

Drugs That Inhibit Levothyroxine Absorption

John R. Horn, PharmD, FCCP, and Phillip D. Hansten, PharmD

Drs. Horn and Hansten are both professors of pharmacy at the University of Washington School of Pharmacy. For an electronic version of this article, including references if any, visit www.hanstenandhorn.com.

Levothyroxine is widely used to treat patients with thyroid disorders. Unfortunately, the bioavailability of levothyroxine can be reduced by a variety of other medications, leading to reduced levothyroxine effect. One would expect that thyroid hormones other than levothyroxine would interact similarly with the drugs described in this article.

Are Some Patients at Greater Risk?

Patients with little or no endogenous thyroid function are likely to be at greater risk, because they cannot increase endogenous thyroid output in response to the reduced levothyroxine absorption. Some patients taking levothyroxine have partial residual thyroid function, and when their thyroid hormone concentrations fall, they can increase endogenous production of thyroid hormones by releasing thyrotropin. This can compensate somewhat for the inhibition of levothyroxine absorption. Variability in endogenous thyroid function probably accounts for the large variation in the outcome of these interactions.

What Types of Drugs Inhibit Levothyroxine Absorption?

The usual suspects of medications known to be involved in reducing levothyroxine absorption include sucralfate, iron, binding resins, and others.

Antacids

Calcium carbonate is well documented to reduce levothyroxine absorption.

Increased thyrotropin concentrations are likely to occur if the calcium carbonate is given chronically with levothyroxine, and in some patients clinical evidence of hypothyroidism may occur. Aluminum hydroxide also appears to inhibit levothyroxine absorption, and limited clinical evidence suggests that magnesium-containing antacids may also interact.

Avoiding Levothyroxine Interactions

- If possible, do not take the levothyroxine (or other thyroid replacement) within 6 hours of the binding agent. The greater the separation the better.
- Try to maintain a constant time interval between taking the levothyroxine and the binding agent. By doing this, any interaction that occurs will tend to be consistent from day to day, and unwanted fluctuations in levothyroxine absorption will be minimized.
- Any time a binding agent is added or deleted from the regimen of a person taking levothyroxine, be alert for clinical evidence of altered thyroid function. The same is true if either the dose of the binding agent or the interval between doses of the levothyroxine and the binding agent have changed. Measurement of thyrotropin concentrations may be needed in some cases.

Sucralfate

Sucralfate contains a considerable amount of aluminum, and this probably accounts for its ability to reduce levothyroxine absorption. In one study, giving the sucralfate 8 hours after the levothyroxine circumvented the interaction.

Phosphate Binders

Patients on hemodialysis may need treatment with drugs that can bind phosphate in the gut, thus reducing their phosphate load. The phosphate binder sevelamer (Renagel) has been shown to

increase thyrotropin concentrations in patients on levothyroxine; hypothyroid symptoms have been reported. Calcium carbonate also can be used as a phosphate binder and it also interacts with levothyroxine, but limited clinical evidence suggests that calcium acetate may not affect levothyroxine absorption.

Iron

Evidence from case reports and clinical studies suggests that iron preparations can inhibit levothyroxine absorption and can result in clinical evidence of hypothyroidism. It seems likely that all iron salts would inhibit levothyroxine absorption, although the magnitude may vary among the various preparations.

Binding Resins

Cholestyramine is known to bind to a number of drugs, and has been shown to reduce levothyroxine absorption as well. The effect of other binding resins such as colestipol (Colestid), colestevlam (Welchol), and ezetimibe (Zetia) on thyroid absorption is not as well established, but be alert for the possibility.

Other Drugs

Other drugs that have been reported to reduce levothyroxine absorption include ciprofloxacin (Cipro), raloxifene (Evista), and caffeine in coffee. More study is needed to establish whether these interactions are likely to be clinically important.

How Can These Interactions Be Avoided?

In general, it is not necessary to discontinue the drug that is reducing levothyroxine absorption (Box). The interactions generally can be circumvented by appropriate adjustment of the dosing times of the levothyroxine relative to the binding agents. ■