) for close monitoring and after being clinically and hemodynamically stable for 12 h, she was transferred to regular floor under the care of psychiatry team. Repeated labs in 24 h were also within normal ranges (Table 1). Upon evaluation by the psychiatry team at our hospital, patient had features suggestive of Borderline Personality Disorder (BPD) that included: A pattern of unstable and intense interpersonal relationships, identity disturbance, impulsivity, recurrent suicidal behavior/threats, and chronic feelings of emptiness. However, a definitive diagnosis needed a more detailed history to be taken after the patient recovered from her suicidal attempt event. The patient left the hospital after signing against medical advice the next day and wanted to follow up with her primary psychiatrist outside our institution.

3. Discussion

Suicide was the tenth leading cause of death overall in the United States and the second leading cause of death for people aged 10–34 according to the Centers for Disease Control and Prevention (CDC), making it a crucial public health burden that needs to be addressed (Xu et al., 2021). In addition, medication ingestion is noted to be one of the most observed methods of suicidal attempts (Bachmann, 2018). On the other hand, suicide and suicidal attempts are largely associated with psychiatric diseases, mainly depression (Ferrari et al., 2014; Read and Williams, 2018). Consequently, the use of antidepressant overdose, mainly by SSRIs, has been commonly utilized in these incidents (Conner et al., 2019; Christiansen et al., 2016).

Vortioxetine differs from traditional SSRIs in that it is a serotonin modulator and stimulator (SMS) that acts on different subtypes of serotonin receptors (partial agonist of the 5-HT1B receptor, agonist of 5-HT1A, and an antagonist of the 5-HT3, 5-HT1D, and 5-HT7 receptors) (Bang-Andersen et al., 2011). It has an absolute bioavailability of 75%, reaches maximal plasma concentration 7 to 11 h after dosing, and has a mean elimination half-life he half-life ($t_{1/2}$) that ranges from 59 to 69 h (PubChem 2021). Vortioxetine is primarily metabolized through oxidation by cytochrome P450 isozymes with its major metabolites being pharmacologically inactive (Identification of the Cytochrome 2021). In addition, it is almost entirely eliminated by the liver ((6) Absorption 2021). Compared to other antidepressants, vortioxetine has shown higher remission and lower withdrawal rates, encouraging its use among physicians. A systematic review assessing the use of vortioxetine for MDD after inadequate response to first line therapy showed that" Vortioxetine had a statistically significantly higher remission rate than agomelatine (risk difference [RD]: −11.0% [95% CI: −19.4; −2.6]), and numerically higher remission rates than sertraline (RD: −14.4% [95% CI: −29.9; 1.1]), venlafaxine (RD: −7.20% [95% CI: −24.3; 9.9]), and bupropion (RD: −10.70% [95% CI: −27.8; 6.4])" (Brignone et al., 2016). Nonetheless, its safety and effectiveness in pediatric population hasn't been confirmed and thus it is not FDA approved (DB09068.pdf 2021). In addition, data in the literature concerning vortioxetine overdose and toxicity is scarce. In preclinical trials, maximum dose of vortioxetine ingested by patients, whether intentionally or by accident, was 75 mg. Side effects demonstrated in the latter were only mild symptoms, including nausea, dizziness, diarrhea, abdominal discomfort, generalized pruritus, somnolence, and flushing (PubChem 2021). Furthermore, in a randomized, double-blind, placebo-

controlled, duloxetine-referenced study, the most common reported side effects for vortioxetine were nausea, headache, diarrhea, and dry mouth (Boulenger et al., 2014). Other possible serious side effects mentioned in the FDA label include hypersensitivity, serotonin syndrome, abnormal bleeding, activation of mania/hypomania, hyponatremia, and increased suicidal risk (especially in adolescents and young adults younger than 24 years old) (DB09068.pdf 2021).

We found only one case report in the literature describing effects of vortioxetine and benzodiazepine overdose in a suicidal attempt. It reports a 50-year-old male who attempted suicide by ingesting 250mg of vortioxetine and 10mg of clonazepam. The case report mentioned no significant clinical signs or symptoms from the overdose and concluded safety of the drug in overdose (Mazza et al., 2018). The former results coincide with those of our case report where no significant side effects occurred after ingestion of 300 mg of vortioxetine. Another paper reports a 20-year-old that was found to have serotonin syndrome after attempting suicide by ingesting multiple medications that included vortioxetine, lamotrigine, lurasidone, and bupropion (extended-release). However, the facility she was in did not have urine screening for vortioxetine and the authors attributed her symptoms to escitalopram overdose (Thumtecho et al., 2021). In addition, none of the FDA mentioned serious side effects occurred in our patient. She only had nausea and vomiting which can occur while taking the daily regular dose.

Our patient mentioned no trigger for her suicidal attempt, this might be an alert that vortioxetine had triggered the event. However, a post hoc pooled analyses by Mahableshwarkar et al. found that vortioxetine was not associated with increased risk of suicidal ideation and behavior (Mahableshwarkar et al., 2020) and thus we cannot consider nor suggest its association with the suicidal attempt in our patient.

Case reports have reported bleeding to be attributed to vortioxetine use with low doses (Okumus, 2020; Kh, 2021). No such complication occurred in our patient after taking a significant amount of the medication. This supports the suggestion that bleeding risk might be associated with an idiopathic reaction to the agent and that toxicity wouldn't increase bleeding risk.

Vortioxetine is a promising antidepressant that has some important advantages over other antidepressants, including tolerability of abrupt discontinuation and low incidence related to sexual dysfunction (Boulenger et al., 2014; Jacobsen et al., 2015) .In addition, data suggest its safety in elderly. A randomized placebo-controlled clinical trial found no effect of 5 mg/day of vortioxetine on vital signs or ECG in older adults (Katona et al., 2012).

Our patient had no major toxicity from vortioxetine overdose. However, the drug was ingested only 3 h prior to presentation, whereby it hadn't reached its peak plasma concentration. In addition, the patient received gastrointestinal decontamination upon presentation which might have contributed to less drug absorption. Furthermore, we did not have vortioxetine levels measured neither in blood nor in urine. All of these factors suggest that toxic levels of vortioxetine could not be precisely assessed in our patient, leading to limitations in the interpretation of our case report results. Another major limitation is the absence of follow up to assess for possible late manifestations or complications.

4. Conclusion

Our case report, like that published in the literature, asserts a safe profile and minimal side effects of vortioxetine overdose, in the setting that the patient visits hospital before the peak absorption into the circulation Thus, it is important that all cases of vortioxetine overdose be reported in the literature in order to establish a more concrete conclusion concerning its safety profile.

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Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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