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Drugs That Interact With Levothyroxine

An Observational Study From the Thyroid Epidemiology, Audit and Research Study (TEARS)

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Abstract and Introduction

Abstract

Objective The aim of this study was to determine the extent of drug interactions affecting levothyroxine, using study drugs often co-administered to patients on long-term levothyroxine therapy.

Design A retrospective population analysis linking biochemistry and prescription data between 1 January 1993 and 31 December 2012 was used.

Patients The study population was Tayside residents prescribed levothyroxine on at least three occasions, within a six-month period, prior to the start of a study drug. Individuals acted as their own controls pre- and postinitiation of study drug. Overall, 10 999 patients (mean age 58 years, 82% female) being treated with thyroxine were included in the study.

Measurements Changes in TSH following initiation of study drug.

Results Iron, calcium, proton pump inhibitors and oestrogen all increased serum TSH concentration: an increase of 0·22 mU/l ($P < 0.001$), 0·27 mU/l ($P < 0·001$), 0·12 mU/l ($P < 0·01$), and 0·08 mU/l ($P < 0·007$), respectively. For these four study drugs, there was a clinically significant increase of over 5 mU/l in serum TSH, in 7·5%, 4·4%, 5·6% and 4·3% patients, respectively. There was a decrease of 0·17 mU/l (*P*-value 0.01) in the TSH concentration for those patients on statins. The TSH decreased by 5 mU/l in 3·7% of patients. There was no effect with H_2 receptor antagonists or glucocorticoids.

Conclusion This large population-based study demonstrates significant interaction between levothyroxine and iron, calcium, proton pump inhibitors, statins and oestrogens. These drugs may reduce the effectiveness of levothyroxine, and patients' TSH concentrations should be carefully monitored.

Introduction

The number of patients treated with thyroxine has increased from 3·12% of the female population and 0·51% of the male population in Scotland in 1994 to 5·14% and 0·88%, respectively, by 2001.[1] In Western society, the most common cause of hypothyroidism is autoimmune thyroiditis.[2] As symptoms and signs of hypothyroidism are neither sensitive nor specific, laboratory assessment of thyroid status is used to confirm the hypothyroid state. TSH is exquisitely sensitive to the plasma concentration of free thyroid hormones and is used to assess the adequacy of levothyroxine (thyroxine) replacement therapy.[3]

Absorption of thyroxine must be efficient and consistent in order for a patient to experience the sustained benefits of treatment. A direct measure of thyroxine absorption is difficult to obtain and so it is important to monitor TSH concentrations to determine pharmacological thyroid homeostasis.[4,5] Many factors[6,7] such as patient compliance, physiological disturbances, drug–drug interactions and mal-absorptive disease states can increase a patient's dosage requirements for thyroxine. Absorption of thyroxine is pH dependent, and on average 60–80% of the dose administered reaches the systemic circulation within three hours.[2,6–8] Thyroxine has its best therapeutic value if taken 1 h prior to breakfast to ensure optimum stomach acidity for absorption.[8]