IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Case Report
March 2023 Vol.:26, Issue:4

A Case Report on Coumarin Induced Coagulopathy

IJPPR
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ISSN 2349-7203
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Submitted: 22 February 2023
Accepted: 28 February 2023
Published: 30 March 2023

Keywords: Oral anticoagulants, Acenocoumarol, INR, PT, Coagulopathy, vitamin K

ABSTRACT

Introduction: Coumarin derivatives have anti-coagulant effects and are useful in preventing and treating arterial and venous thromboembolism. The major complication of coumarin therapy is bleeding. Prothrombin time (PT) and international normalized ratio (INR) are monitored to detect the risk of bleeding. **Case report:** Here we describe the case of a 74-year-old female patient, who presented with major complaints of multiple ecchymosis all over the body for 3 days, along with ruptured Deep Vein Thrombosis (DVT) over her left lower limb. She was already a known case of hypertension and type 2 diabetes mellitus with DVT in the lower limb. She has been taking T. Acitrom 2 mg (acenocoumarol) for the past 5 years without physician's knowledge. Her laboratory reports showed elevated levels of APTT (180 secs), PT (104 secs), INR (>7.5) and D-dimer (935 mcg/L). Based on the symptoms and laboratory investigations, the patient was diagnosed with Acitrom induced coagulopathy. She was treated with Inj. Vitamin K 10mg IV OD for the next 5 days. After 5 days, her INR value gradually reduced from >7.5 to 0.95. **Conclusion:** Coagulopathy associated with coumarins should be treated promptly, or it may become life-threatening. Proper education to the patients regarding early recognition of symptoms and life style modifications will help in preventing major complications.

INTRODUCTION:

Coumarinic oral-anticoagulants (COAs) possess anticoagulant properties and are beneficial for the primary and secondary prevention of arterial and venous thromboembolism in patients with prosthetic heart valves, peripheral arterial disease, atrial fibrillation, antiphospholipid syndrome and recurrent myocardial or cerebral infarction. Some examples of coumarins include warfarin, Acenocoumarol, umbelliferone and phenprocoumon. Though Acenocoumarol (acitrom) and warfarin belong to the same class, acitrom has a longer half-life and lesser interactions when compared to warfarin.[1]These agents are Vitamin K antagonists (VKAs) and work by inhibiting the action of the enzyme, Vitamin K epoxide reductase which is necessary for the activation of vitamin K-dependent coagulation factors II, VII, IX, X and regulatory proteins C, S, and Z. This enzyme is also essential for the regeneration and maintaining required levels of vitamin K for blood clotting.[2]

Overdose of oral anticoagulant therapy leads to a deficiency of vitamin K-dependent proteins, causing bleeding as an adverse effect. To minimize this complication, the prothrombin time (PT) - expressed as the international normalized ratio (INR) is used for achieving optimal therapy and monitoring the degree of coumarin-associated anticoagulation. Normal INR is between 0.8 and 1.2. The INR for patients on VKA therapy varies according to the underlying condition but is typically between 2.0 and 3.5. An INR of less than 2 is associated with an increased risk of thromboembolism and an INR of 4 or more is associated with an increased risk of bleeding.[3]

The potential management options available to counteract the vitamin k antagonist induced coagulopathy include withholding oral anticoagulants and administering vitamin K. Other options available are withholding oral anticoagulants, administering vitamin K and administering fresh frozen plasma.[2]

CASE REPORT:

A female patient age 74 years was admitted in the cardiology department with major complaints of multiple ecchymosis all over the body for 3 days, along with ruptured Deep Vein Thrombosis (DVT) over her left lower limb. She has a history of multiple intramuscular and intravenous injections for treating cough and cold in a day-care centre near her home for past 10 days. She was already aknown case of hypertension and type 2 diabetes mellitus with DVT in her lower limb. She was treated with T. Newtel 40mgOD (telmisartan) for

hypertension, T. glycomet 500mg (metformin) OD for diabetes, T. acitrom 2mg (acenocoumarol) HS for DVT, and several uses of T. dulcoflex (bisacodyl) HS for constipation from past 5 years. She had not visited the physician for the follow-up and continued T. acitrom 2mg for 5 years without physician's knowledge. Her family history was not relatively significant. On general examination she was conscious and oriented; physical examination showed a pulse of 80 bpm, respiratory rate of 20/min and blood pressure of 170/100 mmHg. Her laboratory reports showed a decreased level of Haemoglobin - 6.1 mg/dl and elevated levels of APTT- 180 secs, PT- 104 secs, INR - >7.5 and D-dimer - 935 mcg/L. Based on the symptoms and laboratory investigations, the patient was diagnosed to have Acitrom induced coagulopathy.

The patient's treatment was started with Inj. Vitamin K 10mg IV OD for the next 5 days along with Inj. Rantac 50mg IV BD, Inj. Emeset 4mg SOS, Inj. Tazar 4.5gm Q12H and Inj. Dalacin C 600mg IV BD. On subsequent administration of Inj. Vitamin K for 5 days, her INR value was found to be gradually reducing from >7.5 to 0.95.

DISCUSSION:

Coumarin derivatives can be problematic, as they have a narrow therapeutic index, high variable dosage requirements, and several drug and disease interactions. Assessment of anticoagulants with Vitamin K antagonists is done by International normalized ratio (INR), which is the ratio of prothrombin time of a patient with standard prothrombin time. 0.8-1.2 is considered a normal INR value. INR for patients on Vitamin K Antagonists is typically between 2.0-3.5. INR <2.0 is considered to have a thromboembolic event and >4.0 is associated with increased bleeding risk.[4] Study reports of Dentali et al analysed that bleeding is reduced and INR value is improved when Vitamin K antagonist is withdrawn.[5]Low dose of Vitamin K injection is required for rapid restoration of INR to the

normal range.[6] When the patient is asymptomatic and has an increased INR level, Vitamin K can be administered intravenously, subcutaneously or by oral route to correct the INR value to normal. To treat the bleeding that is life threatening, the following 3 steps are to be followed:

1. Withholding of anticoagulants is required to avoid further bleeding. Withholding only results in a slow reduction of INR value.

2. Administration of Vitamin K in the intravenous route has a rapid rate of onset when compared with the oral route. Vitamin K injection of 5mg is useful in complete correction in the majority of situations.

3. In major life-threatening conditions, coagulation factors should be replaced. This can be achieved by the administration of fresh frozen plasma and prothrombin complex concentrate.[7]

CONCLUSION:

Coagulopathy is the common and most dreadful adverse effect of coumarin derivatives and its management is vital. The bleeding can occur in any part of the body and patients should be advised to report any signs and symptoms of abnormal bleeding or bruising. This undesired outcome can be controlled by withholding the anti-coagulant and administering vitamin K. Parenteral form of vitamin K is widely used in emergency conditions as it has a rapid onset of action. Close collaboration among health care professionals is of utmost importance to achieve normalisation of INR and control bleeding. Appropriate guidelines can be provided to healthcare professionals to guide them in managing patients taking coumarin.

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