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Beyond Therapeutic Boundaries: A Rivaroxaban Overdose Case Analysis

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Abstract

Introduction

Rivaroxaban, a direct factor Xa inhibitor, has revolutionized anticoagulation therapy with its fixed dosing and efficacy in preventing thromboembolic events. However, its use presents challenges due to the absence of a readily available antidote and the potential for bleeding complications. Despite these considerations, Rivaroxaban and other direct oral anticoagulants represent a significant advancement in anticoagulation therapy.

Case Presentation

A 38-year-old female presented after ingesting 200 mg of Rivaroxaban, experiencing symptoms indicative of coagulopathy. Despite initial concerns regarding bleeding risk and coagulation derangement, the patient responded well to activated charcoal lavage and supportive care. Improvement in symptoms and normalization of coagulation parameters were observed over the course of 24 hours, aligning with Rivaroxaban's pharmacokinetics and highlighting the efficacy of supportive measures in managing Rivaroxaban toxicity.

Discussion

This case underscores the complexities of managing Rivaroxaban overdose and the importance of timely intervention and supportive care. Despite the absence of a specific antidote, activated charcoal lavage and supportive measures played a crucial role in improving patient outcomes.

Conclusion

Continued vigilance and further research into antidotes are warranted to optimize management strategies for Rivaroxaban toxicity.

Keywords: Rivaroxaban overdose, Case report, Factor Xa inhibitor, Coagulopathy, Anticoagulation therapy

Introduction

Rivaroxaban is an orally active, direct factor Xa inhibitor. It is approved for the acute and ongoing treatment of venous thromboembolism (VTE), as well as for the prevention of embolic stroke in atrial fibrillation. **[1]** It is effective in preventing stroke in atrial fibrillation, treating deep vein thrombosis, and reducing the risk of pulmonary embolism. Unlike traditional anticoagulants such as warfarin, rivaroxaban offers the advantage of fixed dosing without the need for frequent monitoring. However, this convenience comes with potential challenges, as excessive dosing may lead to bleeding complications, raising concerns regarding the absence of a readily available antidote. Despite these considerations, the advent of direct oral anticoagulants, including rivaroxaban, represents a paradigm shift in anticoagulation therapy, offering patients effective alternatives with more predictable pharmacological profiles. Healthcare providers must carefully weigh the benefits and risks of these agents while individualizing treatment plans based on patient characteristics, medical history, and risk factors for bleeding. Although Prothrombin time (PT) is considered a potential test, there are currently no readily available rapid quantitative tests to promptly assess the timing of blood coagulation with rivaroxaban. **[2]** A normal PT is indicative of a reduced likelihood of its associated clinical anticoagulant effect.

Case presentation

A 38-year-old female presented to the Emergency Department of a private hospital in Lalitpur, Nepal, 22 hours after suicidal ingestion of 200 mg of rivaroxaban, equivalent to ten tablets of 20 mg. The patient had been on a long-term prescription of rivaroxaban 20 mg daily for the management of recurrent deep vein thrombosis (DVT) over the past two years. She travelled from her permanent residence, approximately two hours away from Kathmandu, to seek medical attention. 2 hours after ingestion, she began to exhibit lethargy and nausea, followed by two episodes of non-projectile vomiting, which were foul-smelling and contained food particles, without any signs of blood or bile.

Upon further deterioration characterized by a decreased level of consciousness, the patient was taken to a nearby health clinic. She was referred to our center for advanced care. Upon examination at our facility, the patient's Glasgow Coma Scale (GCS) score was 13/15 (E3V4M6), indicating a mild impairment of consciousness. She was tachycardic with a heart rate of 120 bpm, blood pressure of 150/80 mmHg, respiratory rate of 24 breaths per minute, and oxygen saturation (SpO2) of 98% on room air. The physical examination did not reveal any other significant findings.

Blood samples were immediately drawn for laboratory investigations, and the patient was admitted to the intensive care unit (ICU) for close monitoring. Initial laboratory results indicated an Activated Partial Thromboplastin Time (aPTT) of 45, Prothrombin Time (PT) of 18 s, and International Normalized Ratio (INR) of 1.7. These findings suggest coagulopathy, likely induced by an overdose of rivaroxaban. A nasogastric tube was placed and activated charcoal about 90 grams was installed, followed by lavage. The patient received intravenous doses of ondansetron (4 mg) and pantoprazole (40 mg) as immediate doses to address her nausea and potential gastrointestinal complications. Over the course of 24 hours in the ICU, her symptoms improved significantly, including normalization of her level of consciousness and resolution of nausea. Subsequent laboratory tests showed normal PT and INR values, indicating the resolution of the coagulation abnormalities in this case report.

A psychiatric evaluation was conducted following stabilization, and she was diagnosed with major depressive disorder. Consequently, she was prescribed escitalopram 10 mg daily for her depressive symptoms, along with supervised administration of Clonazepam 0.25 mg at bedtime for five days, to be overseen by her husband. The patient's condition improved, and she was safely discharged with recommendations for ongoing psychiatric follow-up and close monitoring of her mental health status. She was maintained on a reduced dose of 10 mg Rivaroxaban for DVT prophylaxis.

Discussion

The patient, presenting two hours post-ingestion with multiple episodes of vomiting, exhibited an elevated coagulation profile upon admission. Symptomatic improvement and normalization of the coagulation profile followed initial management. Rivaroxaban's half-life of 5-9 hours, peaking at 2-4 hours, correlates with the patient's presentation and subsequent improvement, as shown in Table 1, indicating the drug's elimination post-admission. **[3]**

In our case, the patient showed symptomatic improvement after activated charcoal lavage. In cases of rivaroxaban overdose, activated charcoal is generally effective if administered within the first 1–2 hours of ingestion to prevent further absorption of the drug. **[4]** Although the rivaroxaban concentration could not be estimated due to unavailability, symptomatic improvement suggests reduced post-administration absorption. Despite the Australian guidelines recommending activated charcoal for significant bleeding, the following standard poisoning protocols appear to be effective. **[1,5,6]** In report of Ghodsi et al, activated charcoal was not administered because the ingestion occurred 10 hours prior, exceeding the window of effectiveness, which is typically within 1–2 hours post-ingestion. **[7]**

The long-term use of rivaroxaban may potentially lead to the development of tolerance, resulting in a ceiling effect. Although this effect has not yet been proven, it could theoretically lead to a decreased incidence of bleeding in chronic factor Xa inhibitor users. **[8,9]**

Although we were unable to measure blood rivaroxaban levels owing to unavailability in our setting, we assessed the INR level to estimate the extent of coagulopathy. Although INR is not a direct measure of rivaroxaban activity, it provides a useful surrogate marker to gauge the patient's coagulation status and guide clinical management. **[10]** As demonstrated in the study by Kim et al. **[9]**, where a cutoff of 13.45 seconds for prothrombin time was established, our patient's prothrombin time of 18 s at presentation suggested a high blood rivaroxaban level, despite the inability to perform exact measurements. This elevated prothrombin time indicates significant anticoagulant activity, consistent with the findings of Kim et al., and highlight the severity of the coagulopathy in this case. **[11]**

In the context of rivaroxaban poisoning, the primary concern is the absence of antidotal therapy for overdoses and bleeding events. However, recent clinical trials of andexanet alfa, a novel antidote, have shown promise in reversing the anticoagulant effects of factor Xa inhibitors, including rivaroxaban and apixaban. In our case, Andexanet Alfa was not readily accessible due to its high cost. In patients treated with rivaroxaban, andexanet alfa achieved a 92% reduction in anti-factor Xa activity, compared to an 18% reduction observed in the placebo group. Despite these promising laboratory surrogate endpoints, the efficacy of andexanet alfa in acutely toxic, hemorrhagic patients remains unclear. **[12]**

In line with the case reported by Replinger et al., a single overdose of rivaroxaban in our patient led to elevated PT, aPTT, and INR, but did not result in significant bleeding manifestations. This observation parallels their findings, in which increased coagulation parameters were evident without corresponding severe hemorrhagic events. The similarity in outcomes underscores the potential variability in clinical presentations following rivaroxaban overdose and highlights the importance of monitoring coagulation markers to assess anticoagulation severity without solely relying on the presence of bleeding symptoms. **[13,14]**

In our case, the pharmacokinetics of rivaroxaban were aligned with the presentation, suggesting elimination. Despite the unavailability of blood rivaroxaban measurements, activated charcoal lavage yielded symptomatic improvements.

Table 1: Progression of coagulation profile parameters with time

Lab Parameters	0 hr	12hr	24hr	Normal Range
APTT	45	35	33	21 – 35 secs
PT	18	16	15	11 – 13.5 secs
INR	1.7	1.5	1.14	<1.2

Conclusion

In conclusion, this case illustrates rivaroxaban overdose presentation with PT, aPTT, and INR derangement, despite the absence of significant bleeding. The pharmacokinetics of rivaroxaban suggest elimination, with activated charcoal improving the patient's symptoms.

Conflict of interest

The authors declare that there are no conflicts of interest.

Consent

Written informed consent was obtained from the patient for publication of this case report.

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