

Subclinical Hypothyroidism

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Question

Is it essential to screen and treat with L-thyroxine therapy in order to prevent the progression to overt hypothyroidism in patients with subclinical hypothyroidism?

Define

- **Subclinical Hypothyroidism**
 - **Laboratory Diagnosis:** An elevation in serum thyroid-stimulating hormone (TSH) above the upper limit of the reference range with a normal serum free T4 (FT4) concentration
 - **TSH Normal Reference Range:** 0.45-4.5 $\mu\text{U}/\text{mL}$

Incidence/Prevalence

- Affects approximately 4-10% of the American adult population and 7-26% of the elderly population
- Women, especially those over 50 years of age, are most affected by this life changing disease
- Currently, demographic studies show prevalence among Caucasian women followed by African American and Mexican-American women

Causes:

- Chronic autoimmune thyroiditis (Hashimoto's disease)
- Radiation
- Congenital
- Medication
- Treatment of Graves' disease
 - Radioactive Iodine therapy
 - Subtotal thyroidectomy
 - Antithyroid drugs

Risk Factors

- Family history of thyroid disease
- Personal history of thyroid disease
- Age
- Presence of anti-thyroid antibodies
- Radiation treatment
- Other autoimmune diseases
- Iodine deficiency
- Various medications like lithium and iodine

Manifestations

- Weakness
- Fatigue
- Dry skin
- Coarse hair
- Cold intolerance
- Constipation
- Weight gain
- Muscle cramps
- Nonpitting edema
- Hoarseness
- Hearing loss
- Menorrhagia
- Slowing of reflexes
- Bradycardia
- Elevated Lipids
 - Triglycerides
 - Total cholesterol
 - LDL cholesterol

Treatment

- L-thyroxine has a long half-life and is partially converted to T3 in the body, resulting in a constant physiological blood level of both T4 and T3 with a single dose.
- The goal of this therapy is to maintain the TSH level within normal limits.



Adverse Effects of Treatment

- Nervousness
- Palpitations
- Atrial fibrillation
- Exacerbation of angina pectoris
- Increased appetite
- Insomnia
- Heat intolerance

Course

- TSH level resolves
 - An episode of thyroiditis
- TSH level remains unchanged
- Progression to overt hypothyroidism

Key Evidence

- Randomized, double-blind, placebo-controlled trials
- 73 subjects with subclinical hypothyroidism were selected
- Investigation: 6-12 months

Key Evidence

- Participants: 33 patients
- Mean dose of L-thyroxine: 71.2 µg/dL
- Symptoms: dry or coarse hair
- Results one year later: no change in any variable in the placebo group, but significant decreases in serum TSH levels in the treatment group
- Overall, 8 of the 17 subjects receiving the treatment were symptomatically improved whereas only 3 of 16 subjects in the control group improved

Key Evidence

- Participants: 40 women with mild thyroid dysfunction (serum TSH between 5 to 10 $\mu\text{U}/\text{mL}$ with a normal serum free thyroxine level)
- Dose of L-thyroxine: 50-100 $\mu\text{g}/\text{dL}$
- 6 months later: Significant TSH level decrease of 4.6 $\mu\text{U}/\text{mL}$ in the treatment group compared with a decrease of 1.7 $\mu\text{U}/\text{mL}$ in the placebo group
- Symptom scores improved in both groups

Discussion

- Focusing on screening and disease markers
- Investigators failed to examine whether patients with mildly elevated TSH levels were as likely to improve compared to those with markedly elevated TSH values
- Trial enrollment was limited by the number of participants selected

Discussion

- Researchers noted that symptoms were no more frequent in persons with subclinical hypothyroidism than in the control population
- Correlation between treatment and the development of overt hypothyroidism would be strengthened if data proved that the progression is associated with a substantial burden of illness

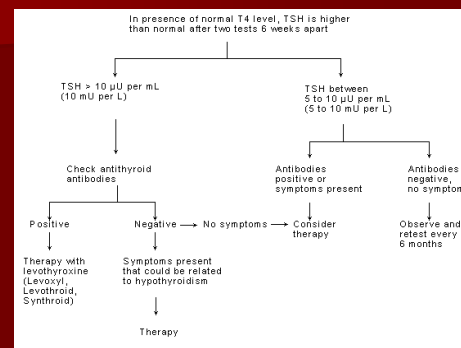
Who to Screen?

- Universal screening
- Selected populations:
 - Women
 - Elderly
 - Pregnancy
 - Family History
- Cost-effective

Clinical Pearls...Who to Treat?

- Though indications for treatment with L-thyroxine remain uncertain, general guidelines can be offered...
 - The greater the TSH level ($>10\mu\text{U}/\text{mL}$) and the higher anti-thyroid antibodies the more likely the patient will overt to hypothyroidism
 - The presences of symptoms related to mild thyroid dysfunction also increases the benefit of treatment even if TSH levels are only slightly elevated ($>5\mu\text{U}/\text{mL}$)

Clinical Pearls...Who to Treat?



Treatment

- Due to the fact that patients with subclinical hypothyroidism have only minimal thyroid dysfunction a daily dose of 25-50µg may be adequate
- Before making dosage adjustments the patient should maintain the initial treatment for 6-8 weeks
- Once the correct dosage is met the patient should have repeat TSH levels every 6-12 months

Conclusions

- Important questions...
 - How often are symptoms causally related to thyroid disease?
 - Focus on screening and disease markers
- L-thyroxine therapy and subclinical hypothyroidism remains undefined unless...
 - TSH level is > 10µU/mL + symptoms/ positive anti-thyroid antibodies
- Screening
 - Evaluate each individual patient (Women, Elderly, pregnant patients and those at higher risk)

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