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Clinical Application of the Levothyroxine Absorption Test in the Diagnosis of Pseudo-Malabsorption

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Abstract We present a variation and clinical application of the Levothyroxine Absorption Test (LAT) in the identification of pseudo-malabsorption of levothyroxine in uncontrolled hypothyroidism, for which there is no current gold standard protocol, and a variety of methods proposed in the literature. The LAT was conducted over 5-days with thyroid function tests conducted pre-LAT, then at day 1 and 5. The thyroid stimulating hormone levels became completely suppressed indicating that there had been previous non-compliance with medication.

Keywords: *levothyroxine absorption test, non-compliance, pseudo-malabsorption*

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1. Introduction

Pseudo-malabsorption of levothyroxine sodium (LT4) in the failure of treatment of hypothyroidism has been recognised as a growing problem and is recognised as one of the commonest causes of persistent TSH elevation. However, the prevalence of pseudo-malabsorption, the name given to non-compliance, is still unknown. [1] The resultant untreated hypothyroidism has its own complications such as adverse effects on body weight, [2] lipid profile and blood pressure.

The recommendations for the investigation of persistently elevated thyroid stimulating hormone (TSH) despite prescribed high-dose levothyroxine sodium tablets advocates the use of a levothyroxine absorption test (LAT) in the first instance to exclude pseudo-malabsorption. [3] However, the form which these tests should take is still under debate.

We present a case study of use of a modified thyroxine absorption test used to identify pseudo-malabsorption and conduct a review on the myriad of methods for the thyroxine absorption test.

2. Case Study

A 38-year old woman was referred by her general practitioner (GP) due to a lack of response to ever-increasing doses of prescribed levothyroxine. Upon referral, she was already on 450 micrograms (mcg) daily. Over the last 3 years in primary care, the TSH had persistently remained elevated between 5-15 (milli-units per litre) mU/L (reference 0.3 – 4.5 mU/L).

On initial assessment she complained of symptomatic hypothyroidism with a hoarse voice, tiredness and inability to lose weight. She admitted to having a good compliance and rarely missed the dose. She had no symptoms of malabsorption or a history of prior gastrointestinal surgery or simultaneous intake of any interfering drugs. Her GP had previously referred her for assessment by the Ear, Nose and Throat surgeons who had found nothing abnormal on endoscopic investigation to account for the hoarse voice.

On the day of the clinic visit, thyroid function tests were rechecked and TSH was 3.49 mU/L and free T4 levels of 13.8 (pica-moles) pmol/l. Subsequent investigations revealed no pathological malabsorption. Computer tomography of the neck and upper thorax was undertaken given the history of hoarse voice which demonstrated a multinodular goitre with no other abnormality.

Despite the normal thyroid function tests in the clinic, we opted for LAT on the basis of persistently elevated TSH for three years and an exceptionally higher dose of thyroxine therapy. With the patient's consent, we arranged two weeks later for an observed modified LAT, requiring the patient's presence every morning for five consecutive days. She was advised to miss her breakfast and on arrival she was offered to use the toilet facility. Later, the nurse observed her taking her normal dose of levothyroxine 450 micrograms (mcg) and observed her swallow the tablets. She remained in the department for an hour after ingestion with no access to toilet facility and later went home.

Bloods were taken for TSH, fT4 and fT3 at the beginning and end of the test. The results are shown in Figure 1 and Figure 2.

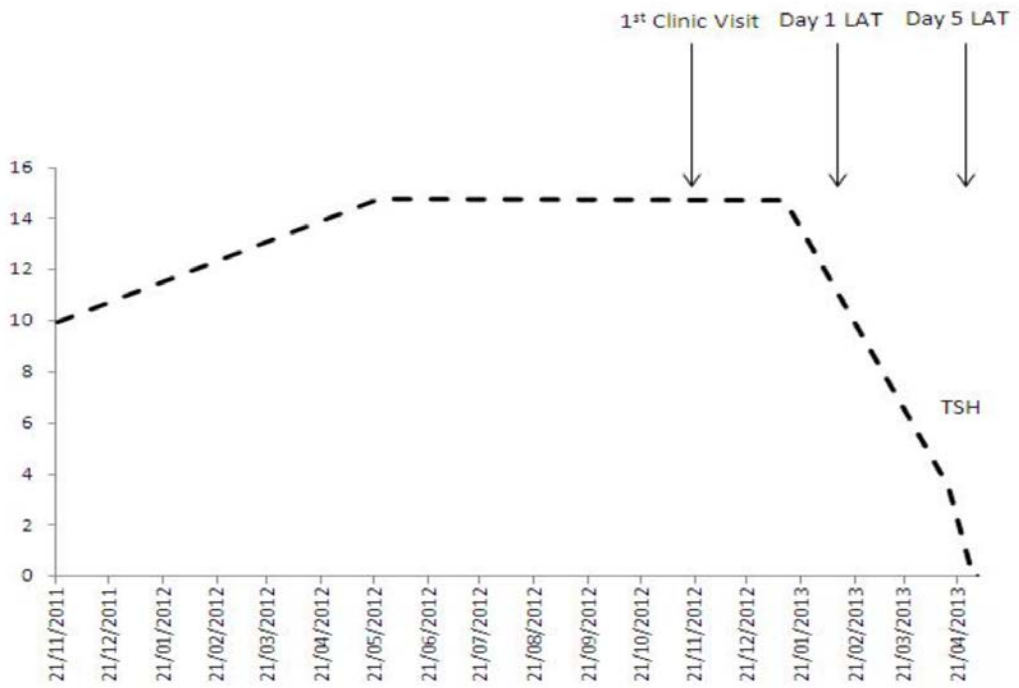

Figure 1. Thyroid Stimulating Hormone (TSH) levels pre, intra and post levothyroxine absorption test

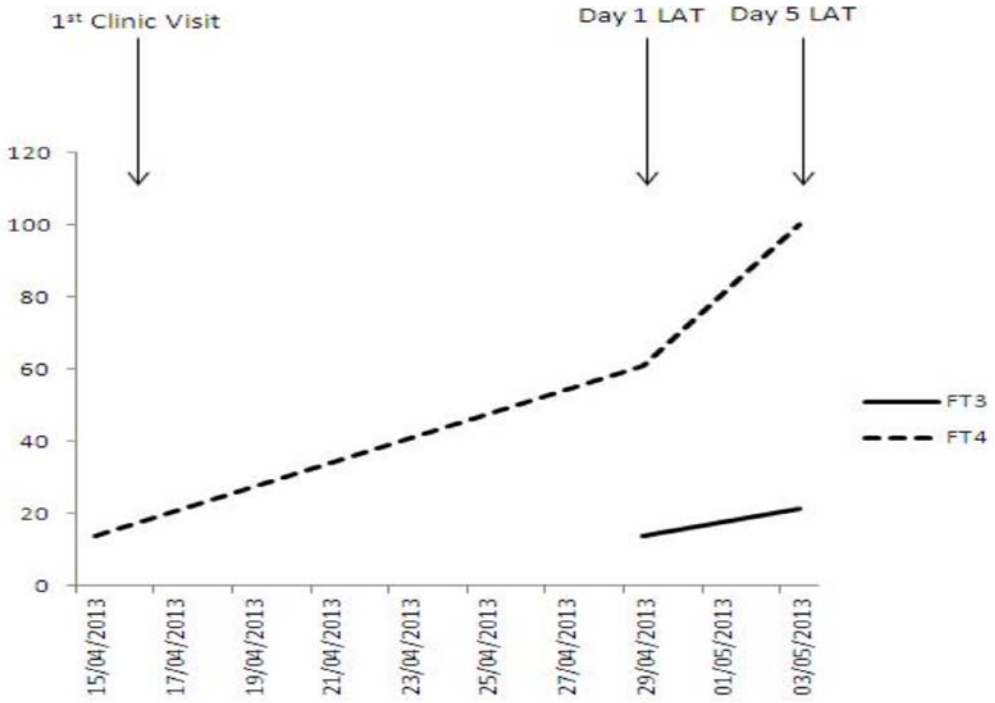

Figure 2. Free thyroxine (FT4) and free triiodothyronine (FT3) pre, intra and post levothyroxine absorption test

The prospect of the investigation for the patient had prompted, we presume, the patient to start taking the medication as prescribed which within 2 weeks period from initial clinic consultation to the day of LAT had resulted in decline of TSH along with the rise in free hormones. The LAT could have been abandoned at this stage as clearly the results proved that when she took her prescribed dose regularly, it was absorbed and was in fact too high a dose for her. However, the test was continued to prove beyond doubt this supposition.

The patient was subsequently advised to cease treatment for two weeks and then re-commence treatment at the dose of 100 mcg per day with ongoing monitoring of thyroid functions by the primary care team.

3. Discussion

Hypothyroidism is very well treated with LT4. One day's tablet accounts for approximately 14% of the total weekly dose. Due to the long half-life, missing a day’s dose intermittently would have an effect on levels over days to weeks; however, it should not affect levels over months to years, as in our patient. The insistence on at least moderate compliance was refuted in our patient in

retrospect with all the information available of adequate levothyroxine absorption. Although the average dose for effective replacement differs to some degree from patient to patient, most hypothyroid patients are managed within a moderately narrow dosing range that varies according to body weight, the average being between 1.6–1.8 µg/kg.

In patients with persistently elevated thyroid-stimulating hormone (TSH) levels, there are a number of causes other than pseudo-malabsorption, including poor administration (i.e. not taking on an empty stomach 30 minutes prior to food ingestion) or ingestion of other food items and drugs, for example large quantities of papaya,[4] fibre-rich diet, [5] ferrous sulphate, calcium carbonate, multivitamins, sucrulfate, cholestyramine, sevelamer, proton pump inhibitors, carbamazepine, rifampicin, phenytoin, oestrogen and so on. [6] Known pathological malabsorption conditions such as inflammatory bowel disease and coeliac's disease are well-recognized to cause malabsorption. However the literature is scanty on the actual degree of malabsorption, in each malabsorption condition.

The Levothyroxine Absorption Test is the primary method for distinguishing between non-compliance and true malabsorption. [7] However, the administration of the test is non-uniform with various protocols advocated in the literature but with no clarity on which one method is the most efficacious, sensitive and specific. Our method, as described, was undertaken over 5 days to allow for out-patient administration, which has been a method found to be of benefit by other Endocrinology colleagues. [8] Another method includes stretching out this process over 5-weeks. [9] While the majority advocate a same-day dosage (1000-2000mcg) of LT4 orally and then measuring TSH and fT4 levels at 2 and possibly 4 and 6 hours, demonstrating a rise in fT4 and a fall in the TSH. [10] Normally 70 to 100% of the administered dose is absorbed within the gastrointestinal tract, with maximal serum levels reached within two to four hours following ingestion. If the biochemical markers rise as expected, then this is indicative of normal gastro intestinal absorption for thyroxine.

The different methodologies described in the literature require differing levels of physician and other healthcare professionals' input. In addition, the results can take from between one and six weeks to determine, depending upon the method used. This results in widely differing results and costs, with an inability for Endocrinologists to interpret the data from individual patients to a gold standard, to determine pseudo-malabsorption from malabsorption.

4. Conclusion

The current LAT options advocated vary widely in the length of time of administration, number of investigations required and clinical input that must also lead to considerable variability in the cost. We advocate robust consensus statement and further research to determine a uniform protocol to undertake the LAT and its interpretation.

References

[1] Roti E, Minelli R, Gardini E, Braverman LE. The use and misuse of Thyroid Hormone. Endocr Rev 1993; 14: 401-23.

[2] Baron DN. Hypothyroidism; its aetiology and relation to hypometabolism, hypercholesterolaemia, and increase in body-weight. Lancet 1956; 271: 277-81.

[3] Molsey R, Swinbourne J & Orme S. Endocrine Abstracts 2007; 13: P298.

[4] Deiana L, Marini S, Mariotti S. Ingestion of large amounts of papaya fruit and impaired effectiveness of levothyroxine therapy. Endocr Pract 2012; 18: 98-100.

[5] Liel Y, Harman-Boehm I, Shany S. Evidence for a clinically important adverse effect of fiber-enriched diet on the bioavailability of levothyroxine in adult hypothyroid patients. J Clin Endocrinol Metab 1996; 81: 857-859.

[6] John-Kalarickal, J., Pearlman, G. & Carlson, H.E. (2007) New medications which decrease levothyroxine absorption. Thyroid, 17, 763-765.

[7] Diagnosis and treatment of Levothroxine Malabsorption. The Netherlands Journal of Medicine 2004; 62 (4) 114-118.

[8] Elmahi E, Vas P & Oyibo S. Levothyroxine absorption testing: a 5-day (suual dose) test as an alternative to the 1-day (100 □ g) test. Endocrine Abstracts 2013; 31: P372.

[9] Walker JN, Shillo P, Ibbotson V, Vincent A, Karavitaki N, Weetman AP, Wass JA & Allahabadia A. A thyroxine absorption test followed by weekly thyroxine administration: a method to assess non-adherence to treatment. Eur J endocrinol 2013; 168 (6): 913-917.

[10] Ain KB, Refetoff S, Fein HG, Weintraub BD. Pseudomalabsorption of levothyroxine. JAMA 1991; 266: 2118-20.