



Thyroid Replacement and Oral Anticoagulants

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Few drug–drug interactions generate more computer alerts for pharmacists than the interaction between thyroid replacement and oral anticoagulants. Yet, with all of this attention, considerable confusion and debate remain about the clinical importance of this interaction. Some are of the opinion that it is perfectly acceptable to give thyroid replacement medication and oral anticoagulants concurrently. Others believe that the combination can cause serious, even fatal, overanticoagulation. Both viewpoints are correct—it just depends on the circumstances under which the 2 drugs are given.

How Does Increasing Thyroid Activity Affect Oral Anticoagulants?

It has been known for several decades that increasing thyroid activity—either through increased output of the thyroid gland or by administering thyroid hormones—increases the anticoagulant response to warfarin and other oral anticoagulants.¹⁻⁴ The mechanism for this effect is not completely established, but it appears that the catabolism of clotting factors increases as thyroid activity increases. So, as a person's thyroid status changes along the continuum (Table), warfarin response changes as well.

When Is This Interaction Dangerous?

This interaction can result in life-threatening overanticoagulation under certain circumstances, but these circumstances do not occur frequently. The typical case would be an ambula-

tory patient stabilized on chronic warfarin therapy, who is then diagnosed with hypothyroidism. Due to the reduced thyroid status, the patient is likely to be taking large doses of warfarin, perhaps up to 20 mg per day or more. When the patient is then started on thyroid replacement therapy, the warfarin response is normalized, and the patient becomes overanticoagulated. This response usually takes place gradually, and it may take up to several weeks for the anticoagulant effect to stabilize. If the patient's anticoagulant response is not monitored during this time, he or she may present with a serious bleeding episode.

The interaction also could be dangerous if a patient stabilized on thyroid hormones and warfarin has a change in thyroid therapy. If the thyroid dose is increased, the anticoagulation would tend to increase, but usually not to the same extent as in a patient who is starting thyroid therapy for the first time. Conversely, a decrease in the thyroid dose would tend to decrease anticoagulation, and the magnitude of the decrease in warfarin effect would depend on the magnitude of the decrease in thyroid dosage. In all of these cases, the changes would tend to be gradual, and it may take up to several weeks before a new steady state is reached.

Discontinuing thyroid therapy in a patient stabilized on warfarin also would tend to reduce the anticoagulant response, but it would be difficult to predict the long-term effects. When thyroid therapy is stopped in patients

who have some thyroid function of their own (or even sometimes a normal thyroid gland), their thyroid gland may “wake up” over a month or 2 and start producing thyroid hormones on its own. Thus, prolonged anticoagulant monitoring may be necessary when thyroid replacement is stopped in the presence of chronic warfarin therapy.

When Is This Interaction Innocuous?

The short answer to this question is, “most of the time.” In most cases, the patient is stabilized on a constant dose of thyroid replacement and is euthyroid (having normal thyroid status) when the warfarin therapy is started. Thus, the patient responds normally to the warfarin, and no additional precautions are necessary (other than the normal monitoring that would be done with any person starting warfarin). Even if the patient on chronic thyroid medication is somewhat hypothyroid or hyperthyroid, the routine monitoring at the start of warfarin anticoagulation should result in achieving the appropriate warfarin dose.

Changing from one brand of thyroid medication to another theoretically should not affect oral anticoagulants, because they should be equipotent. If there is any suspicion, however, that the thyroid preparations are not equal, it would be prudent to monitor for changes in anticoagulation.

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Table

Continuum of Thyroid Status Changes		
Hypothyroid	Euthyroid	Hyperthyroid
Decreased	Normal	Increased
Warfarin	Warfarin	Warfarin
Response	Response	Response

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Conclusions

Be aware that changes in thyroid activity are likely to change the anticoagulant response to warfarin. The greater the change in thyroid activity, the greater the change in warfarin. Most patients who have developed serious reactions have been outpatients stabilized on warfarin who were then diagnosed with hypothyroidism and started on thyroid therapy, without additional monitoring for changes

in anticoagulant effect.

Patients taking warfarin and thyroid hormones concurrently need to be advised that any change in their thyroid may result in alteration in their anticoagulant response. This change would include any change in their thyroid therapy, including discontinuation or changes in doses. This possible outcome also would apply to any nondrug alterations in thyroid status, such as radioactive iodine or

thyroid surgery.

Patients on chronic stable doses of thyroid hormones, who are started on warfarin, appear to be at minimal risk, as are patients on chronic stable therapy with both warfarin and thyroid hormones. ⁷

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.

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