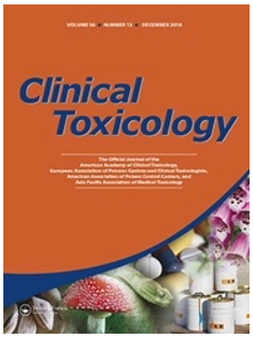

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REVIEW

Vilazodone poisoning: a systematic review

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ABSTRACT

Introduction: Vilazodone is a novel antidepressant approved for the treatment of major depressive disorder. It acts as a serotonin reuptake inhibitor and 5-HT1A partial agonist. It may lead to a more rapid rise in serotonin concentration in the synaptic cleft than selective serotonin reuptake inhibitors (SSRIs), which could potentially cause more severe toxicity in overdose.

Methods: We performed a systematic review of the medical literature to identify all available peer reviewed evidence regarding vilazodone poisoning.

Results: We identified nine unique articles describing vilazodone poisoning. These included eleven unique case reports of vilazodone poisoning, three reviews of data from the National Poison Data System, and one review of data from the Toxicology Investigators Consortium. Children were frequently symptomatic, and many developed seizures and/or serotonin syndrome. Adults and adolescents also developed serotonin syndrome after single-substance ingestion of vilazodone. ICU admission, endotracheal intubation, and parenteral benodiazepines were frequently required.

Discussion: Vilazodone, unlike SSRIs, may frequently cause serotonin syndrome in single-substance ingestions. Children ingesting as little as the minimum daily dose of vilazodone, 10 mg, suffered major clinical toxicity.

Conclusion: Vilazodone poisoning may produce serious clinical effects, including serotonin syndrome and seizures. Young children are at particularly high risk and may become critically ill after ingestion of very small amounts of vilazodone. Admission of poisoned children to a monitored setting and prolonged clinical observation of poisoned adults may be reasonable.

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Introduction

The Food & Drug Administration approved vilazodone hydrochloride (Viibryd®) for the treatment of major depressive disorder (MDD) in 2011. Vilazodone is an indolealkylamine antidepressant which acts as both a selective serotonin reuptake inhibitor (SSRI) and a partial agonist at the serotonin 5-HT_{1A} receptor [1]. It is, thus, a serotonin partial agonist reuptake inhibitor (SPARI) [2]. Vilazodone has been shown to be effective in the treatment of major depressive disorder [1,3,4]. Vilazodone appears to have demonstrable antidepressant effects after 1 week of therapy [5], unlike the SSRIs, which have onset of action 3–4 weeks after initiation of therapy. The usual dose of vilazodone is 20 or 40 mg once daily [1]; tablets of 10, 20, and 40 mg are commercially available. Notably, vilazodone is not approved for use in the pediatric population.

The drug name of vilazodone may lead to confusion with trazodone. Despite the similar names, these two drugs are quite distinct in structure and receptor activity. Trazodone is primarily a serotonin *antagonist* at 5-HT_{2A} and 5-HT_{2C} receptors. Trazodone is a very weak serotonin reuptake inhibitor, although it does possess some partial agonism at 5-HT_{1A} [6]. More importantly, abundant evidence and clinical experience demonstrate that trazodone is generally safe in overdose [7,8].

Vilazodone's unique dual mechanism may explain the more rapid onset of antidepressant efficacy observed in clinical trials. SSRIs increase levels of serotonin in the synaptic cleft by inhibiting reuptake of serotonin by serotonin transporters (SERT) on the presynaptic axon terminal. However, the concentration of serotonin in the synaptic cleft does not rise immediately, in part due to the effect of presynaptic 5-HT_{1A} auto-receptors, which function as a negative feedback mechanism; when serotonin concentrations increase, signaling through 5-HT_{1A} receptors also increases, which causes the presynaptic neuron to reduce serotonin production and release [5,9]. Eventually, the negative feedback response is attenuated (through down-regulation or desensitization of 5-HT_{1A} receptors), and serotonin concentrations increase. Because vilazodone is a 5-HT_{1A} partial agonist as well as an SSRI, it may disrupt the negative feedback loop by occupying 5-HT_{1A} receptors and displacing serotonin [2] or by accelerating attenuation of the 5-HT_{1A} negative feedback signal [5]. It can thus produce rapid increases in the level of serotonin in the synaptic cleft.

We undertook a systematic review of the published medical literature to assess the clinical effects of vilazodone poisoning.

Methods

We performed a systematic review of the medical literature to identify all existing evidence regarding poisoning with

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select novel antidepressant agents. We then classified the results by agent involved, and used evidence relating specifically to vilazodone to construct this qualitative review. We performed this review in accordance with the PRISMA standards for systematic review articles [10].

We searched the published literature using strategies created by a medical librarian for the toxicities associated with overdoses of novel antidepressant agents. A medical librarian established our search strategies using a combination of standardized terms and key words (see Appendix for full list of search terms), and they were implemented in Ovid Medline (1946–present), Embase (1947–present), Scopus (1960–present), Cochrane Central Register of Controlled Trials, Database of Abstracts of Reviews of Effect, Cochrane Database of Systematic Reviews, and Clinicaltrials.gov. We used a "humans" filter and excluded articles not available in English. The medical librarian completed the searches in March 2018, and exported the results to Endnote for a total of 3590 results. She identified 1577 duplicates and removed them, for a total of 2012 unique citations.

We selected articles for this review regarding vilazodone from the above results as described in the results. We included articles describing cases of acute poisoning by novel antidepressants in humans. We included articles regarding patients of all ages and both single and multiple substance exposures. We excluded review or summary articles which did not report novel cases or series, as well as articles describing adverse effects of therapeutic use. Articles identified from the literature search were reviewed for inclusion by one author as detailed below.

Results

We identified a total of 2102 articles using the above search strategy. One author reviewed titles and abstracts for relevance to the research question, and excluded irrelevant articles (defined as articles which in the author's opinion clearly did not meet our inclusion criteria or clearly met our exclusion criteria), leaving 208 relevant articles for more detailed review. At this stage, the author reviewed abstracts in detail, and excluded an additional 106 articles, leaving 104 articles for detailed full-text review. Of these, we identified nine unique articles describing poisoning with vilazodone and included them in this qualitative review. All included articles originated from the United States. See Figure 1 for additional details.

Of the nine included articles, six were novel case reports or case series [11–16], two were reviews of poison center data from the National Poison Data System (NPDS) [17,18], and one included a novel case series, a review of NPDS data, and a review of data reported to the Toxicology Investigators Consortium (ToxIC) [19]. The NPDS is a national database maintained by the American Association of Poison Control Centers (AAPCC) and stores information from calls made to US poison control centers (PCCs). Trained PCC staff, typically nurses and/or pharmacists, collect and enter data, and supervising toxicologists periodically review these data for quality and accuracy [20]. NPDS data are somewhat limited in their granularity and specificity, but still represent a valuable source of information on accidental and intentional poisonings. The American College of Medical Toxicology maintains the ToxIC Registry in order to collect information on poisoned patients cared for at the bedside by medical toxicologists at 47 clinical sites. It typically contains more detailed information on patients' clinical course than the NPDS, but only includes patients seen by a medical toxicology service.

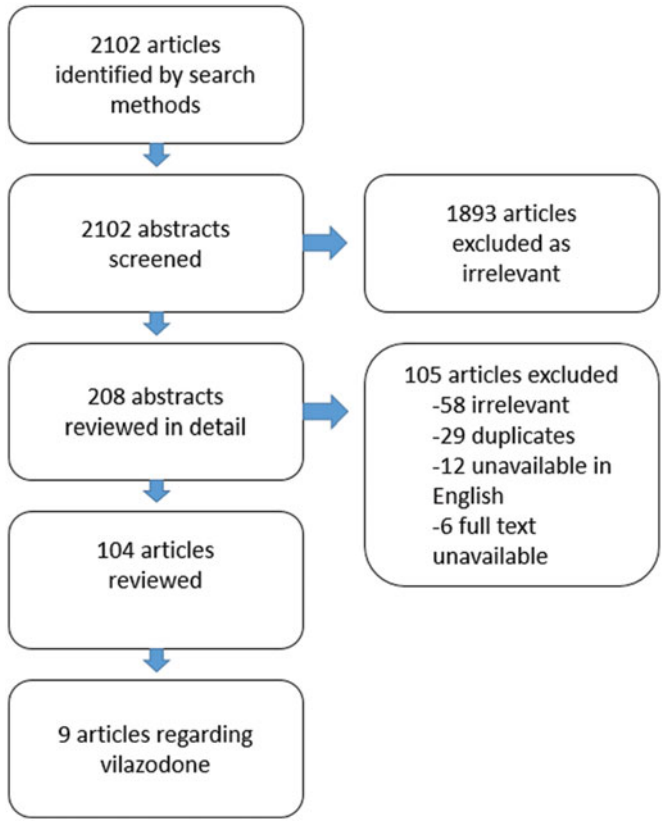

Figure 1. PRISMA flow diagram.

Case reports

Seven articles reported eleven unique cases of vilazodone poisoning. Six articles reported a total of eight cases involving children [11–13,15,16,19]. All eight ingestions in children 3 years of age or younger were accidental or exploratory. Two articles reported a total of three cases involving adolescents or adults [14,19]; all three ingestions were intentional. Table 1 summarizes these case reports.

Children

Children (ranging from 19 months to 3 years of age) ingested varying amounts of vilazodone, ranging from partially chewed tablets to 840 mg. The dose in milligrams per kilogram was available or could be calculated in four cases; it ranged from 5.45 mg/kg to 37 mg/kg. There were no co-ingestants, except in one case in which a child had a bisacodyl tablet in his mouth, which the authors felt was unlikely to contribute to his clinical presentation.

Table 1. Summary of case reports and case series.

Reference	Age	Sex	Amount Ingested	Coingestants	Clinical effects	Serotonin syndrome?	Seizure?	Intubation?	Time course	Vilazodone concentration(s)	Treatment(s)
Acker et al. [11]	19 months	F	400 mg (37 mg/kg)	NR	Tachycardia, altered mental status, seizures, serotonin syndrome	Yes	Yes	Yes	Symptomatic on presentation to ED (t = 1h)	NR	ETI, IV BZD, BZD infusion, CYP
Carstairs et al. [12]	23 months	F	60 mg (5.45 mg/kg)	NR	Tachycardia, somnolence, status epilepticus, possible serotonin syndrome	Possible	Yes	Yes	Asymptomatic but mildly tachycardic at presentation to ED (t = 1h), symptomatic one hour after presentation (t = 2h)	NR	IV BZD, ETI, IV phenobarbital
Del Pizzo et al. [13]	3 years	M	280 mg (15.5 mg/kg)	NR	Status epilepticus, somnolence, nystagmus	Possible	Yes	No	Symptomatic on presentation to ED (t∼0.5h)	1600 ng/mL at t = 4h, 360 ng/mL at t = 27h	IV BZD, normal saline boluses, IV phenobarbital
Del Pizzo et al. [13]	28 months	M	40 mg tablet partially chewed	NR	Seizure, tachycardia, agitation, mydriasis, ataxia	Possible	Yes	No	Symptomatic on presentation to ED (t=?4h)	370 ng/mL at t=?4h	IV BZD
Fung et al. [14]	15 years	M	780 mg	NR	Serotonin syndrome, QRS prolongation	Yes	No	Yes	Symptomatic at t = 3h, unclear when presented to ED	830 ng/mL at t = 9h	ETI, IV sodium bicarbonate boluses and infusion
Pfeiffer et al. [15]	20 months	M	(5.6 mg/kg)	NR	Vomiting, mydriasis, somnolence, seizure, tachycardia, tremors	Possible	Yes	No	Symptomatic on presentation to ED (t=?0.5-1h)	NR	None reported
Rentmeester et al. [16]	3 years	M	320 mg	NR	Vomiting, stupor, tachypnea, mydriasis, hypoglycemia, hyponatremia, sinus pauses and premature junctional complexes (PJC), tachycardia	Possible	No	Yes	Symptomatic on presentation to ED, time point unclear	252 ng/mL at t = 5h, 299 ng/mL at t = 8h, 213 ng/mL at t = 15h	ETI, IV dextrose, IV 3% saline, IV magnesium, sedative infusions (propofol, midazolam, fentanyl)
Heise	23 months	M	Tablet partially chewed, dose not reported	Bisacodyl (partially chewed, dose not reported)	Tachycardia, agitation, serotonin syndrome	Yes	No	No	Symptomatic on presentation to ED, time point unclear	NR	IV BZD
Heise et al. [19]	3 years	M	840 mg	NR	Tachycardia, seizure, serotonin syndrome	Yes	Yes	Yes	Symptomatic on presentation to ED, time point unclear	NR	ETI, sedative infusions (propofol), IV BZD, CYP
Heise et al. [19]	22 years	F	200 mg	NR	Agitation, encephalopathy, tachycardia, serotonin syndrome	Yes	No	Yes	Asymptomatic on presentation to ED (time point unclear), symptoms developed "over the next 3 hours."	NR	IV BZD, ETI, sedative infusions (propofol), BZD infusion, CYP
Heise et al. [19]	39 years	F	800 mg	Ibuprofen (800 mg)	Tachycardia, agitation, encephalopathy, serotonin syndrome	Yes	No	No	Asymptomatic on presentation to ED (time point unclear), symptomatic 4 hours after presentation	NR	IV BZD

NR: not reported; ETI: endotracheal intubation; IV: intravenous; BZD: benzodiazepine; CYP: cyproheptadine.

Table 2. Summary of available EKG data from case reports and case series.

Reference	EKG data
Acker et al. [11]	NSR with "normal intervals," QTc 413 ms
Carstairs et al. [12]	Sinus tachycardia, QRS 58 ms, QTc 373 ms
Del Pizzo et al. [13] Case #1	NSR, QTc 459 ms
Del Pizzo et al. [13] Case #2	Sinus tachycardia, QTc 459 ms
Fung et al. [14]	QRS 130 ms, improving to 96 ms after sodium bicarbonate
Rentmeester et al. [16]	NSR with "normal intervals" and one premature junctional contraction

NSR: normal sinus rhythm.

The most common presenting symptoms & signs in children were mental status changes (agitation or somnolence), tachycardia, nausea & vomiting, and seizures. All children were symptomatic after their ingestions; all but one were symptomatic on presentation to the emergency department (ED). The one patient who was asymptomatic on presentation was actually mildly tachycardic on presentation, and then developed symptoms within 1 h of ED presentation. Six of the eight children had seizures; of these, two had status epilepticus, and one was reported to have "multiple seizures."

Serotonin syndrome, a life-threatening adverse drug reaction caused by excessive serotonergic tone in the central & peripheral nervous system, is a major outcome of interest in serotonergic drug ingestion [21]. Three of the eight children had a reported diagnosis of serotonin syndrome, and the other five had symptoms and signs that suggested serotonergic excess without a reported diagnosis of serotonin syndrome, such as tachycardia, agitation, tremors, and abnormal ocular movements.

The authors provided EKG data in five cases. Table 2 summarizes the available EKG data for the systematic review.

Authors reported vilazodone concentrations in three cases. Initial concentrations, obtained at 4–5 h after ingestion in all three cases, ranged from 252 ng/mL to 1600 ng/mL. Peak concentrations ranged from 299 ng/mL to 1600 ng/mL, although the authors reported serial concentrations in only two cases. The use of activated charcoal, which may affect drug concentrations, was not reported in any case.

The most common treatment administered was intravenous benzodiazepines; treating clinicians administered intravenous benzodiazepines in seven of the eight cases, either for seizures, serotonin syndrome, or sedation after intubation. Four patients underwent endotracheal intubation in the ED. Treating clinicians placed two patients on benzodiazepine infusions, and administered intravenous phenobarbital (in addition to intravenous benzodiazepines) to two patients in order to terminate seizure activity. Enteral cyproheptadine for serotonin syndrome was administered to two patients. Seven of the eight cases required admission to a pediatric ICU; the eighth was transferred to a pediatric general floor. All eight patients were discharged home without long-term sequelae. Case report authors did not report length of stay data.

Adults and adolescents

One 15-year-old patient intentionally ingested 780 mg of vilazodone with no reported coingestants. He developed serotonin syndrome (severe agitation, clonus, hyperreflexia, and tachycardia) and QRS prolongation, with a maximum QRS duration of 130 ms (see Table 2). He underwent intubation (specific indication not reported) and was admitted to an ICU. Treating clinicians administered a sodium bicarbonate bolus and infusion, which normalized his QRS to 96 ms. A vilazodone concentration 9 h after his ingestion was 830 ng/mL. He ultimately recovered to his baseline state of health and was transferred to inpatient psychiatry after a three-day medical hospitalization.

Two adult patients intentionally ingested vilazodone. A 22-year-old patient ingested 200 mg of vilazodone, while a 39-year-old woman ingested 800 mg of vilazodone along with 800 mg of ibuprofen. Both patients were asymptomatic on ED presentation, and did not develop signs or symptoms of vilazodone poisoning until 3–4 h after presentation. Both patients developed serotonin syndrome and significant tachycardia and were admitted to an ICU; neither patient developed seizures, but both received multiple doses of parenteral benzodiazepines. One patient underwent intubation and was placed on a benzodiazepine infusion and enteral cyproheptadine. Both patients ultimately recovered to their baseline state of health and were transferred to inpatient psychiatry. Length of stay was not reported.

Poison center reviews

Three groups conducted retrospective reviews of data submitted to the National Poison Data System (NPDS). All three reviews of NPDS data analyzed established NPDS variables (such as substance of exposure, dose of exposure, level of care, and clinical effects). No free text review of cases was reported. The NPDS manual [22] defines "major" clinical effects as "symptoms that are life-threatening or result in significant residual disability or disfigurement," and "moderate" clinical effects as "more pronounced, more prolonged, or more of a systemic nature than minor symptoms … some form of treatment is or would have been indicated."

Gaw and colleagues [17] performed an NPDS review of single-substance exposures to vilazodone among children younger than 6 years of age from 2011 through 2016. They identified 753 reports regarding pediatric single-substance vilazodone ingestions. Of these, the authors identified 576 who had a true exposure and were followed to a known outcome. Three hundred sixty-nine (64%) experienced one or more "clinical effects." Approximately one-fifth (18.9%) of children had a "serious outcome," defined as moderate or major clinical effects. Notably, there were 11 cases of coma, 21 cases of ataxia, and 40 cases of seizure, including 13 with multiple seizures and 3 with status epilepticus. Seizures were

more common in children 0–2 years of age than in children 3-5 years of age. Twenty-eight patients underwent intubation; the authors did not report the indication for intubation.

Gaw and colleagues also reviewed the dose ingested, when these data were available. They reported that the proportion of serious outcomes, predictably, increased as the ingested dose of vilazodone increased. The median dose associated with major clinical effects was 50 mg (IQR 35–100 mg), and the median dose associated with moderate clinical effects was 40 mg (IQR 20–80 mg). When patient weight was taken into account, the median dose ingested per body weight that was associated with major clinical effects was 3.8 mg/kg (IQR 2.0–8.2 mg/kg), and the median dose ingested per body weight that was associated with moderate clinical effects was 3.4 mg/kg (IQR 1.6–5.7). Notably, the *lowest* dose associated with a major clinical effect in children was 10 mg, the lowest commercially available tablet size. Major clinical effects were associated with doses per body weight as low as 1.0 mg/kg.

Russell and colleagues [18] performed an NPDS review of single-substance and polysubstance exposures to any SSRI or to vilazodone, in children younger than 6 years of age between January 2012 and June 2016. Their primary aim was to compare vilazodone ingestions to ingestions of SSRIs. They calculated that children exposed to vilazodone had significantly higher odds of experiencing a moderate or major outcome in both single-substance exposures (OR 20.5 [15.5–27.1]) and polysubstance exposures (OR 5.9 [3.7–9.0]) than patients exposed to other SSRIs. They also reported an increased rate of hospitalization for both exposure types (single-substance OR 9.0 [7.3–11.2], polysubstance OR 4.1 [2.7–6.2]). Additionally, patients exposed to vilazodone were much more likely to have seizures (RR 54.5 [25.3–129.7]) and coma (RR 137.4 [19.5–5963.3]). The authors concluded that these findings suggested that clinicians treating children exposed to vilazodone should have a high suspicion for clinically important toxicity and a low threshold for hospital admission.

Heise and colleagues [19] performed an NPDS review of single-substance vilazodone exposures in both children and adults from 2012 through April 2016. They identified 1734 single-substance vilazodone exposures; of these, 668 involved patients under the age of 18, leaving 1066 adult exposures. They did not segregate their outcome data by age. 18 patients (1%) had a single seizure, 14 (<1%) had multiple seizures, and 3 (<1%) had status epilepticus. One hundred eighty patients (10%) received benzodiazepines, and 36 (2%) underwent intubation. The authors did not report outcome data separately for children and adults.

ToxIC review

Heise and colleagues [19] also reviewed cases reported to the ToxIC Registry between January 2012 and August 2016. They abstracted coded data from the ToxIC database; no free-text review of cases was performed. A total of 23 cases of vilazodone ingestion were reported to ToxIC during the study period; of these, 17 were "vilazodone-primary" ingestions (vilazodone reported as first or primary agent involved in ingestion), and 10 were isolated vilazodone ingestions. In the ToxIC database, the "primary" substance, or the one felt to be most contributory to the patient's clinical presentation, is determined by the treating medical toxicologist. The authors reviewed only the "vilazodone-primary" cases. These included 7 patients under 18 and 10 patients aged 18 years or older. Nine patients (39%) were specifically diagnosed with serotonin syndrome; seven of these cases involved no serotonergic agents other than vilazodone. In an additional five cases, the treating toxicology team reported symptoms suggestive of serotonergic effects, for a total of 14 of 17 (82%) of vilazodone-primary ingestions with evidence of serotonergic excess.

Discussion

The novel cases reviewed here paint a disturbing picture of vilazodone poisoning. Serotonin syndrome, seizures (even status epilepticus), and need for endotracheal intubation were common. All but one patient required treatment with intravenous benzodiazepines, and some required benzodiazepine infusions and/or barbiturates. All but one patient required ICU care.

The NPDS and ToxIC data are very concerning. While critical clinical findings such as coma, seizure, and respiratory failure were rare, they appear to be much more common in vilazodone poisoning than in SSRI exposures, as specifically illustrated by the NPDS review by Russel and colleagues [18]. Additionally, single-substance vilazodone exposures cause serotonin syndrome, which is not typical of SSRIs. Finally, even miniscule pediatric exposures – as little as one chewed tablet – can result in serious clinical effects. Vilazodone is available in 10 mg, 20 mg, and 40 mg tablets [23], and is typically dosed at 40 mg daily after a brief up-titration period [1]. Exposure to as little as 10 mg, or one quarter of the usual daily dose, can produce major clinical effects in young children, including seizures and serotonin syndrome. A wide range of ingested doses per body weight can produce moderate or major toxicity.

Although several authors reported vilazodone concentrations, the clinical implications of these values are not currently known. Vilazodone concentrations are not typically available in clinical practice, and there is no established therapeutic range. Standard 40 mg daily dosing in adults produces a mean maximum concentration of 156 ng/mL [23].

There are fewer data available on vilazodone poisoning in adults and adolescents as compared to the pediatric population. However, relatively small overdoses (for example, 200 mg or five times the daily dose in case #10) may cause moderate to severe serotonin syndrome.

Additionally, based on the case presented by Fung and colleagues, it seems that vilazodone can act as a sodium channel blocker in massive overdose, as it appeared to cause significant QRS prolongation which corrected with sodium bicarbonate, in a case with no known co-ingestants. To our knowledge, this is the only case of vilazodone-induced QRS prolongation reported, and there are no *in vitro* data

regarding vilazodone-induced sodium channel blockade available. However, it seems prudent to pay close attention to the QRS duration when assessing patients with vilazodone overdoses, and reasonable to consider sodium bicarbonate for patients with a prolonged QRS.

The introduction of novel psychotropic medications such as vilazodone creates a conundrum for emergency clinicians and toxicologists. The data reviewed here suggest that we cannot treat SPARIs such as vilazodone the same way we treat SSRIs. Given the documented morbidity in young children, it seems reasonable to admit all patients <6 years of age who ingest any amount of vilazodone to an appropriate pediatric service for at least 6–8 h of observation. There are no definitive reports of delayed-onset toxicity in children, but caution is likely appropriate given the potential for serious clinical effects. In adults, we know that at least two patients were asymptomatic on presentation but developed symptoms and signs of serotonin syndrome after a period of 3–4 h; this suggests that 6–8 h observation in the ED or an appropriate observation unit may be appropriate even in asymptomatic adults prior to discharge or clearance of inpatient psychiatry.

Limitations

There were several important limitations to this study. Reliance on case reports tends to highlight the most unusual or severe cases, and it is likely that there have been unreported cases in which children or adults have overdosed on vilazodone and suffered no ill effects. Publication bias may limit the availability of useful case reports & series. Studies relying on NPDS and ToxIC data are, by nature, retrospective, and carry all the disadvantages of retrospective reviews, including reliance on existing documentation in the medical record and missing or incomplete data. The ToxIC database collects information in a binary fashion, documenting, for example, the presence or absence of tachycardia over a given cutoff, which may limit the collection of clinically important data points. Additionally, the NPDS database relies on voluntary reporting by patients, families, and clinicians, and is thus subject to significant under-reporting, especially of mild or asymptomatic cases [24]. The three NPDS reviews summarized here had significant temporal overlap, and may have studied near-identical populations; additionally, several of the cases documented in case reports & series occurred during the time period of the NPDS and Toxlc reviews, and may have been included in these data setsIn many of the cases reviewed, both novel cases and in the NPDS and ToxIC data sets, no confirmatory serum or urine drug concentrations were available. The diagnosis of serotonin syndrome, a major outcome of interest, is difficult to determine in retrospect if not specified, as it relies on several specific physical exam findings that the authors did not always report. Finally, a major item of interest is the existence of delayed-onset symptoms, and the NPDS and ToxIC data sets did not report the time course of symptom onset, nor did some authors of novel case reports.

Conclusion

Vilazodone poisoning may produce serious and life-threatening clinical effects, including serotonin syndrome and seizures. Young children, who may become critically ill after ingestions of very small amounts of the drug, are at especially high risk. Clinicians should have a low threshold for admission for any pediatric patient exposed to vilazodone, and should consider at least 6–8 h of observation for asymptomatic adult patients following vilazodone ingestions.

Disclosure statement

No potential conflict of interest was reported by the authors.

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Appendix

Full search strategies including key words and results outlined below.

Ovid medline

387 results
03/30/18

(Exp Drug overdose/OR Overdos*.mp. OR Exp poisoning/OR Cardiotoxicit*.mp. OR Toxicit*.mp. OR toxicosis.mp. OR intoxicat*.mp. OR ((Accident* or Acute) adj2 ingestion*).mp. OR poisoning.mp. OR Poisoning.fs. OR (Poison adj1 center).mp. OR (drug adj1 emergency).mp.

AND

(Milnacipran.mp. OR dalcipran.mp. OR fetzima.mp. OR impulsor.mp. OR ixel.mp. OR levomilnacipran.mp. OR midalcipran.mp. OR savella.mp. OR toledomin.mp. OR Exp atomoxetine hydrochloride/OR Atomoxetine.mp. OR atomoxetin.mp. OR recit.mp. OR strattera.mp. OR tomoxetine.mp. OR tomoxetine hydrochloride.mp. OR Vortioxetine.mp. OR brintellix.mp. OR trintellix.mp. OR Agomelatine.mp. OR Thymanax.mp. OR valdoxan.mp. OR Exp vilazodone hydrochloride/OR vilazozone.mp. OR Viibryd.mp. OR Exp Trazodone/OR Trazodone.mp. OR azonz.mp. OR beneficat.mp. OR bimaran.mp. OR deprax.mp. OR depresil.mp. OR depyrel.mp. OR desirel.mp. OR desyrel.mp. OR manegan.mp. OR molipaxin.mp. OR oleptro.mp. OR pesyrel.mp. OR pragazone.mp. OR pragmarel.mp. OR pragmazone.mp. OR reslin.mp. OR taxagon.mp. OR thombran.mp. OR thromban.mp. OR thrombran.mp. OR tombran.mp. OR tradozone.mp. OR trasodon.mp. OR trasodone.mp. OR trazodil.mp. OR trazodon.mp. OR trazon.mp. OR trazolan.mp. OR trialodine.mp. OR trittico.mp. OR mirtazapine.mp. OR rexer.mp. OR esmirtazapine.mp. OR remeron.mp. OR norset.mp. OR remergil.mp. OR zispin.mp. OR avanza.mp. OR mirtazepine.mp. OR remergon.mp. OR remeron.mp.))
NOT ((Exp Animals/NOT (Exp Animals/AND Exp Humans/)) or rabbit.ti. or rabbits.ti. or rat.ti. or rats.ti. or cattle.ti. or bovine.ti. or mice.ti. or mouse.ti. or ovine.ti. or sheep.ti. or goat.ti. or dog.ti.)

Embase

03/30/18
1,755

(('Drug overdose'/exp OR Overdos*:ti,ab,kw,de OR 'drug intoxication'/exp OR Cardiotoxicit*:ti,ab,kw,de OR 'drug toxicity'/exp OR Toxicit*:ti,kw OR toxicosis:ti,ab,kw,de OR intoxicat*:ti,ab,kw,de OR ((Accident* or Acute) near/2 ingestion*):ti,ab,kw,de OR poisoning:ti,ab,kw OR (Poison near/1 center):ti,ab,kw,de OR (drug near/1 emergency):ti,ab,kw,de)

AND

('milnacipran'/exp OR milnacipran:ti,ab,kw,de OR dalcipran:ti,ab,kw,de OR fetzima:ti,ab,kw,de OR impulsor:ti,ab,kw,de OR ixel:ti,ab,kw,de OR levomilnacipran:ti,ab,kw,de OR midalcipran:ti,ab,kw,de OR savella:ti,ab,kw,de OR toledomin:ti,ab,kw,de OR 'atomoxetine'/exp OR Atomoxetine:ti,ab,kw,de OR atomoxetin:ti,ab,kw,de OR recit:ti,ab,kw,de OR strattera:ti,ab,kw,de OR tomoxetine:ti,ab,kw,de OR 'tomoxetine hydrochloride':ti,ab,kw,de OR 'vortioxetine'/exp OR Vortioxetine:ti,ab,kw,de OR brintellix:ti,ab,kw,de OR trintellix:ti,ab,kw,de OR 'agomelatine'/exp OR Agomelatine:ti,ab,kw,de OR Thymanax:ti,ab,kw,de OR valdoxan:ti,ab,kw,de OR 'vilazodone'/exp OR vilazozone:ti,ab,kw,de OR Viibryd:ti,ab,kw,de OR 'Trazodone'/exp OR Trazodone:ti,ab,kw,de OR azonz:ti,ab,kw,de OR beneficat:ti,ab,kw,de OR bimaran:ti,ab,kw,de OR deprax:ti,ab,kw,de OR depresil:ti,ab,kw,de OR depyrel:ti,ab,kw,de OR desirel:ti,ab,kw,de OR desyrel:ti,ab,kw,de OR manegan:ti,ab,kw,de OR molipaxin:ti,ab,kw,de OR oleptro:ti,ab,kw,de OR pesyrel:ti,ab,kw,de OR pragazone:ti,ab,kw,de OR pragmarel:ti,ab,kw,de OR pragmazone:ti,ab,kw,de OR reslin:ti,ab,kw,de OR taxagon:ti,ab,kw,de OR thombran:ti,ab,kw,de OR thromban:ti,ab,kw,de OR thrombran:ti,ab,kw,de OR tombran:ti,ab,kw,de OR tradozone:ti,ab,kw,de OR trasodon:ti,ab,kw,de OR trasodone:ti,ab,kw,de OR trazodil:ti,ab,kw,de OR trazodon:ti,ab,kw,de OR trazon:ti,ab,kw,de OR trazolan:ti,ab,kw,de OR trialodine:ti,ab,kw,de OR trittico:ti,ab,kw,de OR mirtazapine:ti,ab,kw,de OR rexer:ti,ab,kw,de OR esmirtazapine:ti,ab,kw,de OR remeron:ti,ab,kw,de OR norset:ti,ab,kw,de OR remergil:ti,ab,kw,de OR zispin:ti,ab,kw,de OR avanza:ti,ab,kw,de OR 'mirtazepine'/exp OR mirtazepine:ti,ab,kw,de OR remergon:ti,ab,kw,de OR remeron:ti,ab,kw,de))
NOT (([animals]/lim NOT [humans]/lim) or rabbit:ti or rabbits:ti or rat:ti or rats:ti or cattle:ti or bovine:ti or mice:ti or mouse:ti or ovine:ti or sheep:ti or goat:ti or dog:ti)

Cochrane library

03/30/18
Cochrane Central Register of Controlled Trials – 50 results
Cochrane Database of Systematic Reviews – 1 results
Database of Abstracts of Reviews of Effect – 1 results

([mh "Drug overdose"] OR Overdos*:ti,ab,kw OR [mh poisoning] OR Cardiotoxicit*:ti,ab,kw OR Toxicit*:ti,ab,kw OR toxicosis:ti,ab,kw OR intoxicat*:ti,ab,kw OR ((Accident* or Acute) near/2 ingestion*):ti,ab,kw OR poisoning:ti,ab,kw OR Poisoning.fs. OR (Poison near/1 center):ti,ab,kw OR (drug near/1 emergency):ti,ab,kw)

AND

(Milnacipran:ti,ab,kw OR dalcipran:ti,ab,kw OR fetzima:ti,ab,kw OR impulsor:ti,ab,kw OR ixel:ti,ab,kw OR levomilnacipran:ti,ab,kw OR midalcipran:ti,ab,kw OR savella:ti,ab,kw OR toledomin:ti,ab,kw OR [mh "atomoxetine hydrochloride"] OR Atomoxetine:ti,ab,kw OR atomoxetin:ti,ab,kw OR recit:ti,ab,kw OR strattera:ti,ab,kw OR tomoxetine:ti,ab,kw OR "tomoxetine hydrochloride":ti,ab,kw OR Vortioxetine:ti,ab,kw OR brintellix:ti,ab,kw OR trintellix:ti,ab,kw OR Agomelatine:ti,ab,kw OR Thymanax:ti,ab,kw OR valdoxan:ti,ab,kw OR [mh "vilazodone hydrochloride"] OR vilazozone:ti,ab,kw OR Viibryd:ti,ab,kw OR [mh Trazodone] OR Trazodone:ti,ab,kw OR azonz:ti,ab,kw OR beneficat:ti,ab,kw OR bimaran:ti,ab,kw OR deprax:ti,ab,kw OR depresil:ti,ab,kw OR depyrel:ti,ab,kw OR desirel:ti,ab,kw OR desyrel:ti,ab,kw OR manegan:ti,ab,kw OR molipaxin:ti,ab,kw OR oleptro:ti,ab,kw OR pesyrel:ti,ab,kw OR pragazone:ti,ab,kw OR pragmarel:ti,ab,kw OR pragmazone:ti,ab,kw OR reslin:ti,ab,kw OR taxagon:ti,ab,kw OR thombran:ti,ab,kw OR thromban:ti,ab,kw OR thrombran:ti,ab,kw OR tombran:ti,ab,kw OR tradozone:ti,ab,kw OR trasodon:ti,ab,kw OR trasodone:ti,ab,kw OR trazodil:ti,ab,kw OR trazodon:ti,ab,kw OR trazon:ti,ab,kw OR trazolan:ti,ab,kw OR trialodine:ti,ab,kw OR trittico:ti,ab,kw OR mirtazapine:ti,ab,kw OR rexer:ti,ab,kw OR esmirtazapine:ti,ab,kw OR remeron:ti,ab,kw OR norset:ti,ab,kw OR remergil:ti,ab,kw OR zispin:ti,ab,kw OR avanza:ti,ab,kw OR mirtazepine:ti,ab,kw OR remergon:ti,ab,kw OR remeron:ti,ab,kw)

Scopus

03/30/18
1396 results

((TITLE-ABS-KEY (overdos* OR cardiotoxicit* OR toxicosis OR poisoning)) OR (TITLE-ABS-KEY ("drug intoxication")) OR (TITLE-ABS-KEY (poison W/1 center*)) OR (TITLE-ABS-KEY (drug W/1 emergency)) OR (TITLE-ABS-KEY ((accident* OR acute) W/2 ingestion*))) AND ((TITLE-ABS-KEY (milnacipran OR dalcipran OR fetzima OR impulsor OR ixel OR levomilnacipran OR midalcipran OR savella OR toledomin OR atomoxetine OR atomoxetin OR recit OR strattera OR tomoxetine OR vortioxetine OR brintellix OR trintellix OR agomelatine OR thymanax OR valdoxan OR vilazozone OR viibryd OR trazodone OR azonz OR beneficat OR bimaran OR deprax OR depresil OR depyrel OR desirel OR desyrel OR manegan OR molipaxin OR oleptro OR pesyrel OR pragazone OR pragmarel OR pragmazone OR reslin OR taxagon OR thombran OR thromban OR thrombran OR tombran OR tradozone OR trasodon OR trasodone OR trazodil OR trazodon OR trazon OR trazolan OR trialodine OR trittico OR mirtazapine OR rexer OR esmirtazapine OR remeron OR norset OR remergil OR zispin OR avanza OR mirtazepine OR remergon OR remeron)) OR (TITLE-ABS-KEY ("tomoxetine hydrochloride"))) AND NOT ((KEY (animals)) AND NOT ((KEY (animals)) AND (KEY (humans))))

Clinicaltrials.gov

03/30/18
0 results

(poisoning OR overdose) AND (Mirtazapine OR Trazodone OR Vilazodone OR Agomelatine OR Vortioxetine OR Atomoxetine OR Milnacipran OR levomilnacipran)