ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 9, Issue 2, 2016

Online - 2455-3891
Print - 0974-2441

Case Report

ACENOCOUMAROL OR WARFARIN: WHICH IS THE CLINICIAN'S ALLY?

KARTHIK RAO N[1], NAVIN PATIL[2]*, A AVINASH[2], HANDATTU MANJUNATHA HANDE[1], SUSHIL KIRAN KUNDER[2], RAGHAVENDRA RAO N[1]

[1]Department of Medicine, Kasturba Medical College Manipal, Manipal University, Manipal - 576 104, Karnataka, India. [2]Department of Pharmacology, Kasturba Medical College Manipal, Manipal University, Manipal - 576 104, Karnataka, India. Email: navin903@gmail.com

Received: 16 October 2015, Revised and Accepted: 21 December 2015

ABSTRACT

Warfarin and acenocoumarol are commonly prescribed oral anticoagulant drugs that are used in the prevention and treatment of thromboembolic disorders across the world. Although both these drugs act by a similar mechanism, there are significant differences between them, especially in terms of their half-lives, and more importantly, in their variability in response pharmacogenetically. This case report highlights an instance wherein warfarin proved to provide a much more stable anticoagulant cover, as compared to that provided by acenocoumarol.

Keywords: Thrombosis, Bleeding, Antiphospholipid antibody syndrome, Anticoagulant, International normalized ratio.

INTRODUCTION

Anticoagulants are broadly divided into two groups, based on their routes of administration: Parenteral and oral. While heparin (along with its derivatives) is the most common used parenteral anticoagulant, warfarin is the most widely used oral anticoagulant. As with any other oral medication, warfarin has the advantages of being more convenient and patient-friendly. Acenocoumarol is another commonly prescribed oral anticoagulant. It acts by a mechanism similar to that of warfarin (vitamin K antagonism). The chief clinical application of warfarin and acenocoumarol is in the prophylaxis and treatment of thromboembolic conditions [1].

Anticoagulant therapy is chiefly monitored by two parameters in the laboratory: Prothrombin time and international normalized ratio (INR). Various guidelines available worldwide advice that a patient who is on long-term anticoagulation for secondary prevention of thromboembolism should be maintained on an INR of 2 to 3 for ideal management [2]. Once INR falls below this range, the patient may show features of thromboembolism, whereas if INR is high, the patient may present with bleeding manifestations.

Unstable anticoagulation (INR not being in the target range) can result from various factors: Anticoagulant drug that is used, dose of the anticoagulant, patient-specific features (such as age, weight, and genetic factors), concomitant medications, etc. [3,4]. Variations in the VKORC1 and CYP2C9 genotypes are said to play a major role in response to warfarin and acenocoumarol. Patients who turn out to be positive for variant alleles in these genes usually tend to have bleeding manifestations, as indicated by a high INR [5]. The case report presented here is one such scenario wherein the patient had variability in response to warfarin and acenocoumarol.

CASE REPORT

A 30-year-old male alcoholic (now, reformed) patient walked into our hospital with chief complaints of abdominal pain (periumbilical and colicky pain), vomiting (but no hematemesis) and bloodstained stools for the past 10 days.

The patient's past history revealed that he was diagnosed to have acute porto-superior mesenteric vein thrombosis along with ischemia of distal ileal loops (based on the abdominal contrast-enhanced computed tomography report issued 2 weeks prior to the current visit). As part of the management of the thrombosis, the patient had been initiated on subcutaneous enoxaparin. A repeat abdominal ultrasonography, performed 2 days later, had shown an improvement in his status. Portal vein was now found to be patent, but the superior mesenteric vein was still occluded. The patient had been discharged, owing to the improvement in his condition, on oral acenocoumarol (2 mg/3 mg on alternate days) as maintenance anticoagulant therapy. Oral hyoscine was recommended for symptomatic management of his abdominal pain.

On further evaluation of the etiology of thrombosis in this young ambulatory patient, lupus anticoagulant antibody test turned out to be positive. This turned the diagnosis in favor of antiphospholipid antibody syndrome (APLA). Other tests like routine blood counts (except for mildly elevated erythrocyte sedimentation rate), global ANA, JAK-2 mutation, serum copper levels and sickle cell factors came out negative or within normal limits. Furthermore, liver function tests were normal.

Further, during the current admission, when blood samples were drawn, the patient's INR was found to be high (6.21), which explains the bleeding manifestation. Hence, the dose of acenocoumarol was titrated from the alternate day regimen of 2 mg/3 mg to only 2 mg daily. The INR dropped to 5.3 the next day. As this was still on the higher side, and since the patient was not relieved of blood in stools, the dose was further reduced to 1 mg per day. Following this, the INR dropped to 1.98 on the next day. On the subsequent days, INR kept dropping until a value of 1.18 was seen 3 days later. Since this level is not ideal for a patient with thrombosis, acenocoumarol was stopped, and warfarin was started instead (at a dose of 2 mg per day). The dose of warfarin was titrated up to 5 mg per day, to achieve an optimal INR (2.48, in this case). The patient had no more bleeding manifestations, and he was also under a good maintenance therapy for his thrombotic state.

DISCUSSION

The half-life of warfarin is around 36 hrs, whereas that of acenocoumarol is 10 hrs. Warfarin can thus theoretically provide a more stable anticoagulant cover by preventing the fluctuation of the clotting factors (especially, factor VII). This has been evidenced by Undas *et al*., who concluded from their research that warfarin provides a significantly better control than does acenocoumarol. Based on their study, they have also advised switching from acenocoumarol to warfarin if the patient has unstable anticoagulation [1].

However, a study by Barcellona *et al*. has shown that half-lives of these two drugs may not play a significant role in the clinical setup. The

authors of this study further stated that the anticoagulant profiles of both the drugs are comparable, both clinically and statistically [6].

In the current case, there was unstable anticoagulation, when the patient was on acenocoumarol, as evidenced by bleeding manifestations, despite adjustments in the dose of the anticoagulant. Once he was shifted to warfarin therapy, his anticoagulant status stabilized, and he no longer had bleeding. Although the cause for the same could not be elicited, we think it could be the pharmacogenetic variations that caused this differential response to warfarin, but not to acenocoumarol.

CONCLUSION

Warfarin is the most widely used oral anticoagulant worldwide. However, other drugs like acenocoumarol are occasionally used. From this case report, it is evident that warfarin and acenocoumarol do not have the same amount of credibility in providing stable anticoagulation. Further studies are required to confirm the same, and to understand the cause for this variability in response. Further, if feasible, genetic screening can be done to check for polymorphisms in CYP2C9 and VKORC1 before initiating anticoagulant therapy.

REFERENCES

1. Undas A, Ciesla-Dul M, Zólcinski M, Tracz W. Switching from acenocoumarol to warfarin in patients with unstable anticoagulation and its effect on anticoagulation control. Pol Arch Med Wewn 2009;119(6):360-5.
2. Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G, *et al*. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008;133 Suppl 6:160S-98.
3. Gurwitz JH, Avorn J, Ross-Degnan D, Choodnovskiy I, Ansell J. Aging and the anticoagulant response to warfarin therapy. Ann Intern Med 1992;116(11):901-4.
4. Sconce EA, Khan TI, Wynne HA, Avery P, Monkhouse L, King BP, *et al*. The impact of CYP2C9 and VKORC1 genetic polymorphism and patient characteristics upon warfarin dose requirements: Proposal for a new dosing regimen. Blood 2005;106(7):2329-33.
5. Beinema M, Brouwers JR, Schalekamp T, Wilffert B. Pharmacogenetic differences between warfarin, acenocoumarol and phenprocoumon. Thromb Haemost 2008;100(6):1052-7.
6. Barcellona D, Vannini ML, Fenu L, Balestrieri C, Marongiu F. Warfarin or acenocoumarol: Which is better in the management of oral anticoagulants? Thromb Haemost 1998;80(6):899-902.