

Hypothyroidism With Different Strengths Of Thyroxine

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Background

Hypothyroidism is one of the most common endocrine disorders. Hypothyroidism is the term used for any degree of thyroid hormone deficiency. It can be primary (thyroprivic) or secondary/tertiary (defect lying at pituitary / hypothalamic level). It can be subtle (biochemical/subclinical) or florid (myxedema). It can occur at any age, congenital (thyroidagenesis/dysgenesis, dyshormogenesis, antithyroid drugs), childhood (ectopic thyroid, endemic goiter, dyshormogenesis), adolescent (juvenile thyroiditis), to middle age (Hashimoto's thyroiditis, postablative) and in elderly population.

Thyroid Function Tests

Total T3, T4 or free T3, T4 & TSH are the routine tests ordered for diagnosis of hypothyroidism. Non sensitive & ultrasensitive assays for TSH are available. Rarely T4 may be used in presence of nonthyroidal illnesses. Treatment with thyroxine can reverse the hypothyroidism & restore the euthyroid state. Before commencing therapy, it is important to diagnose whether hypothyroidism is caused by thyroid failure or by the much less common failure as pituitary-hypothalamic level. In the later case, co-existing impairment of ACTH secretion may precipitate an adrenal failure, that had been satisfactorily tolerated during hypothyroidism. It is also important to consider coexisting autoimmune adrenal disorder since treatment of hypothyroidism alone may unmask adrenocortical hormone deficiency by increasing metabolic rate & cortisol metabolism rate. In these settings, cortisol should be administered with the thyroid hormone replacement.

The Better Option

Historically use of oral thyroid medication in hypothyroidism, was described by Raven in 1894. Animal products, such as desiccated thyroid & thyroglobulin, were standard replacement therapy for several decades. These products are being replaced with synthetic preparations of thyroxine, L-tri-iodothyronine or combinations of both. The use of synthetic preparations is preferred because of their stability & standardisation of hormone content. Among them, only thyroxine products relatively unchanged serum T4 & T3 levels throughout 24-hours. Because of its short serum half-life, L-tri-iodothyronine (T3) result in postabsorptive increase in serum T3 to hyperthyroid levels. Also it will not allow assessment of thyroidal state by measurement of serum levels of T3. Therefore one of the well-standardised brands of thyroxine sodium should be used because variations in potency have been reported for some generic preparations.

Dosage In Adults

The initial dosage of thyroxine depends on the severity of the hypothyroid disorder, the age of the patient, and the presence of associated or underlying medical conditions. The half life of thyroxine, which is about 6 days in euthyroid individuals may be significantly prolonged in hypothyroid patients. A full replacement dose has been considered to be between 1.5 to 2 mcg T4/Kg of body weight. Most patients deficiencies are fully replaced with a daily dose of 75 to 150 mcg. In young, otherwise healthy, patients with mild hypothyroidism, a full daily replacement of thyroxine (usually 75 to 100 mcg) may be given at the beginning of the therapy. The initial dose of thyroxine in patients with severe hypothyroidism or in patients with clinically apparent or probable underlying atherosclerotic heart disease or in elderly patients is generally 12.5 to 25 mcg/day. This low dose is recommended because an abrupt increase in metabolic rate & demand for increased cardiac output may precipitate angina pectoris, myocardial infarction, congestive heart failure, or arrhythmias. After this low initial daily dosage of thyroxine is full equilibrated (4

- 6 weeks) and if the patient has no symptoms or signs of cardiac decompensation, the daily dosage may be cautiously increased.

Monitoring

Doses are assessed at monthly intervals until the clinical syndrome is relieved or until laboratory tests demonstrate that full replacement has been achieved. The therapeutic goal for lifelong replacement therapy should be alleviation of the clinical syndrome and the normalisation of serum TSH. In hypothyroidism due to defect at pituitary - hypothalamic level only T3, T4 would get normalised. It is essential to use ultrasensitive TSH assay to detect serum TSH levels that fall below the normal range in response to excess thyroxine. Appropriate practice requires adjustment of thyroxine dosage to normalise serum TSH. Chronic excess thyroxine therapy (suppressed serum TSH) reduces bone mineral density, leading to osteoporosis & possible increased risk of related fractures over prolonged period. Similarly chronic excess (suppressed TSH) or inadequate (increased TSH) can affect cardiac function in different ways. These therapeutic goals may be modified in elderly patients with cardiovascular disease, where optimal therapy would be a daily dosage of thyroxine that relieves most of the symptoms of hypothyroidism without causing myocardial decompensation. Such a dose may not fully normalise serum T4 & TSH.

Neonates And Children

In neonatal & childhood hypothyroidism the treatment goal is to restore euthyroidism as rapidly as is safe for patients. The therapy is essential to protect the brain from damage. However, caution is necessary in the therapy for markedly hypothyroid neonates & infants because of possible presence of a myxedematous myocardium. Vigorous therapy may cause cardiac failure or serious arrhythmias.

Dosage In Neonates And In Children

The initial daily oral dose of thyroxine in full term neonates is 10 to 15 mcg/kg/d. In premature neonates, the starting dose is 10 mcg/kg/d; usually the dose can be increased to 15 mcg/kg/d in 4 to 6 weeks. In infants, children, and adolescents the initial oral dose of thyroxine is approximately 100 mcg/M²/d. In children, suppression of TSH to normal levels is the best index of adequate therapy in primary hypothyroidism. However, neonates and infants with congenital hypothyroidism may have an abnormal "threshold" for the inhibition of TSH secretion: the feedback set point seems to be increased, so that excessive serum levels of T4 are required to suppress the TSH. Serum TSH levels may remain elevated for up to 2 years, despite normal T3 & T4 levels. Therefore, normal TSH levels must not be used as the only criterion of adequate therapy in this age group. Normal growth, development, and skeletal maturation are other criteria. Pseudotumor cerebri may occur after the initiation of therapy. Over treatment may delay neurological development.

Since it is necessary to achieve serum TSH levels in normal range for optimum treatment in adult, and to adjust correct dosages as per weight in neonates, infants and children various dosage ranging from 12.5 to 200 mcg need to be given. This accurate dose adjustment is vital and is not possible with a tablet usually available with single strength. With recent introduction of thyroxine (e.g. Thyronorm) in different strengths (25, 50, 100) clinician can now effectively adjust the dosage & optimise the thyroxine replacement therapy for greater patient benefit.