



## Warfarin Induced Gastrointestinal Bleeding: A Case Report

Jerrin Reji Mathew<sup>1</sup>, Ashley Ann Dilip<sup>1</sup>, Siby Joseph<sup>1\*</sup>, Lakshmi R<sup>1</sup>, George Thayil<sup>2</sup>

1 Department of Pharmacy Practice, St. Joseph's College of Pharmacy, Cherthala, Kerala, India.

2 Department of Cardiology, Lourdes Hospital, Post Graduate Institute of Medical Science & Research, Kochi, Kerala, India.

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### \*Corresponding author:

Email : sibymadappallil@gmail.com

### ABSTRACT

The coumarin derivative Warfarin is effective in prevention and treatment of venous and arterial thrombosis. It is a narrow therapeutic index drug so it may cause bleeding if overdose or thrombosis if the dose is too low. To overcome these complications, the prothrombin time (PT) generally expressed as international normalized ratio (INR) is used to adjust the dose of drug. We describe a case of 61-yr old male patient with Known history of Rheumatic heart disease and mitral valve replacement done in 2012. He was presented with complaints of abdominal pain and vomiting. Laboratory parameter showed increased PT and INR ratio. On further evaluation it was assessed that patient was taking Tab. Warfarin high dose without consulting doctor which resulted in acute intestinal bleeding and subsequently obstruction which required emergency laparotomy - ileocolic anastomosis resection for preventing further complications. So it is important to provide proper patient counselling regarding the use of drugs like warfarin, periodic monitoring of laboratory parameters and importance of consulting clinical practitioner periodically for adjusting the dose.

### INTRODUCTION

Warfarin, a coumarin derivative, produces an anticoagulant effect by interfering with the cyclic interconversion of vitamin K and its 2,3 epoxide (vitamin K epoxide). The proteins, which include the coagulation factors II, VII, IX, and X, require  $\gamma$ -carboxylation by vitamin K for biological activity. It is mainly indicated for atrial fibrillation (AF), venous thromboembolism (VTE) and prosthetic heart valves, but it is contraindicated in certain conditions like recent haemorrhage, bleeding issues due to congenital or acquired disorders of the clotting system, presence of severe liver disease may predispose to bleeding due to insufficiency of liver to synthesize clotting proteins, reduced clearance of warfarin, presence of oesophageal varices [1]. Serious adverse effects of warfarin include bleeding and significant hemorrhage (e.g., intracranial hemorrhage, gastrointestinal (GI) bleed, hematemesis, intraocular bleeding, hemarthrosis etc) can occur at virtually any site on the body. Other adverse effects include nausea, vomiting, abdominal pain, bloating, flatulence and an altered sense of taste. There are reports of rare cases of purple toe

syndrome, warfarin-induced skin necrosis and calciphylaxis with warfarin therapy. Warfarin-induced skin necrosis is a serious condition in which subcutaneous tissue necrosis occurs due to an acquired protein C deficiency following treatment with warfarin. The risk of necrosis increases in patients with protein C or protein S deficiency [2].

### CASE REPORT

A 61-yr old male patient with Known case of Rheumatic heart disease and mitral valve replacement done on 2012, was presented with complaints of abdominal pain and vomiting. He was on Tab. warfarin 5mg (Target INR-2.0) for the past years and he himself adjusted the dose to Tab. Warfarin without consulting a doctor for the past 5 years. His INR values checked outside the hospital shown 1.0 during admission (02-04-22) under cardiology department, it was rechecked in hospital and found INR > 5.0 (Normal: <1.5) with PT >2 minutes (9.4-12.5 seconds). During the physical examination, there was swelling and blackish colour on both legs. USG abdomen done on 4<sup>th</sup> April 2022 and found ileocolic intussusception with intramural hematoma, it

**Table 1.1 :** PT-INR levels of patient during admission.

LAB TESTS	Day1	Day2	Day3	Day4	Day5	Day6	Day7	Day8	Day9
PT (9.4 - 12.5 sec)	>2 mins	20.3 sec	12.7 sec	>2 mins	60.85 sec	41.7 sec	24.5 sec	16 sec	20.2 sec
INR ( )	>5	1.70	1.02	>5	>5	3.58	2.09	1.38	1.72

**Table 1.2:** Serum creatinine values of patient during admission

LAB TEST	2-4-22	7-4-22	10-4-22	12-4-22	15-4-22	17-4-22	18-4-22	20-4-22
S.creatinine (mg/dl)	1.1	1.7	2.7	4.2	2.5	1.7	1.4	1.3

was confirmed by CT abdomen on 5<sup>th</sup> April 2022. Patient was shifted to surgery department and taken for emergency laparotomy on 6<sup>th</sup> April 2022 after preoperative evaluation and optimisation. Intra operatively ileocolic intussusception with multiple subserosal hemorrhagic patches over bowel loops were noted. The intussusception was not reducible and hence proceeded with resection anastomosis. Post-operatively, blood products (Whole blood and Fresh frozen plasma (FFP)) transfusions were carried out. On the 6<sup>th</sup> day patient was found to have deranged renal parameters (Ser. Creatinine: 2.7mg/dl (10/4), 3.0mg/dl (11/4), 4.2mg/dl (12/4) for which nephrology consultation was sought and they advised for restricted fluid intake. Patient was reviewed from cardiology side in view of elevated PT for which regular PT-INR monitoring was advised. Patient developed sudden onset of breathlessness on 11<sup>th</sup> April 2022 with deteriorating renal parameters and he underwent one cycle of hemodialysis in nephrology department. Patient was shifted to ward on 13<sup>th</sup> day after renal parameter values and INR values showed steady improvement, Tab. Acitrom (Acenocoumarol) 2mg was started on 13<sup>th</sup> day. Patient's general condition improved and was discharged after appropriate patient counselling on 20<sup>th</sup> April 2022.

## DISCUSSION

Warfarin is a coumarin anti-coagulant, widely used for the therapeutic and prophylactic anti-coagulation. Although it is considered as a lifesaving medicine, it is associated with the several adverse effects [3]. The most significant adverse effect associated with warfarin is spontaneous subcutaneous or intramuscular bleeding; nevertheless, warfarin may also cause intraabdominal hemorrhages with higher mortality risk.

A case reported by Kavya Vinod et al. shows accidental overdose of warfarin due to poor adherence 80year old male with atrial fibrillation.

A research article was published in British Journal of Medicine on 2015 in which they compared the risk of gastrointestinal bleeding with dabigatran, rivaroxaban, and warfarin. They came with a conclusion that the risk of

gastrointestinal bleeding increased after age 65, such that by age 76 the risk exceeded that with warfarin among atrial fibrillation patients [4]. Another research article in the Circulation, American Heart Association in 2013 conducted a study on the management and Outcomes of major bleeding during therapy with Dabigatran or Warfarin. They found out that the patients who had major bleeding on Dabigatran required more red cell transfusions but received less plasma, required a shorter stay in intensive care and had a lower mortality compared with that of warfarin induced major bleeding [5]. A study in the New England Journal of Medicine in 2013 showed the extended use of Dabigatran, Warfarin and placebo in venous thromboembolism where Dabigatran was effective in venous thromboembolism and also carried a lower risk of bleeding compared to warfarin but carried a higher risk than placebo [6].

Low dose of Oral Anticoagulants (OACs) is effective in the treatment of minor bleedings whereas, surgical and conservative treatment methods are required in case of major intra-abdominal bleedings [7]. Acute abdominal pain may occur in patients receiving warfarin and suffering from non-traumatic intra-abdominal hemorrhage. Coagulation parameters are usually disrupted in such patients. In patients presenting with acute abdominal pain, abdominal ultrasound and computer tomography are the most commonly preferred imaging methods employed for a definitive diagnosis. In the case of hemorrhages associated with the use of warfarin, it is generally sufficient to adjust the dose of oral anticoagulant for the treatment of hemodynamically stable minor bleedings, which are not accompanied by any disorder other than skin manifestations. If vitamin K is to be added to the therapy, it should be noted that INR response may be seen 24 hours after oral intake and within four-six hours after intravenous administration [8].

## CONCLUSION

Warfarin is commonly used to prevent thromboembolic events in patients at risk for stroke and cardioembolic events. The degree of anticoagulation is variable among each patient and is influenced by many factors; therefore, patients must be monitored frequently to assess potential adverse effects related to treatment.

Bleeding associated with warfarin use is an uncommon complication and an important cause of mortality. Consequently, a “black box” warning about warfarin's bleeding risk was added to the US product labeling in 2006. Physicians, clinical pharmacists, nurses and any health workers should educate the patients about the importance of periodic consultation with clinical practitioner, regular monitoring of PT- INR values and seek medical attention if signs and symptoms of bleeding occur. A Medication Guide or leaflet can be provided to patients who are on oral anticoagulant therapy and on high risk medications.

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