

## **Thyroxine Replacement - Need for Fine Tuning and Individualized Treatment** **- Dr. Mala Dharmalingam, Dr. K. M. Prasannakumar** **M. S. Ramaiah Medical College, Bangalore 560054**

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Primary hypothyroidism is a common medical problem occurring in approximately 1-3% of the population with annual incidence rates of 1-2 per 1000 in women and 2 in 10,000 for men. Overt hypothyroidism is associated with typical symptoms and signs. The diagnosis is confirmed by the elevation of TSH (thyrotropin), and a depression of total T4. Primary hypothyroidism occurs at all ages but postmenopausal women are at a greater risk. If left untreated hypothyroidism is associated with high degree of morbidity and may ultimately be fatal.

In primary hypothyroidism, the correct dose would be that which normalizes the serum TSH. High sensitive assays can determine if the TSH is normal or below normal. If TSH were below normal it would indicate over replacement. Over replacement must be avoided because it is associated with features of subtle hyperthyroidism in certain tissues, which include heart, kidney, bone and liver. Adjustment or replacement therapy to maintain the TSH levels in normal range is associated with normalization of peripheral tissue markers of hypothyroidism. However, in patients with secondary forms of hypothyroidism i.e. that resulting from pituitary or hypothalamic disease TSH levels are not useful, and a T4 or fT4 is better.

### **Need for individualizing treatment**

Hypothyroid patients in good health can be started on the full replacement dose of thyroxine. However, caution should be exercised when starting treatment of patients with long-standing hypothyroidism or elderly patients especially those with manifestations of ischemic heart disease. Replacement is started with an oral dose as small as 12.5 or 25 mcg with a stepwise increment depending on clinical response. The availability of multiplicity of tablet strengths with the contents ranging from 25-300 mcg allows precise titration of the daily thyroxine dosage improving compliance significantly.

### **Hypothyroidism in children**

The treatment of hypothyroidism in children should be to raise the serum T4 levels to more than 10 mcg/dl as rapidly as possible. This is usually accomplished with a dose of about 50 mcg/day. This is higher than the adult dose on a weight basis and in keeping with the higher metabolic clearance of the hormone in the infant. The serum TSH does not return to normal quickly due to an apparent residual reset of the pituitary feedback mechanism, but after the age of 2 years a TSH in the normal range is an index of optimal therapy as it is in adults. Monitoring of the child is done more frequently than in the adult. The signs to be monitored are the growth velocity and the pubertal development. The child should have frequent tests for thyroid hormone and TSH levels and the dose titrated as per the requirement. Though a dose is fixed on diagnosis of hypothyroidism, based upon weight, it is to a large extent arbitrary and monitoring of hormone levels and correct dosing is required to prevent delayed puberty, or a final short height in comparison with the genetic potential.

### **Hypothyroidism and pregnancy**

Hypothyroid patients who are planning a pregnancy should be advised to increase their dose by 50% as soon as diagnosis is confirmed. Because the change in requirement occurs soon after implantation. Their increase in requirement persists throughout pregnancy but returns to normal within a few weeks of delivery. A hypothyroid pregnant lady should have her thyroid hormones (fT4 & TSH) done in every trimester to keep the fT4 at the higher levels of normal. Correct dosing is important as it may cause some adverse effects in the child if under/over treated. Patient can switch back to the prepregnancy dose soon after the delivery. Recent data has shown that

untreated hypothyroidism during pregnancy can lead to decrease in the intelligence of the children.

### **Replacement in adults**

Replacement of thyroxine in the young adult is relatively more easy. Thyroxine is started as per the weight of the patient at 100 mcg/d or 150 mcg/d. The dose however need to be adjusted after 6 weeks, which is the half-life of thyroxine. However, the dose may again have to be modified in some patients. After the initiation of the treatment, metabolic rate is normalized, and thyroxine is also metabolised more rapidly than in the initial pretreatment phase. This may require dose modification again after 6 months. Today, with the growing awareness of osteoporosis, it is important not to overtreat the patient, as the excess thyroxine may lead to bone loss. This is more important in postmenopausal women in whom this disease is more common. Mild excess thyroxine can also cause an increased strain on the heart. Thus it is important to individualize the dose for the patient and this requires fine-tuning of the dose by the physician. Earlier when the different strengths of thyroxine were not available the patient used to be instructed to break the tablet, which was but a crude alternative, however with the availability of different strengths of thyroxine it is easier to tailor the dose as per the need of the patient.