

Improper Drug Handling may Result in Treatment Failure: Back to the Basics of Pharmacology

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Abstract

Introduction	The synthetic form of thyroid hormone-tetraiodothyronine is quite useful for the treatment of non-drug induced hypothyroidism including radioiodine-131 therapy induced hypothyroidism. Attention to certain aspects is required while the therapy is instituted with this drug.
Objective(s)	To highlight the precautions which ensure good therapeutic outcome when levothyroxine is being taken as thyroid hormone replacement therapy.
Methods	Case study method was conducted. In a case of hypothyroidism, the patient had purchased levothyroxine preparation without its container and did not store it properly. There was failure of therapy. Repurchase of same drug in its container and its proper storage helped to achieve optimal therapeutic outcome.
Conclusion	Synthetic levothyroxine which is used as thyroid hormone replacement therapy is very unstable if exposed to light and humidity. Further, only very minute amount (in micrograms) being required, any loss of potency can result in failure of therapy. Therefore, it is essential that the drug should be stored in a dark colored container with a tight lid away from sunlight and moisture.
Keywords	Improper drug handling, Treatment failure, Pharmacology.

Introduction

L-thyroxine is the *levo* isomer of *tetraiodothyronine* (T_4) i.e. the primary secretion of thyroid gland. The synthetic form of this hormone, *levothyroxine sodium* (*L-thyroxine*), has been in use for several decades for the treatment of non-drug induced hypothyroidism and post-radioiodine-131 therapy induced hypothyroidism. It has transformed the treatment of hypothyroidism due to its ready availability, ease of administration through oral route and tastelessness. Its other notable qualities are stability, content uniformity, low cost, lack of allergic foreign protein, easy laboratory measurement of serum levels and long half life (7 days), which permits once daily administration. Prior to its introduction, thyroid extract has been employed to treat hypothyroidism which is now obsolete. Despite its time-tested utility in curing hypothyroid state, the improper usage may lead to sub-optimal treatment outcome. The author hereby presents a case of hypothyroidism in which lack of caution while using *levothyroxine* resulted in the failure of therapy.

A 15 years old male child from a poor family presented with the complaints of constipation, lethargy, and anorexia. On physical examination the child had a mild goiter, puffiness of face, dry skin and a pulse rate of 70 per minute. A provisional diagnosis of hypothyroidism was made. Thyroid function tests confirmed the clinical diagnosis. Serum TSH was raised (16 mIU/L; normal 0.5-5 mIU/L) and T_4 was low (40 nmol/L; normal 60-140 nmol/L). The patient was put on thyroid hormone replacement therapy: tablet levothyroxine 50

microgram orally daily. The patient was advised to take the tablet on an empty stomach and to avoid any meals for 1-2 hours thereafter. He was also advised to store the medicine away from direct sunlight.

Case Report

The patient reported for follow-up after 2 months and complained that there was not much improvement in the symptoms. On re-assessment there was not much improvement in the goiter size and other clinical findings were almost same. It is a well known fact that levothyroxine takes 6-8 weeks to take effect. Therefore, the patients are called for follow-up after 8 weeks. In this case there was a lack of effect of thyroxin even after 8 weeks and this called for to verify whether the medicine is being taken on an empty stomach or not. It has been found that the common mistake is that the patient does not take tablet thyroxin on an empty stomach. The patient was asked to show the medicine being taken and explain how it was taken. However, the patient was taking the tablet on an empty stomach and the problem was somewhere else. The patient's attendant has bought the tablet without its bottle i.e. in loose form and has stored it in a piece of newspaper. Though the medicine was being taken on an empty stomach, the storage of medicine was improper and further the potency of tablet could not be verified. The patient was advised to buy the medicine in its container, to keep the medicine in its original container and store it in cool dry place

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away from sunlight. The advice to take the medicine on an empty stomach was emphasized. On the next visit after two months, the patient reported to have a dramatic improvement in his problems. The normalization of thyroid status was confirmed biochemically as well. The patient was advised to continue same treatment and observe the same precautions. In addition, the parents were advised to watch for any sign(s) of Levothyroxine toxicity, which can be due to its overdose. This can manifest in the form of irritability, restlessness, hyperactivity, insomnia etc. The patient was asked to report for follow up after 3 months.

Discussion

Oral levothyroxine sodium is used as replacement therapy for hypothyroidism, a condition characterized by diminished or absent thyroid function. This can occur in conditions, such as congenital hypothyroidism or in functional deficiency, partial or complete absence of the thyroid gland as in auto-immune hypothyroidism, after ablation of thyroid by surgery or radioiodine-131.

Though synthetic levothyroxine is very inexpensive and readily available, it requires certain precautions in its usage for the optimal treatment outcome. These can be stated as follows:

a) Levothyroxine should preferably be taken on an empty stomach because it shows decreased absorption if taken with food¹. Its absorption is also adversely affected by calcium² (even milk), ferrous sulfate, aluminium hydroxide, cholestyramine, sucralfate³ and soy-bean formulations⁴. With all of the above agents, the increased T⁴ dosage may compensate for decreased absorption but its availability still can't be predicted because its absorption varies differently with different food items. Therefore, it is always better to take it on an empty stomach for consistent results. The intake of food should be avoided for 1-2 hours after taking thyroxin. The small children who could not swallow tablets can be given the crushed form of the tablet with plain water, but again on an empty stomach.

b) Levothyroxine is known to be unstable in the presence of heat, light and humidity^{4,5}. In presence of light, levothyroxine can undergo spontaneous de-iodination. Therefore, it is sold in airtight amber colored bottles. It should not be bought loose and always be stored after the cap is tightened, in a cool, dry place away from sunlight.

c) Another important point is that the replacement dose being in micrograms slight variations in dose can be detrimental to the well-being of the patient. The shelf life of the preparation is 1-2 years. Levothyroxine should always be bought in its container not only for its proper storage but also to verify it's correct potency and that the expiry date is not yet over⁴. It has been seen that suboptimal treatment could result in persistent hypothyroidism and its related consequences like growth retardation. Conversely, over treatment is also hazardous. In young children it manifests in the form of irritability, restlessness, hyperactivity, insomnia etc. In addition, shortened attention span and emotional ability may lead to behavioral problems and poor scholastic performance. Because of the risks associated with over treatment or under treatment with levothyroxine, it is critical that levothyroxine

should consist in potency and bioavailability⁴. Similarly it is particularly important to increase the dose very gradually and the dosage must be established for each patient individually⁶.

Conclusion

It need not be over-emphasized that thyroid replacement therapy usually may be required for life-time; therefore, good practices about its usage should be initiated from the beginning especially if the patient is illiterate. Physician should advise the patients to take tablet thyroxin in fasting state and to avoid intake of food for 1-2 hours thereafter for better absorption of levothyroxine. The synthetic form of thyroxin is unstable under the conditions of high temperature, humidity and light. Improper storage can result in loss of potency of the preparation leading to failure of therapy. The treating physician should advise the patients about the importance of expiry date and proper storage of thyroxin tablets. The patient and the parents should also keep a watchful eye on any over-treatment of the condition. The childhood period is important from the point of physical growth, therefore, maintenance of euthyroid status should be highlighted and this is only possible if the patient and the parents co-operate very well with the treating physician

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