A Case of Funny Thyroid Function Test

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Abstract

The preferred treatment for hypothyroidism is oral levothyroxine (LT4) ingestion, in doses that ensure a sustained state of hormonal balance. Yet, despite physician's best effort in dose titration, up to 20-50% of patient fail to achieve optimal thyroid function test, in a condition known as refractory hypothyroidism. Impaired absorption of levothyroxine through the gastrointestinal tract is one of the major causes of not achieving adequate thyroid function control. We describe a case of the effect of bile acid malabsorption syndrome on reducing levothyroxine absorption.

Case presentation :

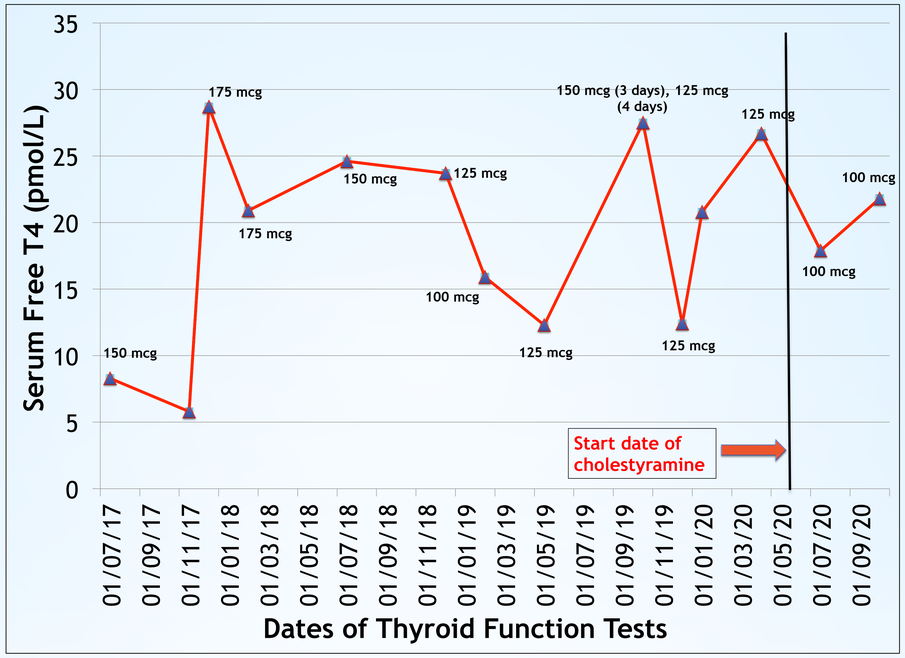
A 49 year old Caucasian woman was referred to the Endocrinology Team with 24 years history of primary hypothyroidism, co-morbidities included premature ovarian failure, depression, and recent changes in bowel habit. To optimise her TFTs, primary care physician altered her Levothyroxine dose several times over the past few years. However patient was left with on-going symptoms of hypothyroidism, mild-moderate diarrhoea, and multiple vitamin deficiencies. She reported full compliance, no dietary changes or overt interacting medications. Malabsorption syndrome was suspected and further investigations were arranged by the gastroenterology team, including faecal elastase, Hydrogen Breath Test for lactose intolerance, and Radionuclide SeHCAT bile study. Bile acid malabsorption syndrome was confirmed and this was thought to be the cause of her inadequate thyroid function control. Since starting a bile acid sequesterant (cholestyramine), her gastrointestinal signs and symptoms have settled and this was associated with a significant clinical and biochemical improvement in her thyroid function tests. Her recent TFTs have completely normalised.

Blood Results

Test	Result	Interpretation
TTG, Serum (u/ml)	0.70	Normal
Vitamin D	17	Profound Deficiency
Folate (nanogram/ml)	2.8	Deficient
B12 (nanogram/ml)	262	Lower end of normal
Ferritin (nanogram/ml)	51	Lower end of normal
Iron	14.2	Normal
TIBC	69.3	Higher end of normal
Transferrin Saturation (%)	20	Lower end of normal

Gastroenterology Results

Test	Result	Interpretation
Colonoscopy	Normal	Normal
Faecal elastase	>500 ug/g	Normal – no signs of pancreatic insufficiency
Faecal Calprotectin	52 ug/g	Normal – no signs of inflammation
NM Radionuclide SeHCAT bile study	Tracer Uptake at 7 days = 2.7%	Abnormal and would be in keeping with a diagnosis of bile salt malabsorption
NM Hydrogen Breath Test Lactose	No significant H_2/CH_4 production	Normal – no evidence of lactose intolerance



Discussion

Gastrointestinal conditions affecting LT4 absorption

- The therapeutic efficacy of levothyroxine (LT4) may be impaired by behavioural, pharmacological, and pathological issues acting as interfering factors.(1) Gastrointestinal malabsorption of oral T4 represent an emerging cause of refractory hypothyroidism and may be more frequent than previously reputed. Approximately 60-82% of the orally administered LT4 is absorbed within the first 3h of ingestion. (2) LT4 is mainly absorbed in the small intestine with 15% absorbed in the duodenum, 29% in the upper jejuno-ileum, and 24% absorbed in the lower jejuno-ileum. (3) This explains the higher dose requirement of levothyroxine in GI malabsorption. T4 and T3 are conjugated to glucuronic and sulphuric acids. These conjugated hormones undergo enterohepatic circulation as partial de-conjugation occurs in small intestine hence releasing small amount of T4 and T3 for reabsorption. (2) Interference with the enterohepatic circulation of thyroid hormone leads to deranged thyroid hormone absorption. Gastrointestinal conditions such as bile acid malabsorption syndrome can play an integral role in reducing levothyroxine malabsorption. Hypothyroidism that persists despite escalation of levothyroxine dose should prompt investigation into underlying GI malabsorption or medication interference.

Bile acid synthesis and circulation

- Bile acids are synthesized in hepatocytes from cholesterol and secreted into small intestine.(4) Bile Acid play a critical role in emulsification and absorption along the small intestine.(4) Enterohepatic circulation is a very efficient system allowing most of bile acid (95%) to be reabsorbed along the small intestine and 5% of bile acid reaches large intestine for excretion

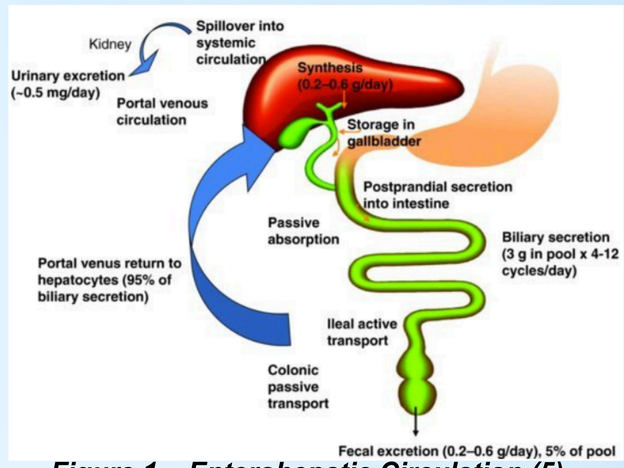


Figure 1 – Enterohepatic Circulation (5)

Bile acid Malabsorption Syndrome

Bile acid diarrhoea can occur idiopathically (type 1), a complication of small bowel resection, post cholecystectomy (type 2) or in association with other conditions such as microscopic colitis, chronic pancreatitis, coeliac disease, small intestinal bacterial overgrowth or diabetes mellitus.(6) The population prevalence is around 1% and is under-diagnosed. Many patients diagnosed with diarrhoea-predominant irritable bowel syndrome have evidence of bile acid diarrhoea. Unabsorbed bile salts pass into the colon, stimulating water and electrolyte secretion and causing diarrhoea. (4) If hepatic synthesis of new bile acids cannot keep pace with faecal losses, fat malabsorption occurs. Contrast studies and tests of B12 and bile acid absorption, such as the 75 Se-homocholic acid taurine (SeHCAT) test are useful investigations.(6)

Management – Diarrhoea usually responds well to bile acid sequestrants, such as colestyramine or colesevelam, which bind bile salts in the intestinal lumen. Aluminum hydroxide can be used as an alternative. (4)

Conclusion

These findings suggest that pre-existing malabsorption can reduce the bioavailability of levothyroxine. The need to use high LT4 doses in the substitutional treatment of hypothyroidism is often the very first sign of one of the pathologies that are connected with malabsorption syndrome, which might have been asymptomatic and undiagnosed previously.

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