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Editorial

The treacherous use of thyroxine preparations.

Stability of thyroxine preparations

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Endocrinologists not infrequently confront the problem of inconsistent blood values of thyroxine among patients receiving L-thyroxine preparations. The question is how universal this problem is.

Before the use of L-thyroxine or thyroid gland preparations, hypothyroid patients were left untreated. It was therefore a landmark in the history of medicine when for the first time Murray in 1891 treated hypothyroidism with injections of an extract of sheep thyroid glands[1]. The preparations from animal thyroid glands were later standardized according to their iodine content, but nevertheless had a variable content of the active thyroid hormones L-thyroxine (T_4) and L-triodothyronine (T_3), and also had a relatively short "shelf-life", i.e. their biologic potency decreased with time, especially if not properly stored. Hence, they were replaced in the sixties by pure preparations of T_4. These have a more consistent biologic effect and a longer shelf-life. Nevertheless, T_4 tablets, although certainly preferable to animal thyroid gland preparations, may still have some problems with potency, bio-availability and storage.

In 1997, Olveira et al[2] and Peran et al[3] noticed in Spain that some batches of the preparation "Levothroid" had a reduced effect. These batches possessed the correct T_4 dose, but this was a "non-micronized" raw material with a reduced bioavailability. Olveira et al[2] concluded that "Simple changes in the manufacture of levothyroxine tablets may produce important variations in their bioavailability, having an adverse effect on the clinical control of the patients, and causing extra expense by the need for repeated patient visits". This is highly reminiscent of the problems Greek endocrinologists have not infrequently come up against.

Recently Hennesey[4] published a provocative paper citing the problems faced by American endocrinologists. For instance, subpotency was noted in 47/58 batches, in 9 superpotency and in 2 inconsistent thyroid test results. The conclusion was that "L T_4 products were unstable, influenced by factors such as light, temperature, air exposure, humidity and the use of some excipients which actually accelerate the degradation of active ingredients"[5]. To sum up: 1) All thyroxine preparations do not have the same biovailability, and 2) the shelf-life of thyroxine preparations is longer than that of preparations from animal thyroids, but still limited.

To deal with this serious issue, I believe a number of things should be done. Firstly, the authorities should insist on biovailability studies of thyroxine preparations. Secondly, physicians should instruct their patients to take T_4 while fasting for at least 4 hours, and not take any other food for at least 20-30 min, as well as to avoid other drugs such as calcium carbonate[6] for at least 30 min before or after the T_4 tablet. Many drugs, food items and even fruit juices may interfere

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with T_4 absorption, and this should be explained to the patient. Thirdly, physicians should not frivolously change from one T_4 brand to the other on the assumption that 100 μg T_4 from brand A equals 100 μg T_4 from brand B. Fourthly, physicians should report to authorities if they have a "suspicious" result in several patients. One or more patients may be non-compliant, for instance, taking their T_4 with food or with other drugs, but if this occurs frequently, the brand used may be responsible.

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