

Does Ginseng Affect Warfarin Response?

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Much has been written about the effect of herbal supplements on prescription medications, particularly those with a narrow therapeutic index such as oral anticoagulants. Nonetheless, considerable confusion remains, because much of the data comes from isolated case reports or small studies in healthy individuals.

A recent well-controlled study assessed the effect of ginseng on the anticoagulant response to warfarin, and it provides—for the first time—credible evidence that ginseng does interact with warfarin in a way that may be clinically important in some patients.

What Did the Recent Study Reveal?

Twenty healthy people took warfarin for 3 days with and without pretreatment with American ginseng for 2 weeks. Ginseng was associated with a modest reduction in both the international normalized ratio (INR) and the warfarin area under the plasma concentration-time curve.¹

Although the mean reduction in warfarin effect and plasma concentrations was modest, it did occur in most of the people. The effect also was quite variable from person to person, with some individuals having a substantial change.

This study was performed in healthy people, and it seems likely that the effect on warfarin could result in adverse outcomes in at least some patients who receive the combination.

How Does This Result Compare with Results of Previous Studies?

In a previous case report, a 47-year-

old man who had been stabilized on warfarin with an INR of about 3 had a reduction in his INR to about 1.5 after he took ginseng for 2 weeks.² After stopping the ginseng for 2 weeks, his INR returned to about 3 again. In another case of possible reduction in warfarin effect with ginseng, thrombosis occurred in a prosthetic aortic valve.³ Both of these cases are consistent with the findings of the controlled study cited above—namely, that ginseng can reduce the effect of warfarin.

Another study in healthy individuals failed to find any effect of ginseng on a single oral dose of warfarin.⁴ Although this study appears to conflict with the studies cited above, the ginseng was given for only 7 days, which may have been an insufficient period to see the interaction. Also, the dose and type of ginseng were different from those in the studies that found a reduced warfarin effect with ginseng.

What Is the Mechanism for This Interaction?

The mechanism for the effect is not established. Available evidence suggests that ginseng administration does not result in enzyme induction, at least for CYP1A2 and CYP3A4.^{5,6} Little evidence exists, however, on whether or not ginseng affects CYP2C9, which is the cytochrome P-450 isozyme primarily responsible for S-warfarin metabolism. So it is possible that ginseng modestly induces CYP2C9, but other potential mechanisms have not been rigorously ruled out.


What Are the Limitations of the Available Data?

Numerous ginseng products are available, with different sources of the ginseng root, different methods of preparation, and different recommended doses. Indeed, some ginseng products have been found to have no

ginseng at all. It is difficult, therefore, to compare one study of a ginseng drug interaction with any other study. For the same reasons, it is difficult to apply the results of published studies to a specific patient, because it would be rare for the patient under consideration to be taking the same brand as in the study. Moreover, even if the same ginseng brand is used, different lots of the product are likely to have different amounts of active constituents.

How Should This Interaction Be Handled?

To reduce the likelihood of an adverse drug interaction between warfarin and ginseng, pharmacists should consider the following recommendations:

1. Ideally, patients on warfarin should avoid taking any ginseng products, and it would be prudent to warn patients accordingly. Indeed patients on warfarin would be well advised to avoid all herbal medications.
2. If a warfarin-treated patient insists on taking ginseng, the patient should be advised not to switch from one brand to another, and not to vary the dose of ginseng. This course of action will not guarantee a stable interaction, of course, because the same brand can vary from lot to lot, but it is probably a sensible precaution.
3. If a patient on warfarin has any change in his or her ginseng intake (eg, starting, stopping, change in dose, change in brand), it would be prudent to monitor for any change in the anticoagulant effect of warfarin. 

For a list of references, send a stamped, self-addressed envelope to: References Department, Attn. A. Stahl, Pharmacy Times, 241 Forsgate Drive, Jamesburg, NJ 08831; or send an e-mail request to: astahl@mwc.com.