JPPT | Case Report

# Acute Tramadol Ingestion With Transient Acute Kidney Injury in an Adolescent Female

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Renal toxicity has been described with tramadol overdoses; however, it is typically associated with rhabdomyolysis, multiorgan failure and/or mortality. Our patient was a 16-year-old female who was evaluated following an intentional tramadol ingestion, estimated 27.8 to 37 mg/kg, and had a seizure prior to arriving at our health care facility. Her symptoms were consistent with a tramadol ingestion; however, she developed transient acute renal impairment (peak serum creatinine, 4.04 mg/dL), which improved over 6 days with minimal intervention. No other causes were identified to explain her acute renal impairment thus it was attributed to the tramadol overdose. Providers should be aware that transient acute renal impairment could occur with an intentional tramadol ingestion and may not require aggressive intervention.

**ABBREVIATIONS** BUN, blood urea nitrogen; CK, creatine kinase; ED, emergency department; IV, intravenous; QTc, ECG interval from the QRS complex to the end of the T wave where "c" in QTc stands for corrected; SCr, serum creatinine

**KEYWORDS** acute kidney injury; adolescent; adverse drug effect; analgesics; case report; drug overdose; tramadol

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## Introduction

Tramadol is a centrally acting synthetic analgesic medication with both opioid and non-opioid affects, and it inhibits the re-uptake inhibitor of norepinephrine and serotonin. It is hepatically metabolized via CYP2D6 to its active metabolite, O-desmethyltramadol, which has greater pharmacologic activity than the parent compound. Both are excreted in the urine. Renal toxicity has been described with tramadol overdoses; however, it is typically associated with rhabdomyolysis, multiorgan failure, and/or mortality.[1-3] We describe an adolescent who developed transient intrinsic renal injury, not associated with rhabdomyolysis, following an intentional overdose of tramadol.

## Case

A 16-year-old (54 kg) female was admitted 2 to 3 hours after reportedly ingesting 30 to 40 50-mg tramadol tablets (27.8 mg/kg–37.0 mg/kg). Her mother found her with pale and clammy skin, altered mental status, confusion, an unsteady gait, and bite marks on her tongue and drove the patient to the ED. En route, she experienced a seizure that spontaneously resolved without therapy soon after arrival to the ED (estimated length of seizure 3–8 minutes). She was postictal, tachycardic (heart rate 140 seconds beat/min), hypertensive (systolic blood pressure of 130 seconds mm Hg) and had a normal QTc of 400 ms. Laboratory results were unremarkable except for a serum bicarbonate concentration of 8 mEq/L, anion gap 37.5 and 2+ proteins on urinalysis. About 4 hours after tramadol ingestion, her serum creatinine (SCr) was 0.9 mg/dL and blood urea nitrogen (BUN) was 14 mg/dL; i.e., within normal limits (Table). She was transported to our facility for further evaluation and monitoring.

In our ED, now 7 hours post-ingestion, she continued to be tachycardic and hypertensive but was otherwise well appearing and her mental status and neurologic examination were improved. She received 4 mg of IV ondansetron for nausea and was admitted to the acute care floor with maintenance IV fluids of 5% dextrose 0.45% normal saline and 20 mEq/L of potassium acetate. Soon after arrival to the floor, her serum bicarbonate concentration had improved, but her SCr had increased (Table).

By the following morning, she was hemodynamically stable, her mental status remained at baseline, and her IV fluids were switched to 5% dextrose and normal saline. Patellar reflexes were found to be 4+ along with 3 to 4 beats of ankle clonus bilaterally. Repeat laboratory studies were obtained 22 hours post-ingestion revealed that her SCr had increased to 2.44 mg/dL, which caused concerns about acute kidney injury. Her creatine kinase (CK) was only slightly elevated at 278 units/L. Further review of her medical record noted a normal SCr was 0.7 mg/dL approximately 1 month prior to this admission. She confirmed her intentional ingestion of up to 2000 mg of tramadol. Her home medications included aripiprazole, fluoxetine, melatonin, alprazolam, and hydroxyzine, which were unlikely causes of her acute kidney injury.

**Table.** Pertinent Laboratory Results During Hospital Admission Following an Acute Tramadol Ingestion

| Time After Tramadol Ingestion (hr) | SCr, mg/dL | BUN, mg/dL | Bicarbonate, mEq/L | CK, units/L |
|---|---|---|---|---|
| 5 | 0.9 | 14 | 8 | — |
| 10.5 | 1.35 | 16 | 21.5 | — |
| 22 | 2.44 | 18 | 21.5 | 278 |
| 25.5 | 2.76 | 18 | 21.9 | — |
| 31 | 3.18 | 19 | 19.4 | — |
| 37.5 | 3.57 | 20 | 17.3 | — |
| 43.5 | 3.85 | 19 | 16.6 | 177 |
| 49.5 | 4.04 | 21 | 20.8 | — |
| 55.5 | 4.02 | 21 | 21.2 | — |
| 64 | 3.79 | 19 | 21.6 | — |
| 73.5 | 3.25 | 19 | 22.1 | — |
| 79 | 2.96 | 19 | 23.9 | — |
| 85.5 | 2.37 | 16 | 25.8 | — |
| 89 | 2.2 | 15 | 26.3 | — |
| 97 | 1.8 | 12 | 26.8 | — |
| 109.5 | 1.44 | 9 | 19.1 | — |
| 121.5 | 1.28 | 9 | 23.4 | — |
| 136 | 1.03 | 9 | 20.4 | — |
| 161 | 1.01 | 11 | 20.6 | — |

*BUN, blood urea nitrogen; CK, creatine kinase; SCr, serum creatinine*

Approximately 25 hours post-ingestion, her SCr continued to increase (2.76 mg/dL), and nephrology was consulted. A recommended renal ultrasound showed kidneys >95th percentile in size (incidental finding); urinalysis was notable for 1+ hemoglobin, 1+ protein, and a specific gravity of 1.004. Nephrology attributed this to non-oliguric intrinsic kidney injury secondary to the tramadol ingestion. They recommended continued IV fluids with the goal of a net positive fluid balance and laboratory assessment of her renal function every 6 hours. Despite 24 hours of adequate fluid resuscitation, her BUN and SCr continued to increase, but her serum bicarbonate began to decrease (nadir 16.6 mEq/L) (Table). Maintenance IV fluids were changed to 5% dextrose with 0.45% normal saline and 77 mEq/L of sodium acetate and her bicarbonate improved. Approximately 48 hours post-ingestion, her SCr peaked at 4.04 mg/dL with a BUN of 21 mg/dL.

Over the next few days, she was in the polyuric phase of kidney recovery, with net fluid balance of negative 2 to 3 L despite aggressive IV and oral fluid intake. Given the negative fluid balance, IV fluids were changed to 5% dextrose with 0.45% normal saline with 10 mEQ/L of KCl at 1.5 times maintenance requirements. By day 5, her patellar reflexes were 2+ and her ankle clonus had improved to 2 beats bilaterally. Her fluids were discontinued on day 6 of admission (SCr 1.03 mg/dL, BUN 9 mg/dL). After 24 hours without IV fluids, her SCr and BUN remained stable. She was discharged from the acute care floor and transferred to an inpatient psychiatric unit 8 days post-ingestion.

## Discussion

Our case describes an adolescent patient who developed transient intrinsic renal injury, not associated with rhabdomyolysis, following an overdose of tramadol. She had no other coingestions to explain her transient renal injury and her seizure was non-contributary to this injury. Her home medications have not been associated with acute renal injury and no other reports of isolated renal injury associated with tramadol were identified in a literature review. One case report described a patient with a significant rise in SCr, but the CK was also elevated following the tramadol ingestion and multiple seizures.[1]

Even at therapeutic dosing, tramadol is known to

cause seizures that typically respond to benzodiazepines. The minimum dose required to induce seizures has been difficult to define. However, in 1 study 11% of the patients had a seizure following a median ingested dose of 2100 mg tramadol;[3] fatalities in adults have occurred with 5000-mg ingestions.[2] In pediatric patients, Stassinos et al[4] found that serious toxicity was rare, with respiratory depression and seizures occurring in 0.6% of patients with median doses of 225 mg (range, 50–600 mg) and 525 mg (range, 50–1050 mg), respectively. In pediatric case reports, minimum doses of 4.8 mg/kg have been associated with adverse effects. Coingestions with a selective serotonin reuptake inhibitor or a monoamine oxidase inhibitor increase the theoretical risk for serotonin toxicity, although notably 1 study failed to show this association out of 71 patient cases reviewed.[3]

Proposed mechanisms for tramadol-associated nephrotoxicity have included rhabdomyolysis, secondary amyloidosis, and decreased renal perfusion. Our patient only had a modest rise in serum CK making it unlikely that rhabdomyolysis contributed to her renal impairment. Multiple rat models have shown acute kidney injury following tramadol overdose.[5-7] Large doses of μ-receptor agonists are known to decrease renal perfusion due to decreased systemic arterial blood pressure in conjunction with increased antidiuretic hormone secretion and increased sympathetic outflow. These actions lead to transient decrease in urinary flow rate and glomerular filtration rate. It is likely that transiently decreased renal perfusion played a large role in the acute kidney injury that our patient developed and required only supportive IV fluids.

## Conclusion

We described a case of isolated acute renal impairment following a tramadol overdose that resolved without significant intervention over 6 days. Although renal impairment has rarely been reported following tramadol overdose, it is typically associated with rhabdomyolysis or multiorgan failure. Providers should be aware that transient acute renal impairment following acute ingestions of large doses of tramadol could occur independently, but may not require aggressive intervention.

### Article Information

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