Lurasidone Ingestions Reported to Texas Poison Centers

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Abstract

Background: Lurasidone is an atypical antipsychotic approved for the treatment of schizophrenia in 2010. There is limited information on potentially toxic events involving lurasidone outside of clinical investigations. **Objective:** This investigation describes potentially toxic lurasidone ingestions from a single data source. **Methods:** Cases were lurasidone ingestions reported to Texas poison centers during 2011 to 2013. The distribution was determined for selected characteristics. For management and outcome factors, analyses were limited to those cases without coingestants. **Results:** There were 140 lurasidone ingestions. Of the 72 cases with a reported dose, the mean dose was 536 mg (range = 20–4000 mg). The patient age was 5 years or less in 8.6% of the cases, 6 to 12 years in 2.1%, 13 to 19 years in 17.9%, and 20 years or more in 70.7%; 65.7% of the patients were female. The most commonly reported reason for the exposure was suspected attempted suicide, reported in 54.3% of the cases. No coingestants were reported in 55 (39.3%) of the cases. For these cases, the management site was 56.4% already at/en route to health care facility, 29.1% managed on site, and 10.9% referred to a health care facility. The medical outcome was known or suspected to not be serious in 65.5% of the cases. The most commonly reported clinical effects were drowsiness, agitation, and nausea. **Conclusions:** The majority of lurasidone ingestions reported to Texas poison centers involved adults and females. Over half were suspected attempted suicides and most involved coingestants. The majority of lurasidone ingestions without coingestants did not have serious outcomes.

Keywords

atypical antipsychotic, lurasidone, poison center, management, outcome

Introduction

Lurasidone (Latuda, Sunovion Pharmaceuticals Inc, Fort Lee, NJ) received regulatory approval by the US Food and Drug Administration (FDA) on October 28, 2010.¹ Lurasidone is a second-generation atypical antipsychotic belonging to the benzothiazol derivative class.² The medication is indicated for the treatment of schizophrenia and bipolar depression.²

Lurasidone has a strong affinity for the dopamine D₂ and serotonin 5HT_{2A} and 5HT₇ receptors, moderate affinity for the serotonin 5HT_{1A} and noradrenaline α_{2c} receptors, minimal affinity for the noradrenaline α_1 receptors, and negligible affinity for the histamine H₁ and cholinergic M₁ receptors.^{2,3} The medication is rapidly absorbed, reaching peak serum concentration in 1 to 3 hours, with a mean elimination half-life of 18 hours.² It is mainly metabolized in the liver by the CYP3A4 enzyme system.²

Adverse events reported with therapeutic use as well as accidental exposures and overdoses involving lurasidone include insomnia, somnolence, sedation, akathisia, nausea, vomiting, headache, extrapyramidal symptoms, agitation, diarrhea, anxiety, and tachycardia.^{2,4,5} Several deaths where the person had taken lurasidone have been reported, although these deaths involved other substances as well.⁶

There is limited information on adverse events involving lurasidone outside of clinical investigations. One possible source of information is poison centers. US poison centers are telephone consultation services that assist in the management of potentially adverse exposures to a variety of substances, including atypical antipsychotics. In 2012, 40 435 atypical antipsychotic exposures were reported to US poison centers, including 15 deaths.⁶ The intent of this investigation was to characterize potentially toxic lurasidone ingestions reported to poison centers.

Methods

The data source for this retrospective, descriptive epidemiology study was the Texas Poison Center Network (TPCN), a system consisting of the 6 poison centers that service the entire state, a population of over 25 million. The 6 poison

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centers use a common electronic database to collect a variety of information on all received calls in a consistent manner. The data fields and allowable data options are standardized by the American Association of Poison Control Centers (AAPCC).^{6,7}

Cases were all lurasidone ingestions reported to the TPCN during 2011 to 2013. No lurasidone exposures had been reported to the TPCN prior to 2011. Exposures by routes other than ingestion were excluded. Cases involving coingestants were included in the study. Cases not followed to a final medical outcome also were included because 25.7% of the lurasidone ingestions were not followed to a final outcome.

The distribution of lurasidone exposures was determined for year, reported dose, patient age and gender, exposure site, the circumstances of (reason for) the exposure, presence of coingestants, management site, medical outcome, adverse clinical effects, and treatments. The mean dose was calculated for the subgroups among most of the other variables. Since the presence of coingestants might affect the management and outcome of the patient, the analysis of management site, medical outcome, adverse clinical effects, and treatments was limited to those cases without reported coingestants.

Descriptions of the groupings within the variables are defined in the AAPCC National Poison Data System (NPDS) Reference Manual.⁷ The circumstances of (reason for) the exposure are based on the intent of the exposure. Unintentional exposures result from unforeseen or unplanned events such as accidental exposures or therapeutic errors. Intentional exposures result from purposeful actions such as attempted suicide or abuse of a substance. Adverse reactions involve unwanted effects reported by a patient while taking a medication, regardless of whether or not the medication use is related to the reaction.

The medical outcome or severity of an exposure is assigned by the poison center staff and is based on the observed or anticipated adverse clinical effects. Medical outcome is classified according to the following criteria: no effect (no symptoms due to exposure), minor effect (some minimally troublesome symptoms), moderate effect (more pronounced, prolonged symptoms), major effect (symptoms that are life-threatening or cause significant disability or disfigurement), and death. A portion of exposures are not followed to a final medical outcome because the poison center staff assess the exposures to be nontoxic or minimally toxic, resource constraints, or the inability to obtain subsequent information on the patient. In these instances, the poison center staff record the expected outcome of the exposure based on what is known about the exposure. These expected outcomes are assigned the following categories: not followed but judged as nontoxic exposure (symptoms not expected), not followed but minimal symptoms possible (no more than minor symptoms possible), and unable to

follow but judged as a potentially toxic exposure. Another medical outcome category is unrelated effect where the exposure was probably not responsible for the symptoms. A further medical outcome category is confirmed nonexposure where it becomes known with certainty that a patient was not exposed to a substance. Exposures assigned this category were excluded from the analysis. The medical outcomes were grouped into those known or expected to not be serious (no effect, minor effect, not followed but judged as nontoxic, not followed but minimal symptoms possible) and those known or expected to be serious (moderate effect, major effect, death, unable to follow but judged as potentially toxic).

Information on specific clinical effects and treatments is recorded in the electronic records in a set of check-boxes as well as in a text notes (narrative) field. Since such information is not consistently recorded in the notes field, the analyses of clinical effects and treatments were restricted to information recorded in the check-boxes.

The Texas Department of State Health Services Institutional Review Board considers this analysis exempt from ethical review.

Results

There were 140 lurasidone ingestions: 26 in 2011, 42 in 2012, and 72 in 2013. The dose was reported for 72 (51.4%) of the cases. For these cases, the mean dose was 536 mg (range = 20–4000 mg).

Table 1 presents the distribution of lurasidone ingestions by selected demographics. The majority of patients were adults, who also had the highest mean reported dose. Most of the ingestions involved female patients; the mean dose was higher for this gender. The highest proportion of ingestions involved intentional suspected attempted suicide followed by unintentional-general and therapeutic errors. The mean dose was higher for suspected attempted suicides than for any other exposure reason group. Over half of the exposures were acute. The majority of lurasidone cases involved coingestants; these ingestions had a higher mean dose than cases not involving coingestants.

Table 2 provides information on the management site and medical outcome of those lurasidone ingestions that did not involve coingestants. Over half of the patients were already at or en route to a health care facility when the poison center was contacted. The mean dose was higher among those cases seen at a health care facility than those managed on site. Of those patients seen at a health care facility, over one third were treated or evaluated and released. The mean dose was higher for those patients who were admitted to the health care facility. The majority of lurasidone ingestions were known or expected to not be serious. The mean dose was higher for those cases that were known or expected to be serious.

Table 1. Demographic Characteristics of Lurasidone Ingestions Reported to the Texas Poison Center Network During 2011 to 2013^a.

Factor	Total Cases		Cases With Reported Dose		
	n	%	n	Mean Dose (mg)	Range (mg)
Total	140		72	536	20-4000
Patient age (years)					
5 or less	12	8.6	11	82	20-200
6-12	3	2.1	1	20	
13-19	25	17.9	14	340	40-1200
20 or more	99	70.7	46	715	20-4000
Unknown	1	0.7	0		
Patient gender					
Male	48	34.3	27	398	20-3680
Female	92	65.7	45	618	20-4000
Circumstances of exposure					
Unintentional—General	20	14.3	15	155	20-1000
Unintentional—Therapeutic error	19	13.6	13	89	20-320
Unintentional—Misuse	1	0.7	1	160	
Unintentional—Unknown	2	1.4	1	160	
Intentional—Suspected suicide	76	54.3	33	1012	100-4000
Intentional—Misuse	5	3.6	1	240	
Intentional—Unknown	3	2.1	1	100	
Adverse reaction	12	8.6	6	73	40-120
Unknown	2	1.4	1	600	
Chronicity					
Acute	76	54.3	43	418	20-2600
Acute-on-chronic	52	37.1	26	695	40-4000
Chronic	4	2.9	1	80	
Unknown	8	5.7	2	1220	600-1840
Coingestants					
No	55	39.3	37	447	20-4000
Yes	85	60.7	35	629	20-3680

^aIncludes all exposures whether or not coingestants were involved.

The most frequently reported adverse clinical effects were drowsiness or lethargy followed by agitation or irritability and nausea (Table 3). No conduction disturbance, dysrhythmia, or electrocardiogram (ECG) changes were reported among the cases. The most commonly reported treatments were administration of intravenous fluids, activated charcoal, and benzodiazepines (Table 4).

Discussion

This study describes the pattern of lurasidone ingestions reported to a large poison center system. The majority of lurasidone ingestion patients reported to the TPCN were adults and female, and most of the ingestions were reported to be intentional, particularly suspected attempted suicide. These findings are similar to those included in a previous study of lurasidone ingestions reported to all US poison centers, although exposures involving coingestants and exposures not followed to a final medical outcome were excluded.⁴ In this previous study, 24% of the patients were 19 years or younger and 61% were female, and 64% of the

Table 2. Management Site and Medical Outcome of Lurasidone Ingestions Reported to the Texas Poison Center Network During 2011 to 2013^a.

Factor	Total Cases		Cases With Reported Dose		
	n	%	n	Mean Dose (mg)	Range (mg)
Total	55		37	447	20-4000
Management site					
On site (non-HCF)	16	29.1	12	90	20-200
Already at/en route to HCF	31	56.4	21	493	20-2400
Referred to HCF	6	10.9	3	1380	40-4000
Other	2	3.6	1	80	
Managed at HCF ^b					
Already at HCF: Treated/evaluated, released	13	35.1	10	146	20-600
Already at HCF: Admitted noncritical care	4	10.8	3	1347	600-2240
Already at HCF: Admitted to psychiatric	8	21.6	5	344	100-600
Already at HCF: Lost to follow-up	6	16.2	3	1040	120-2400
Referred to HCF: Admitted critical care	1	2.7	1	1000	
Referred to HCF: Lost to follow-up	5	13.5	2	2020	40-4000
Final medical outcome					
No effect*	18	32.7	14	424	20-2240
Minor effect*	8	14.5	7	28	80-1000
Moderate effect**	7	12.7	5	216	80-600
Not followed—Judged nontoxic*	1	1.8	1	80	
Not followed—Minimal effects*	9	16.4	5	80	20-160
Unable to follow—Potentially toxic**	10	18.2	5	1416	40-4000
Unrelated effect	2	3.6	0		
*Not serious	36	65.5	27	310	20-2240
**Serious	17	30.9	10	816	40-4000

Abbreviation: HCF, health care facility.

^aIncludes only those exposures without coingestants.

^bIncludes only those cases that were already at, en route to, or referred to a health care facility (n = 37).

exposures were intentional. In the present investigation, the mean dose was higher among adults, females, and suspected attempted suicides. The higher mean dose among suspected attempted suicides might be expected considering that individuals who attempt suicide may ingest large amounts of medications or other substances to end their life. The higher mean dose among adults is likely due to the observation that 60.6% of the suspected attempted suicides occurred among adults, with the remainder among patients age 13 to 19 years. Moreover, the higher mean dose among females may be related to the observation that females comprised a higher proportion of the adult patients (66.7%) than young children (50.0%).

Over half of the patients ingesting lurasidone were already at or en route to a health care facility when the poison center was contacted, and slightly over 30% were known or expected to result in serious outcomes. In the previous study of lurasidone ingestions reported to poison centers nationally, 23% had serious outcomes (21% moderate, 2% major).⁴ The mean dose was higher among cases known

Table 3. Adverse Clinical Effects of Lurasidone Ingestions Reported to the Texas Poison Center Network During 2011 to 2013^a.

Clinical Effect	Total Cases		Cases With Reported Dose		
	n	%	n	Mean Dose (mg)	Range (mg)
Total	55		37	447	20-4000
Cardiovascular					
Hypertension	4	7.3	1	40	
Tachycardia	3	5.5	2	420	240-600
Gastrointestinal					
Nausea	6	10.9	4	225	40-460
Oropharyngeal problem	1	1.8	0		
Vomiting	3	5.5	1	40	
Neurological					
Agitation/irritability	7	12.7	5	196	80-600
Confusion	2	3.6	1	100	
Drowsiness/lethargy	8	14.5	5	188	80-460
Dystonia	1	1.8	1	80	
Hallucinations/delusions	2	3.6	1	600	
Slurred speech	3	5.5	2	140	40-240
Tremor	2	3.6	2	60	40-80
Respiratory					
Hyperventilation/tachypnea	1	1.8	1	1200	
Miscellaneous					
Hyperglycemia	1	1.8	1	40	
Hypoglycemia	1	1.8	1	240	
Other (unspecified)	7	12.7	4	390	80-1000

^aIncludes only those exposures without coingestants.**Table 4.** Treatments of Lurasidone Ingestions Reported to the Texas Poison Center Network During 2011 to 2013.

Treatment	Total Cases		Cases With Reported Dose		
	n	%	n	Mean Dose (mg)	Range (mg)
Total	55		37	447	20-4000
Decontamination					
Activated charcoal	13	23.6	10	470	20-2240
Cathartic	4	7.3	3	507	320-600
Dilution/irrigation/wash	4	7.3	4	160	20-460
Other emetic	1	1.8	1	4000	
Other					
Antiemetics	1	1.8	1	320	
Antihistamines	3	5.5	0		
Benzodiazepines	5	9.1	3	333	80-600
Glucose	1	1.8	1	240	
Intravenous fluids	15	27.3	10	578	100-2240
Naloxone	1	1.8	1	460	
Vasopressors	1	1.8	1	2240	
Other (unspecified)	4	7.3	2	340	80-600

^aIncludes only those exposures without coingestants.

or suspected to be serious. Since higher doses of a medication might be more likely to result in adverse effects, and the presence of adverse effects are used by poison center staff to determine the severity of the exposure, then higher doses might be expected to be associated with more serious outcomes. Moreover, since patients known or expected to

have serious effects from ingestion of lurasidone might be expected to not only be seen at but also admitted to a health care facility, then those cases involving health care facilities might be expected to have higher mean doses of the medication. This investigation did find higher mean doses among those cases involving health care facilities.

The most frequently reported adverse clinical effects reported in the lurasidone ingestions in this study were consistent with the adverse events reported in the literature.^{2,4,5}

This study is subject to various limitations. Reporting of potentially adverse lurasidone ingestions to the TPCN is voluntary. Consequently, those exposures that are reported might not be representative of all such exposures that occur in the population. This was a retrospective study using data already collected via normal poison center operations and not specifically for this investigation. There may be reporting bias. Moreover, the ingestion was primarily based on the caller's report and not verified clinically; that is, that an actual ingestion of lurasidone had occurred was not confirmed. Also, the reported dose was known for only slightly over half of the cases and was based on information provided by the patient or caller and therefore might not be accurate. Furthermore, as described in the methodology, all the cases were not followed to a final medical outcome. For cases not followed to a final medical outcome, information on the management and clinical effects might be incomplete. In addition, analysis of the clinical effects and treatments was restricted to the information provided in the checkboxes and did not include any information on clinical effects or treatments recorded in the notes field.

In conclusion, the majority of lurasidone ingestions reported to Texas poison centers involved adults and females. Over half were suspected attempted suicides and most involved coingestants. The majority of lurasidone ingestions without coingestants did not have serious outcomes.

Declaration of Conflicting Interests

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