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Case Report: Menorrhagia in Women After the Administration of Novel Oral Anticoagulants, Like Rivaroxaban: A Case Report

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ABSTRACT

Background: The Novel Oral Anticoagulants (NOACs), despite numerous benefits, such as the ease of use and less drug involvement, provide extensive adverse effects. One of the most significant, but rare side effects of them in women is severe and dangerous bleeding

Case presentation: In this study, we reported a case of severe vaginal bleeding (manometric hemorrhage) in a woman receiving rivaroxaban to prevent pulmonary thrombosis.

Conclusion: The oral anticoagulant rivaroxaban could present a rare adverse effect on women.

1. Introduction

Anticoagulant is a substance with medicinal characteristics that prevents blood clotting. Blood coagulation or thinning is a process that causes blood clotting. This process converts fibrinogen to fibrin and activates coagulation factors. Besides, it leads to platelet aggregation through internal and external pathways [1].

Oral anticoagulants are absorbed through the gastrointestinal tract and metabolized extensively in the urine prior to excretion. Contrary to the venous anticoagulant medications, the oral anticoagulant drugs pass through the placenta. Their consumption may lead to bleeding in the fetus and impairment in the formation of the fetus [2]. The most prevalent adverse effect of oral anticoagulant drugs is bleeding. Such bleeding may range from a minor nasal blooding to a menorrhagia hemorrhage due to the oral anticoagulants, abnormal blood clotting, the rupture of the healthy menstrual cycle, or the abnormalities of the uterus endothelial lining [3]. By reason, menorrhagia may be accompanied by periods, i.e., painfully abnormal (painful dysmenorrhea).

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Types of the Novel Oral Anticoagulants (NOACs) include rivaroxaban, i.e., used for the treatment of Deep Venous Thrombosis (DVT) and dabigatran, a Pradaxa brand (Pradaxa) with a direct thrombin inhibitor which prevents blood clots formation. This medication prevents the blood platelets in the blood to be clotted (coagulation) [4, 5].

Apixaban is an inhibitor of the factor A10 inhibitor; by controlling the selective and reversible inhibition of the active site of factor 10a without the need for any cofactor (antithrombin 3), it inhibits the activation of the platelets [6]. Apixaban, without directly affecting the platelet aggregation or inhibiting the free or clot-linked factor 10a and controlling the prothrombinase activity, inhibits the thrombin-induced platelet aggregation [7].

There is a rare side effect for the oral anticoagulant rivaroxaban. In this study, we reported a case of severe vaginal bleeding presented two months after consuming rivaroxaban in a woman.

2. Case Report

A 41-year-old woman with severe vaginal bleeding, vertigo, tachycardia (pulse rate=110 beats/minute), and hypotension (systolic blood pressure=60 mm Hg), referred to Shahid Mostafa Khomeini Hospital and visited an infectious diseases specialist. The patient was immediately admitted to the hospital. Laboratory samples were obtained and 2 blood bags were provided to the patient due to low hemoglobin level (Hb=6 g/dL).

Other laboratory tests data were as follows: Erythrocyte Sedimentation Rate (ESR)=40 mm/h, C-Reactive Protein (CRP)=4 mm/L, Prothrombin Time (PT)=12 s, International Normalized Ratio (INR)=1.0, Blood Urea Nitrogen (BUN)=7 mg/dL, and creatinine=2.2 mg/dL.

Concerning medical history, she has suffered from deep venous thrombosis and pulmonary embolism for several times. On examining the patient, the congenital deficiency of protein-C was diagnosed as a rare genetic trait; accordingly, the patient was treated with warfarin due to the recurrent nature of the thrombosis. At the time of warfarin administration, the patient's menstrual cycles were healthy. The patient failed to co-operate to monitor the time of Prothrombin (PT). To study the International Standard Tests (INRs) for managing the dose of warfarin, the physician decided to replace warfarin with rivaroxaban (15 mg orally twice a day for the first 21 days, followed by 20 mg orally once a day; because creatinine clearance was normal).

Approximately 2 months after the onset of the treatment, the patient was suffering from the adverse effects of rivaroxaban in the form of severe vaginal bleeding and was admitted to the emergency department.

3. Discussion

As recommended, with the presence of rivaroxaban as a non-vitamin K antagonist oral anticoagulant, no coagulation monitoring is required; therefore, no longer the changes in coagulation parameters require adjustment in terms of dose and dosing interval [8].

Although all anticoagulants are accompanied by bleeding, it is not always responsible for elevated concentrations in some medications. It is unclear whether or not the risk of abnormal vaginal bleeding is increased by rivaroxaban consumption; only a few cases with an incidence rate of 20% to 27% have been described in this respect [9].

As per some meta-analysis clinical trials, no trace of Heavy Menstrual Bleeding (HMB) [10] was reported due to rivaroxaban therapy. Perhaps this should come as no surprise; according to the International Society on Thrombosis and Hemostasis (ISTH), HMB may not be specified as a subcategory of bleeding as far as clinical non-major bleeding [11] is concerned. The absence of formal recognition is due to the missing of some specific information in this area. HMB is rarely associated with serious events; however, it usually imposes negative impacts on the quality of life of the women and eventually contributes to direct and indirect costs [12]. The increased incidences of abnormal vaginal bleeding in women of reproductive age receiving rivaroxaban and apixaban, compared to warfarin consumers have been reported in several studies [13, 14].

Lower-dose Direct Oral Anticoagulants (DOAC) were appeared to be effective in preventing recurrent thrombosis in patients receiving apixaban and rivaroxaban for ≥6 months. Shifting from rivaroxaban to apixaban in 5(70%) of 7 women was reported as a successful HMB management as well [14].

According to another observational study, a high incidence of mucosal bleeding, especially uterine or ovarian bleeding was reported in women with VTEs who were treated with rivaroxaban [15].

Based on a cohort from the AMPLIFY study, clinically-relevant non-major vaginal bleeding was observed in 28(2.5%) of 1122 women, and 24 (2.1%) of 1106

women treated with apixaban and warfarin, respectively (Odds Ratio (OR), 1.2; 95% CI, 0.67-2.0)) [14].

Coagulation monitoring is not required for the use of rivaroxaban, according to most of the studies. The increased risk of bleeding should be addressed by clinicians. Moreover, monitoring the coagulation status of these patients should be considered during rivaroxaban therapy.

4. Conclusion

The oral anticoagulant rivaroxaban could present a rare adverse effect on women.

Ethical Considerations

Compliance with ethical guidelines

The study is compatible with the ethical guidelines of the Helsinki Declaration. All private information will remain confidential.

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Author's contributions

All authors contributed in preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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