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Anticoagulation instability with life-threatening complication after dietary modification

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Summary: Anticoagulation instability due to a change in intake of vitamin K after dietary modification was observed in 2 patients on long-term oral anticoagulants. One patient developed diffuse bruises treated conservatively with fresh frozen plasma transfusion and the other had a thrombosed aortic prosthesis which required emergency operation. To prevent such complications, dietary modification especially with food rich in vitamin K should be undertaken with care in patients on long-term oral anticoagulants.

Introduction

Dietary modification has been reported to affect anticoagulation therapy.[1,2] In this paper, we describe two patients who manifested anticoagulation instability with life-threatening complications after major alterations in their usual diets.

Case reports

Patient 1

A 50 year old man had mitral valve replacement in 1984 from which he made an uneventful recovery and was taking warfarin with an international normalized ratio (INR) of 2.0 to 3.0, on an average daily dosage of 5.0 mg. His anticoagulation regime had remained stable. In October 1989, he was admitted because of an attack of gouty arthritis which responded promptly to colchicine therapy. He was discharged and advised for a low purine diet. No alteration in anticoagulation regime was necessary. Two weeks later at follow-up, he was, however, noted to have diffuse bruises. The INR was high at 5.6. The platelet count and liver function test were normal. He admitted to taking no additional drugs and his gouty arthritis had been controlled adequately on a low purine diet alone. As a result, he had given up his former long-standing dietary habit of ingesting porcine liver about 1 kg every week (250 μg vitamin K).[3] He was hospitalized and 300 ml fresh frozen plasma transfused. On the next day, his INR fell to 3.6. He was then discharged and observed closely at the anticoagulation clinic. In the interim, because of the reduced intake of vitamin K, the dosage of warfarin had to be decreased gradually in order to achieve an INR of 2.0 to 3.0. Three months later, when reviewed at clinic, he remained asymptomatic and was taking warfarin 1.5 mg daily with an INR of 2.6.

Patient 2

A 42 year old housewife underwent aortic valve replacement in 1987. Postoperatively, she remained well and was taking warfarin 5 mg daily with an INR of 2.5 to 3.0. Her anticoagulation status had remained stable and throughout her visits to the anticoagulation clinic, major alteration in dosage of warfarin was unnecessary.

In December 1989, she was admitted because of shortness of breath for 3 days. Physical examination revealed signs of heart failure and severe aortic regurgitation. Her INR was low at 1.2. Platelet count and liver function tests were normal. She denied omission of warfarin anticoagulation. Electrocardiogram revealed sinus tachycardia at 120 beats/min. Chest radiograph showed pulmonary oedema. Cross-sectional and Doppler echocardiography confirmed the presence of severe aortic regurgitation. Prosthetic valve dysfunction was diagnosed and she was taken immediately to the operating theatre. At operation, the disc of the aortic prosthesis was noted to be in a fixed and semi-open position, being held by thrombi in the valve annulus. The thrombi were then removed carefully and the aortic prosthesis regained its normal function. She had an uneventful recovery.

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Direct questioning revealed that her family, because of the cold winter, were having 'hot pots' frequently for the past 4 weeks. As a result, she had been taking about 5 kg broccoli (10 mg vitamin K) and 0.5 kg porcine liver (125 μg vitamin K)[3] weekly for 4 weeks. The resulting excess of ingested vitamin K antagonized the effects of warfarin and accounted for her state of under-anticoagulation. Two months later at follow-up, she was taking her previous warfarin dosage of 5 mg daily with an INR of 2.9.

Discussion

Many drugs are known to affect warfarin anticoagulation.[4,5] The dangers of dietary modification in patients on long-term oral anticoagulants, however, are less often considered. Leafy vegetables (dark-green and deep-yellow), which provide 50–800 μg vitamin K/100 g, are the best sources of vitamin K.[6] Small but significant amounts (5–50 μg/100 g) are also present in milk and dairy products, meats, eggs, cereals, fruits, and other vegetables.[6] Liver is the only animal tissue containing significant amounts of vitamin K (porcine, 25 μg/100 g; bovine 92 μg/100 g) since it is concentrated there after absorption.[3] As warfarin interacts with the inactive precursors to the vitamin K dependent proteins,[7] it is conceivable that irregular intake of food rich in vitamin K may modify the effect of anticoagulant therapy. Dietary modification resulting in a lower intake of vitamin K would be expected to potentiate warfarin anticoagulation. Severe coagulation defect has occurred with dietary vitamin K deficiency[8] and life-threatening bleeding tendency observed in one patient on warfarin anticoagulation after he had stopped consuming liver.[9] Dietary modification resulting in a higher intake of vitamin K, on the other hand, would be expected to cause warfarin resistance. It occurred in patients who had taken liquid-nutrition preparations with vitamin K supplementation[10,11] or ingested excessive green leafy vegetables.[1,2,12] The degree of anticoagulation instability depends to a great extent on the amount of vitamin K consumed and duration of dietary modification.[13]

In patient 1, the introduction of a low purine diet strikingly potentiated the anticoagulation effect of warfarin. On adherence to his usual maintenance dosage of warfarin, the INR was greater than 5.0 and he had bleeding manifestation which necessitated the transfusion of fresh frozen plasma. No other drugs known to potentiate warfarin anticoagulation had been administered. The anticoagulation instability was temporally related to and caused by his recent dietary modification. With the introduction of a low purine diet after the attack of gouty arthritis, he was told not to consume porcine liver. Continuation of the same dosage of warfarin thus eventually led to the enhancement of anticoagulation described because of a reduction in dietary intake of vitamin K.

In patient 2, her anticoagulant regime had been unaltered since operation and there had been no addition of other drugs. The cause for her state of under-anticoagulation leading to thrombosis of the aortic prosthesis was again due to dietary modification. Because of frequent 'hot pots' in the cold winter, she had an unusual increase in consumption of broccoli and porcine liver. The resulting excess of ingested vitamin K antagonized the effects of warfarin, leading to the life-threatening complication of thrombosed aortic prosthesis. Fortunately, she was operated on in time and has remained well.

Our patients illustrate well how dietary modification can affect anticoagulation stability. Patients on long-term oral anticoagulants who are contemplating a major dietary modification for any reasons require a careful assessment of the consequent changes in intake of vitamin K. Frequent monitoring of the INR with appropriate adjustment in warfarin dosage should then be performed until anticoagulant stability has been restored. Furthermore, to prevent potential life-threatening complications, drastic changes in diet especially food rich in vitamin K are to be avoided.

References

1. Qureshi, G.D., Reinders, T.P. & Swint, J.J. *et al.* Acquired warfarin resistance and weight-reducing diet. *Arch Intern Med* 1981, **141:** 507–509.
2. Kempin, S.J. Warfarin resistance caused by broccoli. *N Engl J Med* 1983, **308:** 1229.
3. Olson, R.E. Vitamin K. In: Goodhart, R.S. & Shils, M.E. (eds) *Modern Nutrition in Health and Disease.* Lea and Febiger, Philadelphia, 1980, pp. 170–180.
4. Udall, J.D. Drug interference with warfarin therapy. *Clin Med* 1970, **77:** 20–25.
5. Watson, P.G., Lochan, R.G. & Redding, V.J. Drug interaction with coumarin derivative anticoagulants. *Br Med J* 1982, **285:** 1045–1046.
6. Olson, J.A. Recommended dietary intakes (RDI) of vitamin K in humans. *Am J Clin Nutr* 1987, **45:** 687–692.
7. Stenflo, J., Fennland, P., Egan, W. & Roepstorff, P. Vitamin K dependent modifications of glutamic acid residues in prothrombin. *Proc Mol Acad Sci* 1974, **71:** 2730–2733.
8. Colvin, B.T. & Lloyd, M.J. Severe coagulation defect due to a dietary deficiency of vitamin K. *J Clin Pathol* 1977, **30:** 1147–1148.
9. Kalra, P.A., Cooklin, M., Wood, G., O'Shea, G.M. & Holmes, A.M. Dietary modification as cause of anticoagulation instability. *Lancet* 1988, **ii:** 803.

10. Michaelson, R., Kempin, S.J., Navia, B. & Gold, J.W.M. Inhibition of the hypoprothrombinemic effect of warfarin (Coumadin) by Ensure Plus, a dietary supplement. *Clin Bull* 1980, **10:** 171–172.
11. O'Reilly, R. & Rytand, D. Resistance to warfarin due to unrecognized vitamin K supplementation. *N Engl J Med* 1980, **303:** 160–161.
12. Fletcher, D.C. Do clotting factors in vitamin K-rich vegetables hinder anticoagulant therapy? *JAMA* 1971, **237:** 1871.
13. Karlson, B., Leijd, B. & Hellstrom, K. On the influence of vitamin K-rich vegetables and wine on the effectiveness of warfarin treatment. *Acta Med Scand* 1986, **220:** 347–350.