Drug Interaction Report

Patient: CF URI test  Date: 01/30/2012 14:58

Warfarin Sodium with Food

Onset: Delayed  Severity: Major  Documentation: Probable

Warfarin Sodium
Member of interaction class: Anticoagulants
Interacting Ingredient(s): Warfarin

Food
Member of interaction class: Food
Interacting Ingredient(s): Food

Effect: Hypoprothrombinemic effects of Warfarin Sodium may be decreased by vitamin K-enriched foods or increased by grapefruit or cranberry juice.

Mechanism: Large quantities of vitamin K from food may competitively inhibit Warfarin Sodium binding on end-organ cell receptors. Grapefruit juice, and possibly cranberry juice, may inhibit intestinal cytochrome P450 3A4 and increase the bioavailability of warfarin.

Management: All patients receiving Warfarin Sodium should be advised to avoid abrupt changes in dietary vitamin K content. Large quantities of grapefruit juice or cranberry juice should be avoided. Strict vegetarian diets should be avoided. Monitor international normalized ratio and adjust warfarin dosage accordingly.

Discussion: Acquired warfarin resistance has been linked to high or irregular intake of vitamin K (VK) (2,6). Two studies have found high intake of VK or VK-rich foods for 1, 2, or 7 days interfered with anticoagulation therapy (5,10). Case reports have shown changes in anticoagulant effect in patients on stable warfarin who began consuming more VK-rich foods (3,4,8,15,18,19). One study showed that a diet rich in brussel sprouts stimulated warfarin elimination (7); another showed that food decreased the rate, but not extent, of warfarin absorption (1). In 2 case reports, avocado, although low in VK, decreases the effects of warfarin (9). A 44-year-old white male with stable INR had an abrupt decrease of INR from 3.8 to 1.37 (12). He had recently started drinking at least 1/2 gallon of green tea daily. After stopping green tea, INR increased to 2.6. Green teas may contain large quantities of VK (13). INR values in a 70-year-old man on stable warfarin for 7 months decreased from 2.5 to 1.6 after 4 weeks of soy milk and no other dietary or drug changes (17). The effect of frozen grapefruit juice (GFJ) on PT in 9 patients on stable warfarin doses was studied (11). Patients ingested 250 ml of GFJ 3 times/day for 1 week while taking warfarin. There was no significant difference in PT or INR in any patient (11). In a separate randomized crossover study of 24 patients on routine doses of warfarin (14), the frequency of dose adjustments in a GJ versus orange juice group were similar. Grapefruit Seed Extract (GSE) products have been shown to increase INR (29). Mango has been reported to increase INR in 13 patients by an average of 38% (16). Nineteen cases (20,22,24,25,27,28,31,38) indicate that increases in INR and death (31) have occurred in patients on warfarin who ingested cranberry juice (CJ) or cranberry juice (30). In contrast, 3 well controlled studies have found 250 ml of CJ once to twice daily for 7 to 14 days does not affect the plasma warfarin concentration, PT, and/or INR (26,32,37). Caution is advised against drinking large quantities of CJ; however, questions remain regarding the validity of the scientific conclusions being extrapolated to moderate amounts of cranberry juice ingestion (36). An INR increase has been demonstrated in a patient taking fish oil (21) and pomegranate juice (33,34), and milk (35) while decreased warfarin effect has been reported with high-protein, low carbohydrate diets (23).


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