

Anticoagulation Overdose When Receiving Anticoagulant Therapy Vitamin K Antagonists Who Had Use Of The Cruciferous Family Green: A Review Of The World's Medicine

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ABSTRACT

Objective: Study to find out the influence of risk factors that are green vegetables of the cruciferous family that can cause anticoagulation over-dosage drugs who received anticoagulant therapy with vitamin K antagonists.

Methods: Present case series study and review of the medical literature, Study on 5 case series of heart failure, mechanical mitral valve after mitral heart valve surgery, and atrial fibrillation had coagulation disorders who receiving anticoagulant therapy with vitamin K antagonists and have used greens vegetables of the cruciferous family.

Results: A Study on 5 cases of the main disease as atrial fibrillation (AF), heart failure with dilated heart chambers, and artificial heart valve surgery who were using vitamin K antagonist anticoagulants (VKAs) drugs with green vegetables of the Cruciferous family that can cause anticoagulation overdose and was discovered when they were medical examination at an International General Hospital in Vietnam in 2022. Clinical cases found to have anticoagulation overdose including the subcutaneous hemorrhagic bruise and who had an anticoagulant overdose disorder with an INR of 7.32, 5.11, 7.63, 8.22, and 10.91, respectively. We were acutely managed in timely resuscitation and returned the coagulation index to normal.

Conclusion: It is recommended that patients who are using vitamin K anticoagulant drugs, should balance their diet, and limit green vegetables that contain a lot of vitamin K such as the Cruciferous family to avoid possible blood clotting disorders or the bleeding may to happen.

Keywords: Anticoagulation overdose, vitamin K antagonist anticoagulants, Cruciferous family.

INTRODUCTION

Coagulation disorders in patients taking vitamin K antagonist anticoagulants (Vitamin K antagonists are coumarin derivatives, including warfarin, acenocoumarol, phenprocoumon and ethylbiscoumacetate) when treating patients with cardiovascular diseases that cause embolism such as artificial heart valves surgery, atrial fibrillation, heart failure with severe dilated heart chambers, severe left atrial dilatation, etc. but complications may occur [1], [2], [3], [4], [5]. When complications occur, it is a medical emergency accounting for about 11% of cases [6] or more [2], [3]. An overdose of Anticoagulant (INR > 3.5 for patients with artificial heart valves surgery and INR > 3.0 in the rest) [2], [6]. Many cases of late arrival or late detection can lead to severe blood loss, hemodynamic instability, hemorrhagic shock, even hemorrhagic stroke [7], [8] requiring both resuscitation and intervention and/or emergency surgery [1], [2], [6].

In the past time, Haiphong-Vinhbao International General Hospital at Vietnam is an international standard general hospital established in 2020, there have been many cases of medical examination and treatment in the state of blood clotting disorders requiring timely emergency treatment, even with bleeding complications, which were detected and promptly treated by us, caused by many factors to affects blood clotting disorders, including patients who are taking vitamin K antagonists anticoagulants (VKAs) but are consuming green vegetables of the Cruciferous family [9], [10]. Therefore, we proceed to report typical cases using vitamin K anticoagulants drugs with Cruciferous family greens in a long time and these are only 5 case **series** out of many detected cases.

METHODS

Present case series study and review of the medical literature, Study on 5 case series of the heart failure, mechanical mitral valve after mitral heart valve surgery and atrial fibrillation had an coagulation disorders who receiving anticoagulant therapy with vitamin K antagonists and have used greens vegetables of the cruciferous family.

RESULTS

Study on 5 patients receiving anticoagulant therapy with vitamin K antagonists when using green vegetables of the Cruciferous family [9], [10] who have an anticoagulation overdose, they were discovered when visiting for medical examination and showed bleed symptoms at Hai Phong - Vinh Bao International General Hospital at Vietnam in 2022.

The first case is a 76-year-old, male patient who was admitted to the hospital because of chest pain with atrial fibrillation and ventricular tachycardia on the background of mitral regurgitation grade 2/4, aortic regurgitation grade's 2/4 and heart failure improved function with EF's 64%, ischemic heart disease, bilateral lower extremity venous insufficiency, overweight and obesity with a Body Mass Index (BMI) of 22.04, heart rate of 77 heart beats/min, blood pressure's 92/56 mmHg. The patient with an anticoagulation overdose has an INR index of 7.32 and Platelet (PLT) count within normal limits (PLT's 181 U/L); We inquired carefully for the information about the medical history to discover that the patient had a habit of often consuming green vegetables of the cabbage vegetables and Chinese Broccoli vegetables belong to the Cruciferous family in a long time. For patients with atrial fibrillation and ventricular tachycardia with hypertension as well as heart valve disease, there is an indication for vitamin K anticoagulation drugs and it is necessary that the INR target ranges from 2-3 levels.

The second case is a 74-year-old, female patient, was admitted to the hospital because of weakness and check-ups for coagulopathy. The result of the INR test showed that a high INR index (INR = 5.11), the platelet's 119 U/L and the patient using many episodes of green vegetables such as the Cabbage and turnip family in a long time [9]. The clinical examination showed a heart beat of 86 beats/min, blood pressure of 110/54 mmHg, BMI of 21.33. The main disease is mechanical mitral valve after mitral heart valve surgery due to mitral stenosis, atrial fibrillation and heart failure improved function (EF of 52%) with atrioventricular and ventricular two-chambers pacemaker, on the background of the mitral regurgitation grade 2/4, aortic regurgitation grade 2/4, there is an indication for vitamin K anticoagulation drugs and it is necessary to the INR target ranges from 2.5-3.5 levels.

The third case is a 82-year-old, male patient with atrial fibrillation, Heart Failure mild reduce Ejection Fraction with EF's 48% on the background of multiple dilated heart chambers, chronic renal failure, BMI's 22.04, heart rate of 82 beats/min, blood pressure's 120/70 mmHg. The patient with an anticoagulation overdose has an INR of 7.63, the platelet's 187 U/L and the patient had a habit of often consuming green vegetables as Broccoli (Calabrese) and cabbage of the Cruciferous family [9]. The patients with mitral heart valve surgery, atrial fibrillation and dilated heart chambers, so the INR target ranges of the patient should be from 2.0-3.0 levels.

Although, three patients as above had a coagulation disorder with a high INR index, but there are no signs of bleeding complications, so we just need to indicated for the patients to stop anticoagulation drug in two days and re-evaluate the INR index; The results after 2 days of stopping anticoagulation with INR test results reaching the safe threshold is 1.13, 1.80 and 1.19, respectively. The patients continued to receive anticoagulants with dose adjustment, besides being advised not to use cruciferous vegetables as well as some other foods that interact with vitamin K anticoagulants.

The 4th case is a 84 year old, female patient who was admitted to the hospital because of subcutaneous hemorrhagic bruises under the skin on the arm skin and thigh skin area, the main disease is the heart failure improved (EF: 51%) with dilated heart chambers on the background of slow atrial fibrillation, hypertension, mitral valve regurgitation and aortic regurgitation grade 2/4, cerebral infarction, BMI's normal (BMI: 16.44), heart rate of 61 beats/min, blood pressure's 104/60 mmHg. The patient with an anticoagulation overdose has an INR of 8.22, the platelet's 239 U/L; However, this patient had a habit of often using Cauliflower vegetables which belong to the Cruciferous family. For patients with atrial fibrillation, there is an indication for vitamin K anticoagulation drugs and it is necessary that the INR target ranges from 2-3 levels.

The 5th case is a 57 year old, female patient, the test found that the INR was high (INR: 10.91), the platelet's 258 U/L, had sinus tachycardia 126 heart beat/min, blood pressure's 90/54 mmHg with the main disease is the atrial fibrillation, diabetes, chronic renal failure and coronary artery stents, Chronic Obstructive Pulmonary Disease (COPD), BMI normal (BMI's 25.40); The exploiting information in the history shows the patient used the cabbage vegetables which is belong to Cruciferous family in a long time and was admitted to the hospital because of signs of the subcutaneous hemorrhagic bruises under the skin of the left leg area and left ankle area arms. We conducted emergency treatment, resuscitation and intravenous vitamin K treatment for anticoagulation overdose, after treatment, the patient's coagulation disorder has been stabilized [2].

There two patients as above had a coagulation disorder with a high INR index, there are signs of bleeding complications, The patient was treated urgently in resuscitation, deal with the factors that cause severe coagulation disorders by injecting a dose of 10 mg of vitamin K1 intravenously immediately and 12 hours after repeating a dose of 10 mg of

vitamin K after 12 hours to reverse the blood clotting, the disease is soon stabilized [2], [3]. After resuscitation with intravenous vitamin K treatment for anticoagulation overdose, the patient's coagulation disorder has been stabilized with INR index's 2.45 and 1.19, respectively [2], [3]. The patients continued to receive anticoagulants with dose adjustment, besides being advised not to use cruciferous vegetables as well as some other foods that interact with vitamin K anticoagulants

DISCUSSION

The results showed that the INR test index of all 5 patients of coagulation disorder with bleeding complications above Who had INR index's anticoagulation overdose in the group with high bleeding risk's INR > 5 (INR index of 7.32, 5.11, 7.63, 8.22 and 10.91, respectively) while the Platelet (PLT) count within normal limits [1], [2], [6]. All three cases of patients above used foods containing nutritious green vegetables belonging to the Cruciferous family in the past period in which the vegetables have a lot of vitamin K rich properties [5], [6], [9].

The pathophysiological causes of the increased risk of bleeding events are multifactorial [3]. They may be a direct consequence of urea-associated platelet dysfunction or impaired platelet adhesion and aggregation; impaired platelet glycoprotein IIb or IIIa receptor activation and subsequent glycoprotein binding [6]. Vitamin K is a group of fat-soluble vitamins that are structurally similar and play an important role in the regulation of blood clotting, which is necessary for the assistance of blood clotting. The function of vitamin K as a coenzyme for carboxylase is dependent on vitamin K, an enzyme required for the synthesis of proteins involved in hemostasis (blood clotting) and bone metabolism, and diverse physiological functions. is different. Prothrombin (clotting factor II) is a plasma vitamin K-dependent protein directly involved in blood clotting. Therefore, patients taking these anticoagulants need to maintain a consistent intake of vitamin K to avoid coagulopathy [2], [6]. The study of Eichinger S. (2016) in Austria reported that the complication of anticoagulant overdose had a bleeding rate of about 11% [6], in addition, the study of Karen EG. (2004) statistics show that the rate of bleeding can be up to 10% but up to 25% of patients are likely to bleed at least once a year [4]. Statistics by Connolly SJ. (2009) showed a dangerous complication rate with a hemorrhagic stroke rate of 3.36% and a mortality rate of 4.13% per year in the warfarin group [1].

Patients are using vitamin K anticoagulants with green vegetables containing a lot of vitamin K should moderate and stabilize their diet, because green leafy vegetables such as Cruciferous family containing a lot of vitamin K will reduce the effect of vitamin K anticoagulants drugs [9], this invisibly leads to the need to increase the dose of anti-vitamin K antagonists to achieve the dose or adjust the increase or decrease erratically depending on the INR test index, which is more difficult to control in the adjustment of anticoagulants, When there is an imbalance in the nutritional source of green vegetables rich in vitamin K, it is easy to cause coagulation disorders, including bleeding complications with high INR index.

In principle, in the case of overdosage with vitamin K antagonists, if there is any sign of bleeding with an increase in INR of any value, the vitamin K anticoagulant should be stopped immediately with 10 mg of vitamin K1 intravenously, can re-inject vitamin K1 after 12 hours. Blood transfusion, fresh frozen plasma transfusion depending on clinical condition. For cases with coagulation disorders but no signs of bleeding, depending on the level of INR, we treat differently: In cases with INR < 5, the dose of warfarin can be reduced or stopped 1 warfarin dose and dose adjustment; With an index of $5 < \text{INR} < 9$ usually stop 2 doses of warfarin and then retest and adjust the dose again (or stop 1 dose of Warfarin and take 1-2,5 mg of Vitamin K1); With an INR > 9 but no bleeding, warfarin is usually discontinued with a 10 mg dose of vitamin K1 followed by reevaluation and dose adjustment [2]. All cases of coagulopathy, especially hemorrhagic events, are treated quickly and promptly stabilized by anticoagulation to bring INR back to normal, depending on the patient's condition. As well as the degree of bleeding to choose the time to re-use Vitamin K antagonists or other anticoagulants to ensure safety and stable treatment. When the INR is stable, continue to be monitored periodically every 4 weeks. We can completely handle the situation in time and control the situation.

CONCLUSION

The cases of coagulation disorders who patients receiving anticoagulant therapy with vitamin K antagonists when using green vegetables of the cruciferous family may be considered a risk factor for coagulation disorders and an increased risk of the anticoagulation overdose complications including who had the subcutaneous hemorrhagic bruise complications, so further research is needed into risk factors in coagulation disorders such as an cruciferous family as well as other green vegetables group with a larger sample to confirm that these side effects for patients when they using vitamin K anticoagulants drugs.

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