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Suicidal Vilazodone Overdose Presenting as Serotonin Syndrome in a Young Woman With Major Depressive Disorder

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Vilazodone is a novel dual-acting selective serotonin reuptake inhibitor approved for treatment of adult depressive disorders.[1] Serotonin syndrome is a rare but serious adverse drug reaction of vilazodone that produces toxic systemic effects and may lead to coma or death. The risk is higher when combined with other serotonergic drugs such as monoamine oxidase inhibitors (MAOIs).[2–4] Available literature, however, is limited with regard to risk of serotonin syndrome in suicidal vilazodone overdose in adults.[5] We hereby report a case of serotonin syndrome in a young woman with suicidal vilazodone overdose with no coingestion.

Case Report

A 27-year-old unmarried woman suffering from major depressive disorder for the last 10 years presented with a severe depressive episode since November 2018. In the current episode, she was given adequate trials of escitalopram, fluoxetine, venlafaxine, and bupropion (November 2018–May 2019). Augmentation was also tried (May 2019) with lithium and lamotrigine. Later, tablet vilazodone was started (July 2019) and was increased to 40 mg/day, as she tolerated it well. She also received additional brain stimulation therapies along with vilazodone but with no added benefit (August–September 2019). In October 2019, she consumed 30 tablets of vilazodone 20 mg (ie, 600 mg [2 mg/kg] in total). Approximately 4 hours after consumption, she developed delirium and was taken to the emergency department (ED).

In the ED, she developed marked agitation, restlessness, hyperactive delirium, profuse sweating, tachycardia up to 140 bpm, and hypotension up to 90/60 mm Hg and was given a 2-mg injection of intravenous (IV) lorazepam twice half an hour apart. Later, she was transferred to the intensive care unit (ICU) for further management given her deteriorating vital signs. During the detailed examination, her deep tendon reflexes (knee/ankle jerk) were brisk and planter reflex was flexor, and she developed spontaneous jaw clonus, which was confirmed by repeating inducible patellar clonus and ocular clonus. Urine drug screen was positive for only benzodiazepines. Other blood investigations were within normal limits. Electrocardiogram showed no abnormality (QT_c of 390 ms). A diagnosis of serotonin syndrome was considered as per Hunter's diagnostic algorithm,[6] and supportive treatment (IV fluids and midazolam infusion 0.05 mg/kg/h) in the ICU was continued. After 24 hours, her delirium had resolved, and she was able to recognize her family members and the treating doctor.

She was transferred to the psychiatry inpatient unit after 72 hours of stabilization and was kept off psychotropic medications for the next 2 weeks. Later, she was started on sertraline (was not tried previously) on the psychiatry inpatient unit.

Discussion

Life-threatening suicide attempts with medication overdose are not uncommon among patients with depressive disorder. This case was challenging not only because the patient responded poorly to the treatment but also due to the uniqueness of presentation with suicidal vilazodone overdose and serious adverse reaction in the form of serotonin syndrome.

While previous literature has provided a cautionary note for tricyclic antidepressants and MAOIs, most studies have argued that selective serotonin reuptake inhibitors are safe in suicidal overdoses.[3,4] However, this may not be true for vilazodone. Being a relatively newer molecule, literature is sparse about assessing risk associated with vilazodone in the context of overdose. It has been hypothesized in the literature that the possible higher risk of serotonin syndrome with vilazodone is due to partial agonism of serotonergic 5-HT_{1A} receptors in addition to selective serotonin reuptake inhibition.[5] And, it is possible that the risk increases many fold when combined with other serotonergic drugs.[2,3,7]

At present, available literature predominantly (9 of 14 cases) consists of case reports with accidental overdoses in the pediatric population (Table 1), with a dose range of 40–800 mg and symptoms of serotonin syndrome usually appearing after 1–6 hours. Most common symptoms reported in these cases were tachycardia, agitation, and hyperreflexia. Treatment seeking was prompt and often before appearance of any symptoms in cases of accidental ingestion. Most patients (11 of 14) required ICU admission and were frequently treated conservatively with parenteral

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Table 1. Summary of Case Reports and Case Series on Vilazodone Overdose

Author, Year	Age/ Sex	Ingestion Mode	Dose	Serum Level	Time to Treatment Seeking After Ingestion	Symptom Onset After ingestion	Agitation	Sweating	Tachycardia	Tremor	Hyperthermia	Hyperreflexia	Clonus	Seizure	Treatment	Discharge
Clevenger and McCabe, 2020[8]	21 y/ female	Suicidal*	400 mg (6.8 mg/kg BW)	NA	45 min	6 h	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Lorazepam IV, propofol infusion (50 mcg/kg/min), phenobarbital (10 mg/kg)	80 h
Heise et al, 2017[5]	23 mo/ male	Accidental	NA	NA	NA	NA	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	Lorazepam IV	72 h
	22 y/ female	Suicidal*	200 mg	NA	3 h	3 h	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Cyproheptadine 12 mg and GA with midazolam and propofol	96 h
	39 year/ female	NA	800 mg	NA	NA	4 h	Yes	Yes	Yes	Yes	Yes	Yes	NA	NA	Lorazepam IV	72 h
	3 y/ male	Accidental	840 mg	NA	NA	NA	Yes	NA	Yes	NA	Yes	Yes	Yes	Yes	Benzodiazepine, cyproheptadine 4 mg	72 h
Laliberte and Kishk 2018[9]	14 mo/ NA	Accidental	120 mg (10 mg/kg BW)	NA	3 h	3 h	Yes	NA	Yes	Yes	No	Yes	Yes	No	Lorazepam IV	26 h
Del Pizzo et al, 2018[10]	3 y/ male	Accidental	280 mg (15.5 mg/kg BW)	1,600 ng/mL, 4 h post ingestion	15 min	1 h	Yes	NA	Yes	NA	No	Yes	NA	Yes	Lorazepam IV 0.1mg/kg twice, phenobarbital IV 7.5 mg/kg twice	48 h
	28 mo/ male	Accidental	40 mg (3.2 mg/kg BW)	370 ng/mL, 4 h post ingestion	4 h	4h	Yes	Yes	Yes	NA	No	Yes	NA	Yes	Lorazepam IV 0.2 mg/kg twice	24 h
Pfeiffer et al, 2015[11]	20 mo/ male	Accidental	5.6 mg/kg BW	NA	20 min	2 h	Yes	NA	Yes	Yes	NA	Yes	NA	Yes	GA	96 h
Acker et al, 2015[12]	19 mo/ female	Accidental	400 mg (37 mg/kg BW)	NA	1 h	1 h	Yes	NA	Yes	NA	Yes	NA	NA	Yes	Cyproheptadine, midazolam IV infusion	57 h
Butler et al, 2014[13]	28 y/ female	On therapeutic dose*	40 mg, day 17 of treatment	NA	…	…	No	Yes	Yes	Yes	NA	Yes	No	NA	Discontinuation of drug	…
Fung et al, 2014[14]	15 y/ male	Suicidal*	780 mg	830 ng/mL, 9 h post ingestion	3 h	3h	Yes	NA	Yes	NA	NA	Yes	Yes	NA	GA, sodium bicarbonate 200 mEq IV bolus	96 h
Rentmeester et al, 2014[15]	3 y/ male	Accidental	320 mg	252 ng/mL, 5 h post ingestion	3 h	3h	Yes	Yes	Yes	NA	NA	Yes	NA	NA	Propofol, midazolam, fentanyl IV infusion	48 h
Carstairs et al, 2012[16]	23 mo/ female	Accidental	60 mg (5.45 mg/kg BW)	NA	1 h	2h	Yes	NA	Yes	NA	Yes	Yes	NA	Yes	Lorazepam IV, midazolam IV, phenobarbital IV, GA	24 h

*On prescribed treatment with vilazodone.
Abbreviations: BW = body weight, GA = general anesthesia, IV = intravenous, NA = not available.

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benzodiazepines, general anesthetics, or oral cyproheptadine (because of its 5-HT receptor–blocking properties). All patients were discharged after 24 to 96 hours of ICU admission.[8–16]

Vilazodone is metabolized predominantly by hepatic cytochrome P450 enzymes, peak plasma level is reached in 3–5 hours (explaining the time of appearance of the symptoms), and it usually has a half-life of 25 hours (explains usual time to recovery after initial supportive care).[1,5]

In this case, we could not obtain a serum vilazodone level, but the patient denied consuming any other medication and she was not on any other prescription medication during that time (also, family members retrieved 3 empty strips of vilazodone). The appearance of serotonin syndrome coincided with reported plasma peak level (ie, 3–5 hours after ingestion), and the consumed dose was also similar (12 mg/kg body weight) to the average reported in cases.[9,10]

This case highlights the risk of serotonin syndrome in suicidal overdose (where treatment seeking may not be as prompt as in the case of accidental ingestion) of vilazodone, even with no coingestion in a patient with major depressive disorder, raising the issue about safety of vilazodone as an antidepressant in patients with higher suicide risk. Hence, it is necessary to inform family members about risk of serotonin syndrome in case of overdose and the need to give medications under supervision. Further studies are needed to establish the risk versus benefit to guide the real-world decision making.

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