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Internal Medicine Section

Importance of the Levothyroxine Absorption Test in an Adolescent Girl

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ABSTRACT

Hypothyroidism is a commonly encountered problem in daily clinical practice. Although the management of hypothyroidism may seem straightforward, it can become challenging when patients' Thyroid-Stimulating Hormone (TSH) values remain elevated despite treatment. Various factors, including non-adherence and malabsorption, can contribute to this issue. Consequently, it is crucial to identify the underlying cause of increased levothyroxine demand, as this will prevent unnecessary dosage adjustments of levothyroxine tablets. In this case, a 13-year-old girl patient, presented with a TSH level greater than 200 and an fT4 level of 0.34, along with absent secondary sexual characteristics, impaired memory, delayed puberty, easy susceptibility to anxiety, difficulty with memorisation, and poor academic performance. Despite repeated inquiries, neither she nor her mother reported any instances of non-compliance. Additionally, there were no signs suggestive of malabsorption, such as diarrhoea or oedema. Therefore, a levothyroxine absorption test was conducted to rule out pseudo-malabsorption. This test aids in distinguishing patients with non-compliance from those with true malabsorption, thereby avoiding unnecessary dosage adjustments of levothyroxine supplementation, a problem frequently encountered in day-to-day clinical practice.

Keywords: Hypothyroidism, Malabsorption, Non-compliance

CASE REPORT

A 13-year-old girl patient (height 118 cm and weight 18 kg) presented to the hospital with a diagnosis of hypothyroidism (high anti-TPO antibodies, suggestive of autoimmune hypothyroidism) and a history of ingesting 200 mcg of levothyroxine tablets for four months. Prior to that, there had been a gradual increase in the levothyroxine dosage over the past six months, eventually reaching 200 mcg, yet her TSH level remained high at >200 mIU/mL. Upon further inquiry, it was discovered that the girl exhibited absent secondary sexual characteristics and had not yet started menstruating. Her mother reported that she was easily apprehensive, had a weak memory, and performed poorly in school. Further investigation into her birth and developmental history did not reveal any significant abnormalities. When questioned about compliance and malabsorption, her mother confirmed that there was no history of non-compliance or any symptoms suggestive of malabsorption such as diarrhoea. Due to a strong suspicion and after consulting with other endocrinologists in the department, a decision was made to conduct a levothyroxine absorption test on the patient. She was admitted to the hospital for the test, which was planned to be conducted without any dietary restrictions. She was instructed to take her medication at her usual time of 6 am, and the examination began at that time.

A baseline blood sample was collected at 6.00 am to evaluate TSH and fT4 levels. After the blood sample was collected, she ingested 200 mcg of levothyroxine, ensuring that she had swallowed the medication and had not spit the tablets out. A careful examination of her oral cavity confirmed that she was not holding the tablets in her mouth. Blood samples were collected from the girl serially at one-hour intervals, resulting in a total of six blood samples from morning 6.00 am to 11.00 am every hours. The results at each time interval were as follows: At 6.00 am -fT4- 0.44, after 1 hour fT4- 0.58; after 2 hours, fT4- 0.86; after 3 hours, fT4- 0.93; after 4 hours, fT4- 0.91; and after 5 hours, fT4- 0.86, with a TSH value of >150 mIU/mL. The exact TSH value at each time interval could not be obtained as the highest detectable TSH level in the institutional laboratory was 150 mIU/mL. During the test, fT3 values were not measured. However, a pre-test fT3 value was obtained, which was 0.78 pg/mL (2.3-4.2). The results of this test showed that the fT4 value had nearly doubled from the baseline to the 3-hour value.

DISCUSSION

The maximum replacement dose of levothyroxine for a patient with no thyroid hormone in their body is 1.6 to 1.8 mcg/kg/day [1]. In the case of this girl, who weighed 18 kg, the maximum replacement dose of levothyroxine for her body would be 32.4 mcg. However, according to the history provided by her mother, she was taking nearly eight times of her maximum replacement dose, yet still not achieving adequate replenishment. The main causes could be malabsorption or non-compliance. Based on the clinical history and examination, there was no history of chronic diarrhoea, anaemia, generalised oedema, recurrent nausea and vomiting, major surgery involving the resection of a large portion of the bowel, anaemia in blood parameters, abnormal levels of other micronutrients in the biochemical parameters, epigastric pain, or black, semisolid stool that would suggest gastric erosion.

Although an upper Gastro-intestinal (GI) endoscopy was planned, the authors performed this test to rule out malabsorption. The test result showed a nearly doubled fT4 value from baseline in the 3-hour sample, which indicates no malabsorption but rather poor compliance [2]. Finally, further inquiry was conducted with the girl alone regarding poor compliance, and she confessed that her mother used to give her the tablets in her hand, and then the mother would leave and the girl would throw the tablets away under the bed. Using a levothyroxine absorption test, patients with a high TSH on an adequate dose of levothyroxine can be clearly identified as non-adherent to treatment [2]. A study that conducted the levothyroxine absorption test over two hours showed that it may offer a more rapid alternative to the commonly used, much longer protocols for evaluating levothyroxine absorption [3].

Additionally, this study showed that some people may be encouraged to begin adhering to levothyroxine therapy prior to the test by scheduling a levothyroxine absorption test [3]. A study utilised (2-hours FT4 minus baseline FT4) and (2-hours TT4 minus baseline TT4) as criteria and found that the rapid LT4 absorption test is effective in distinguishing between non-compliance and malabsorption [4]. The

levothyroxine absorption test is useful in differentiating malabsorption from pseudo malabsorption [5,6]. Another study suggests using total T4 trends for at least four hours in combination with the calculated absorption percentage to determine if true absorption is occurring [6]. This levothyroxine absorption test can be used as an easy tool for appropriate diagnosis and for avoiding unnecessary treatments and investigations in situations where a normal level of TSH is not obtained despite utilising high dosages of tablet levothyroxine therapy [7]. Thus, this test can also be used for better management of patients with refractory hypothyroidism [5]. In summary, the levothyroxine absorption test can differentiate between true malabsorption and non-compliance or pseudo malabsorption, thereby helping us avoid unnecessary high dosing of levothyroxine supplementation.

CONCLUSION(S)

Based on the aforementioned test and further inquiry about the girl, it was concluded that she didn't have any malabsorption. Therefore, the inference from this test was that the patient had poor compliance. After diagnosing poor compliance, she was prescribed 50 mcg of tablet levothyroxine daily and instructed to follow-up. There was also a suggestion of administering 350 mcg of levothyroxine once weekly under supervision, but the mother disagreed and chose daily home medication. The key message is that sometimes it can be extremely difficult for a clinician to obtain an accurate compliance history, but by performing this test, true malabsorption and poor compliance can be easily differentiated, thus avoiding unnecessary high doses of levothyroxine supplementation.

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