



PIC QUESTION OF THE WEEK: 4/16/07

Q: Does cranberry juice alter the INR in patients receiving warfarin?

A: Cranberry (*Vaccinium macrocarpon* and other species) products are used extensively as foods and beverages. The fruit is available in various forms including juice, concentrated extract, cranberry juice cocktail (~ 26-33% pure cranberry juice), capsules, etc. For years, cranberry *juice* has been recommended as an alternative remedy for the prevention of acute cystitis in women. Warfarin, the standard oral anticoagulant in the United States, has been associated with countless drug and food interactions. Foods rich in vitamin K (e.g. spinach, broccoli, etc.) are known to antagonize the effects of warfarin and reduce INR values. In general, it appears patients must ingest large amounts (≥ 250 g daily) of these vegetables for 5-7 days before a significant decrease in INR is observed. In 2003, the United Kingdom's Committee on Safety of Medicines (a voluntary reporting system similar to FDA's MedWatch) received initial reports of possible interaction between warfarin and cranberry juice. Although many of these cases lacked sufficient detail to prove causality, there was a consistent temporal relationship to cranberry juice intake. In most of these cases, as well as subsequent reports, the amount of cranberry juice ingested each day was quite large and ranged from approximately 750 ml – 2 L. A recent randomized, placebo-controlled, double-blind, cross-over study evaluated the effects of daily ingestion of 250 ml of cranberry juice cocktail on INR values in seven male patients chronically treated with warfarin for atrial fibrillation. There was little effect of cranberry juice cocktail on INR values in these study patients. The authors concluded that cranberry juice consumption did not have to be completely eliminated in patients receiving warfarin, but their INR values should be monitored. The mechanism by which cranberry may alter the INR during warfarin administration has not been established. The fruit contains several phenolic compounds including various flavonoids. Proposed mechanisms include the ability of some flavonoids to inhibit the CYP2C9 isoenzyme, thus decreasing metabolism of warfarin's more active S-enantiomer with resultant increases in INR. Others have suggested that the relatively high concentration of salicylic acid in cranberries may alter platelet function or displace warfarin from its binding sites. None of these mechanisms are supported by the known pharmacokinetic characteristics of cranberry juice. This food-drug combination is cited in most of the standard databases used in screening for potential drug interactions. In summary, it appears that small amounts of cranberry juice will not affect the INR in patients taking warfarin.

References:

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