Is levothyroxine availability enhanced by grapes?

Ishrat Khan, Ruhina Ahmed, Andrew Aldridge, Onyebuchi Okosieme

Diabetes and Endocrinology Department
Prince Charles Hospital, Cwm Taf University Health Board
Merthyr Tydfil, Mid Glamorgan, Wales

INTRODUCTION

Patients with hypothyroidism are routinely advised to take levothyroxine without food or beverages on the assumption that food substances reduce its availability[1]. However, the pharmacokinetic effect of many common foods are unknown. We describe a patient with high levothyroxine requirements who only achieved adequate replacement by taking grapes along with levothyroxine. Through a cycle of challenge, withdrawal, and-re-challenge, we were able to demonstrate that levothyroxine availability was enhanced by grapes in this case.

Figure 1: Grapes may enhance levothyroxine availability

CASE REPORT

A 30-year-old lady underwent total thyroidectomy for papillary thyroid cancer which had developed on a background of long-standing Hashimoto's thyroiditis and pre-existing hypothyroidism. Prior to this a stable euthyroid state had been maintained for many years with 100 mcg daily of levothyroxine which she regularly took with grapes to make the tablets palatable. Following surgery she continued taking 100 mcg of levothyroxine but on discharge from hospital she was advised, as is routine, to avoid taking her tablets with all foods or beverages. At clinic follow-up we noted that her thyroid status had deteriorated significantly and initially we attributed this to the added impact of total thyroidectomy on the background Hashimoto's disease. Over a number of visits her dose was titrated upwards but serum TSH rose to peak doses of 300 mcg daily (figure 1).

Box 1:
Approach to persistent hypothyroidism in patients on levothyroxine.

1. Check compliance
2. Check dose : 0.8 -1.6 mcg/kg/day
3. Check administration: first thing in the morning or bedtime
4. Exclude interference from diet and drugs
5. Consider co-morbid conditions
6. Consider other causes of elevated TSH: e.g. thyroid hormone resistance, interfering antibodies, TSH secreting pituitary adenoma
7. Consider trial of inpatient therapy
8. Consider supervised weekly dosing

Adapted from reference 1

Box 2:
Factors affecting levothyroxine availability

Reduced absorption: dietary fibre, soy, wholegrain, antacids, omeprazole, calcium carbonate, ferrous sulphate, cholestyramine

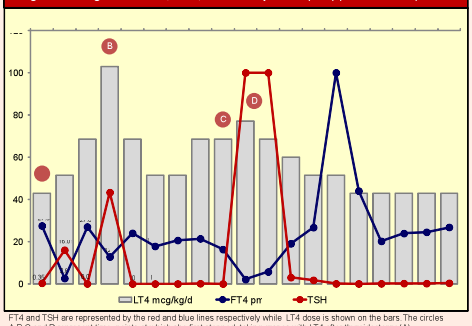
Malabsorption: coeliac disease, atrophic gastritis, helicobacter pylori gastritis, diabetic gastroparesis

Increased clearance: phenobarbitone, phenytoin, rifampicin, carbamazepine, oestrogen compounds, sertraline, nephrotic syndrome

Other mechanisms: tyrosine kinase inhibitors, pregnancy, amiodarone

Adapted from reference 1

Figure 2: Longitudinal FT4, TSH, and levothyroxine (LT4) profile in the patient



FT4 and TSH are represented by the red and blue lines respectively while LT4 dose is shown on the bars. The circles A,B,C and D represent time points at which she first stopped taking grapes with LT4 after thyroidectomy (A), recommenced taking grapes (B), stopped grapes again on a second occasion (C), and finally recommenced grapes (D).

We therefore reviewed her treatment following the approach outlined in box 1. She was compliant with her medication which she took each morning with water at least an hour before breakfast. She was not obese, was not receiving other medications, and we excluded coeliac disease, pernicious anaemia, malabsorption, and other pathological causes of high levothyroxine requirements (box 2). Supervised inpatient treatment and switching to a liquid formulation did not improve thyroid profile. At this stage she highlighted that she had achieved stable thyroid profile in the past by eating a handful of dark grapes along with her tablets. We asked her to resume this practice resulting in a remarkable reduction of levothyroxine requirements to 150 mcg daily (figure 1). A year later she stopped taking grapes during a three week holiday abroad but continued to take levothyroxine appropriately. Thyroid profile a week after she returned showed that she had become hypothyroid again. Re-introduction of grapes once more restored normal thyroid status (figure 1).

CONCLUSIONS

To the best of our knowledge this is the first report of high levothyroxine requirements corrected by ingestion of grapes. A contributory role for grapes is compelling in this case given the demonstration of a challenge-withdrawal-re-challenge cycle. Grapes are small rounded berries of the deciduous vines of the genus *vitis* and are a good source of vitamin C which may increase gastric acidity. Low Gastric pH appears to enhance thyroxine absorption[2] and a recent study showed that administration of levothyroxine with vitamin C improved thyroxine availability[3]. Therefore, it is plausible that ingestion of grapes with levothyroxine provided a favourable acidic environment for levothyroxine absorption in this case. Clinicians and pharmacists should be aware of this potential interaction and further studies will be required to confirm and elucidate the underlying pharmacokinetic mechanisms.

REFERENCES

(1)Okosieme OE. Thyroid hormone replacement: current status and challenges. Expert Opin Pharmacother **12:** 2315-28, 2011.
(2)Centanni M, Gargano L, Canettieri G, Viceconti N, Franchi A, Delle Fave G, Annibale B.I. Thyroxine in goiter, Helicobacter pylori infection and chronic gastritis. N Engl J Med **354**: 1787-95, 2006.
(3)Antúnez PB and Licht SD Vitamin C improves the apparent absorption of levothyroxine in a subset of patients receiving this hormone for primary hypothyroidism. *Rev Argent Endocrinol Metab* **48**: 16-24, 2011.