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Hematuria in Patient on Rivaroxaban on Consumption of Saffron

[1.] Dr. Vishnu Sharma
Department of General Medicine
SMS Medical College
Jaipur, India

[2.] Vansh Bagrodia
Final MBBS Student
SMS Medical College
Jaipur, India

Abstract:- Herb-drug interactions is a known entity which arises due to taking medications from different branches like allopathy, naturopathy, herbal medicine, etc. at the same time by many patients in the hope of achieving better and faster treatment. Here, we report a case of hematuria seen in patient on rivaroxaban for DVT-PTE on consumption of saffron.

I. INTRODUCTION

Herb-drug interactions are those interactions which occur between herbal medicines and conventional drugs on simultaneous ingestion. These types of interactions may be more common than drug-drug interactions since herbal medicines often contain multiple pharmacologically active ingredients, while conventional drugs usually contain only one.

Approximately 70% of the world's population has been using medicinal herbs as a complementary or alternative medicine with significant increase seen in the past 20 years. The main routes proposed for HDIs include cytochrome P450 (CYP450)-mediated inhibition or induction and transport and flow proteins.[1]

Examples of herb-drug interactions include:

- Warfarin combined with ginkgo leading to bleeding (Ginkgo biloba)
- Neuroleptic drugs and betel nut leading to exacerbation of extrapyramidal effects;
- Liquorice potentiating oral and topical corticosteroids;
- Chinese herbal product xaio chai hu tang causing decreased blood concentrations of prednisolone .[2]

II. CASE

We report a case of 31 year old male, who presented with swelling in both legs and breathlessness in November 2021. Patient gave a history of long haul intercontinental travel and was suspected of having Bilateral Leg Deep Vein Thrombosis with Pulmonary Thromboembolism. A two point compression ultrasound and Doppler study confirmed the diagnosis. Patient was found to have elevated D-dimer levels (2467 ng/mL FEU) and was started on Enoxaparin. Due to Bilateral Leg Deep Vein Thrombosis with massive Pulmonary Thromboembolism, patient was advised long term Direct Oral Anticoagulant therapy and was put on rivaroxaban. Patient was asymptomatic on rivaroxaban but started taking saffron supplements on the pretext that they would boost the general immunity of the patient. Patient said to have observed hematuria within 1 day of taking saffron supplements and then stopped the same after 4 days. Patient repeated the same thing before finally reporting to us with the complaint of hematuria. Drug levels in blood, basic blood and urine investigations and coagulation profile were done, all of which came to be normal. No causative pathology for hematuria was found on urinary tract examination done by USG. On detailed history, patient told about his recent saffron supplementation with the hematuria occurrence observed and was thus advised to stop them. Having not consumed saffron supplementation again, patient reported no complaints of hematuria and is asymptomatic on Rivoraxaban therapy.

III. DISCUSSION

The possibility of direct toxicities, drug interactions, and contamination with active pharmacological agents are among the health concerns about dietary and herbal supplements.

Research and public opinion have opposing views regarding the safety of herbs and botanical products in dietary supplements with the former demonstrating that these products carry similar dangers as other pharmaceutically active compounds. Interactions may occur between prescription drugs, dietary supplements, over-the-counter drugs and even small molecules in food—making it a real issue to understand interactions that may be clinically concerning.

Though much stern and solid research about herb-drug interactions hasn't been done or is inconclusive and most of the presently identified herb-drug interactions are either hypothetical, inferred from animal studies, or based on other indirect means; however, attention to this issue is needed for drugs with narrow therapeutic indexes like cancer chemotherapeutic agents, digoxin, and warfarin.

Rivaroxaban is a novel oral anticoagulant (NOAC) drug. DOACs like rivaroxaban interact with potent CYP3A inhibitors and P-glycoprotein (P-GP) inhibitors, and breast cancer resistance protein Bcrp (ABCG2) inhibitors (such as azole-antimycotics, apart from fluconazole and HIV protease inhibitors), which are multi-pathway inhibitors of rivaroxaban clearance and elimination.[3]

The use of rivaroxaban to reduce a persistent risk of venous thromboembolism is FDA-approved and was thus given to the patient.

Saffron and its main constituents crocetin and its glycosidic esters, called crocins, and safranal have been identified as powerful antioxidants. Their beneficial effects have been illustrated on various body systems like cardiovascular, gastrointestinal, endocrine, immune, with CNS being the most studied.

Usage of herbal products as complementary and/or alternative medicine is famous worldwide. Low reporting from patients and the inability to accurately recognize HDIs by healthcare providers are identified to be major factors limiting formation of a compilation of clinically relevant HDIs.

Though a randomised controlled trial done by Ayatollahi et al on the effect of saffron on coagulation and anticoagulation systems in healthy volunteers ruled out this possible herb-drug interaction in their given study parameters[4], the occurence of hematuria in our patient on use of saffron while on rivaroxaban without any other clear causative pathology warrants further study on this topic. Such an occurrence was also reported by Heidari et al[5] which is dated after the above mentioned RCT which further strengthens the need for more study on this topic.

IV. CONCLUSION

Elaborate studies need to be done on this possible drug-herbal interaction of saffron and DOACs for possible increased risk of bleeding in such patients and such co-administrations should be avoided until proper studies have confirmed of the existence or non-existence of this particular drug-herbal interaction.

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