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[Short Communication] Advisory caution message on retail packaging of Levothyroxine and its significance in the treatment of hypothyroidism

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Abstract

Levothyroxine is extensively used for overt hypothyroidism. Most of the time, it is also prescribed by general practitioners in developing countries for subclinical hypothyroidism at the initial stages, despite adequate recommendations for the treatment, causing the manifestation of new health disorders. Therefore, it is opined that an advisory caution message be inscribed on the retail packaging of Levothyroxine to give an indication to the non-endocrinologist general practitioner about the correct treatment protocol and also make aware the patient.

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Short Communication

Thyroid hormones are critical regulators of various body functions and any disorder in their functioning causes a host of diseases. Hypothyroidism is a widespread common endocrine disorder that results from reduced activity of the thyroid gland causing deficient production of thyroid hormone. In developed countries, the incidence of subclinical hypothyroidism is approximately 8% in women and 3% in men ^[1]. The global thyroid disorder market was valued at \$2,057 million in 2017, and is estimated to reach \$2,771 million by 2025 at a Compounded Annual Growth Rate (CAGR) of 3.8% from 2018 to 2025 ^[2]. The most prevalent treatment for hypothyroidism is supplementation with a synthetic thyroid hormone called Levothyroxine. In the USA alone levothyroxine is a top-selling drug since 2016 and prescribed to over 114 million retained

its number one position among the top 300 drugs in 2019 [3]. In India, every third person suffers from hypothyroidism [4] and the immediate line of treatment is levothyroxine for overt or subclinical hypothyroidism (SCH) even if the patient does not show any symptoms like tiredness, muscle aches, constipation, dry skin, weight gain, slow heartbeat, or sensitivity to cold. The usual dosage of levothyroxine ranges from 25 µg to 300 µg per day for an adult with an initial dose at a rate of 1.6µg/kg of body weight. It is experienced during the treatment of chronic subclinical hypothyroidism patients in India, most of the consulting general medical practitioners (GP) kept on increasing levothyroxine doses to an upper limit of 300µg/day or even more up to 500µg/per in some isolated cases to keep TSH within standard pathological limits irrespective of T3 and T4 levels. More strangely the treatment is governed on the pathological test for TSH alone whereas it has been found that in some isolated cases T3 and/or T4 goes beyond recommended limits while TSH remain within recommended limits. Further, most of the GP developed the false premise that levothyroxine cannot be discontinued once started.

Thyroid disorders in initial stages is not life threatening and remain asymptomatic over a long period. High quality treatment for thyroid disorders in developing or underdeveloped countries is limited to certain metropolitan pockets due to the dismal availability of practicing endocrinologists. In such a scenario GP handles most of the thyroid disorder cases. Every GP is not expected to be knowledgeable in all domains of medicine. They acquire most of the practicing knowledge from marketing executives of pharmaceutical companies. Indeed, they don't get time to update their knowledge in state-of-art research and development (R&D) in advanced medicine. It is surprising to note that many practicing GP at reasonably good multi-specialty hospitals have limited awareness of thyroid disorders especially subclinical hyperthyroidism (SCH). They prescribe levothyroxine at the moment level of Thyroid Stimulating Hormone (TSH) approaching the upper recommended limit 5.0 mIU/L despite the fact that enough literature is available on the initiation of SCH treatment [5][6]. Levothyroxine reduces TSH in SCH as long as it is continued, satisfying the patient with numbers. Once the administration of levothyroxine started its dosage progressively increases along with the burden of manifestation of other morbidity like cardiovascular disease, tremors, weight gain/loss, headache, vomiting, diarrhoea, change in appetite, hair loss, skin dryness, joint pains, leg cramps, changes in the menstrual cycle, and mood swings for which the patient is unaware and accepts it on account of advancing age.

In my more than four decades of general practicing, I have come across patients with the following chronic complaints:

- weight gain or loss
- chronic headache
- persistent vomiting
- remittent fever
- changes in the menstrual cycle
- sensitivity to heat
- dryness of hairs and loss
- premature joint pain, and
- leg cramps

who had been on levothyroxine or its variants like Eltroxin and Thyroxin for more than a decade and high doses as 50 mcg to 350 mcg. Moreover, despite such high doses the TSH level was still beyond upper limit. Nominal increase in level of TSH while T3/T4 is within recommended pathological limits can be comfortably managed with physical exercises coupled with suitable medication for limited time.

Nowadays most of the patients and their caretakers have better awareness about medicines on account of increased literacy and ready availability of the Internet. Most of them look for an “Expiry Date” before going for any medicine. In view of the recommendations [5][6] for treatment for SCH and to mitigate various side effects of excessive or unwarranted use of levothyroxine, it is opined that an “Advisory Caution” message needs to be inscribed on retail packaging of levothyroxine. It will educate GP to update their knowledge and would be helpful in the correct treatment of hypothyroidism. Further, the patient can also cross reference his treatment with laboratory results and flag the discrepancy to GP, if any.

The suggested format for an “ Advisory Caution” may be as below in one or more most popular native languages e.g. for India it can be in widely spoken languages English and Hindi following format:

[illegible]

Inscription of such an advisory caution on drug leaflet may not serve purpose because invariably majority of patients feel that leaflet is meant for practicing doctors. Such an “Advisory Caution” will significantly help in healthcare and reduce burden of new morbidities on account of side reactions of levothyroxine.

Conflict of interest

None.

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