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Clinical Evidence Concise

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Hyperthyroidism

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What are the effects of drug treatments for primary hyperthy

LIKELY TO BE BENEFICIAL

Antithyroid Drugs (Carbimazole, Propyl-thiouracil, and Thiamazole)

We found no randomized controlled trials (RCTs) comparing antithyroid drug persons with hyperthyroidism, although there is consensus that treatment is b RCTs comparing antithyroid drugs (carbimazole, propylthiouracil, or thiamaz systematic review found that fewer persons relapsed with 18 months of highe treatments than with six months; however, it found no significant difference f compared with 12 to 18 months of lower-dose treatment. One systematic revi number of persons relapsed to hyperthyroidism with antithyroid drugs alone (drugs plus thyroxine (block replace). One RCT found a similar proportion of who became euthyroid between high-and low-dose thiamazole. However, it f were lower with titration regimens. There have been concerns about bone ma neutropenia, and agranulocytosis with antithyroid drugs. The doses of antithy studies are higher than are generally used in practice. (Based on consensus be considered unethical.)

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By Topic

Radioactive Iodine (in Persons Without Ophthalmopathy; May Increase Ophthalmopathy with Graves' Disease)

We found no RCTs comparing radioiodine with placebo in persons with hyperthyroidism. There is consensus that treatment is beneficial. Cohort studies found that radioiodine increased thyroid and extrathyroid cancers but not overall incidence of cancer. RCTs found that radioiodine worsened ophthalmopathy in persons with Graves' disease compared with other treatments. (Consensus because RCTs would be considered unethical.)

UNLIKELY TO BE BENEFICIAL**Adding Thyroxine to Antithyroid Drugs (Carbimazole, Propylthiouracil, and Methimazole)**

One systematic review found that a similar number of persons relapsed to hyperthyroidism with antithyroid drugs plus thyroxine (block and replace) and antithyroid drugs alone. (Consensus because the review found that adverse effects were higher with block and replace regimens. Another review found a significant difference in relapse between thyroxine and no treatment after antithyroid drug treatment.)

What are the effects of surgical treatments for primary hyperthyroidism?**LIKELY TO BE BENEFICIAL****Thyroidectomy**

We found no RCTs comparing surgery with placebo in persons with hyperthyroidism. There is consensus that treatment is beneficial. One systematic review and subsequent RCT found that thyroidectomy decreased hyperthyroidism and increased euthyroidism and hypothyroidism compared with subtotal thyroidectomy. However, another subsequent RCT found no significant difference between bilateral subtotal, unilateral total, and contralateral subtotal, and total thyroidectomy. (Consensus because the review and RCTs did not find sufficient evidence that effects were worse with total or subtotal thyroidectomy. (Based on consensus because RCTs would be considered unethical.)

What are the effects of treatments for subclinical hyperthyroidism?**LIKELY TO BE BENEFICIAL****Any Antithyroid Treatment**

One controlled clinical trial found that thyroid-stimulating hormone (TSH), alkaline phosphatase, and bone mineral density were higher in women given radioiodine compared with women with no compression symptoms from a nodular goiter.

DEFINITION

Hyperthyroidism is characterized by high levels of serum thyroxine (T₄), high triiodothyronine (T₃), or both, and low levels of TSH. Subclinical hyperthyroidism is characterized by decreased levels of TSH (less than 0.1 mIU per L) but with levels of T₄ and T₃ (total T₄: 5 to 11 mcg per dL [64 to 142 nmol per L]; total T₃: 65.19 to 162.9 nmol per L), depending on assay type).¹ The terms hyperthyroidism and thyrotoxicosis are used synonymously; however, they refer to slightly different conditions. Hyperthyroidism refers to the overactivity of the thyroid gland leading to excessive production of thyroid hormones. Thyrotoxicosis refers to the clinical effects of unbound thyroid hormones, whether or not the thyroid gland is the primary source.²

Secondary hyperthyroidism owing to pituitary adenomas, thyroiditis, iodine-induced hyperthyroidism, and treatment of children and pregnant or lactating women are not covered in this review. Hyperthyroidism can be caused by Graves' disease (diffusely enlarged thyroid gland with ophthalmopathy and dermopathy), toxic multinodular goiter (thyrotoxicosis with multinodular goiter on palpation), or toxic adenoma (benign hyperthyroidism with a single toxic nodule on palpation).

neoplasm presenting as a solitary thyroid nodule).¹ We have not included treatment of ophthalmopathy in this review, although we do report on worsening of Graves' disease with radioiodine. We also have not included euthyroid sick syndrome (a condition for example, pneumonia, acute myocardial infarction, cancer, and depression; levels of TSH and T₃).

Diagnosis

The diagnosis of hyperthyroidism is established by a raised serum total or free thyroxine (T₄) level, and reduced TSH level, and high radioiodine uptake in the thyroid gland with few exceptions. Usual symptoms are irritability, heat intolerance and excessive sweating, palpitations, increased appetite, increased bowel frequency, and oligomenorrhea. Persons with hyperthyroidism often have tachycardia, fine tremors, warm and moist skin, muscle weakness, and weight loss.¹

Incidence and Prevalence

Hyperthyroidism is more common in women than in men. One study (2,779 persons in the United Kingdom; median age 58 years; 20 years' follow-up) found an incidence of 0.8 per 1,000 women a year (95% confidence interval [CI], 0.5 to 1.4 per 1,000 women a year); the study reported that the incidence was negligible in men.

In areas with low iodine intake, the incidence of hyperthyroidism is higher than in areas with high iodine intake because suboptimal iodine intake induces nodular goiter, and by the time the disease becomes autonomous, hyperthyroidism develops.⁴ In Denmark, with moderate iodine intake, the incidence of hyperthyroidism (defined as low levels of TSH) is 9.7 percent compared with 3.7 percent in Iceland with high iodine intake. The prevalence in the Danish study was 38.7 percent in women and two per 100,000 men a year.⁵

Etiology

Smoking is a risk factor, with an increased risk of Graves' disease (odds ratio 3.5) and toxic nodular goiter (OR = 1.7; 95% CI, 1.1 to 2.5).⁶ In areas with high iodine intake, the major cause is Graves' disease, whereas nodular goiter is the major cause in areas with low iodine intake. A correlation between diabetes mellitus and thyroid dysfunction has been described in a study of a population with diabetes, the overall prevalence of thyroid disease was 13 percent, the highest in women with type 1 diabetes (31 percent). As a result of screening, hyperthyroidism was diagnosed in 7 percent of persons with diabetes (hyperthyroidism in 1 percent of persons with diabetes).

Prognosis

Clinical hyperthyroidism can be complicated by severe cardiovascular or neurologic complications requiring hospital admission or urgent treatment.

MORTALITY

One population-based 10-year cohort study of 1,191 persons at least 60 years of age found an excess in mortality among persons who had a low initial TSH level. The excess in mortality was due to cardiovascular diseases. However, the persons in this study who had a low TSH level also had a higher prevalence of other illnesses, and adjustment was done only for age and sex. We found another population-based study evaluating 3,888 persons with hyperthyroidism. An increased risk was found in all-cause mortality or serious vascular events in persons whose hyperthyroidism was treated and stabilized, but an increased risk of dysrhythmias was found in persons with hyperthyroidism compared with the standard population (standardized incidence ratio 1.63 to 4.24).⁹

ATRIAL FIBRILLATION IN PERSONS WITH OVERT HYPERTHYROIDISM

We found one cohort study evaluating the incidence of atrial fibrillation in persons with low serum TSH concentrations (0.1 mIU per L or less). It found that low TSH values were associated with an increased risk of atrial fibrillation (diagnosed by electrocardiogram) over 10 years (61 persons with low TSH and 1,576 persons with normal TSH; incidence 28 per 1,000 person-years with low TSH values versus 11 per 1,000 person-years with normal TSH values; 13 out of 61 [21 percent] persons with low TSH values versus 133 out of 1,576 [8.5 percent] persons with normal TSH values; relative risk [as calculated by *Clinical Evidence* to 4.20).¹⁰ A population-based study including 40,628 persons diagnosed with hyperthyroidism in Denmark from 1977 to 1999 found that 8.3 percent were diagnosed with atrial fibrillation within 30 days from the date of diagnosis of hyperthyroidism.¹¹

QUALITY OF LIFE

The quality of life of persons with thyroid problems can be reduced in many ways, and this can continue in the long term. In a long-term follow-up (179 persons, treated before investigation), persons with Graves' disease had diminished vital and functional aspects even after years of treatment compared with a large Swedish reference population.

FRACTURE RATE AND BONE MINERAL DENSITY

Hip and spine bone mineral density levels can decrease if hyperthyroidism is not treated; when treated, bone mineral density can increase to normal levels. The risk of fracture is increased in persons with hyperthyroidism. Progression from subclinical to overt hyperthyroidism is more likely in persons with nodular goiter but not in persons found by screening without other thyroid disease.¹⁴ A meta-analysis (search date 1996), based on data from screening studies, found that 1.5 percent of women and 1.0 percent of men who had a low TSH level at baseline developed an elevated free T₄ or T₃ level.¹⁴ Ophthalmopathy is a complication of hyperthyroidism. Treatment can be problematic and usually involves topical corticosteroids and radiation of the eye muscles.

THYROID VOLUME AND THE NODULARITY OF THE GLAND INFLUENCE THE COURSE OF OVERT HYPERTHYROIDISM

In a controlled study of 124 persons with newly diagnosed hyperthyroidism, the relapse rate was calculated after treatment with a combined antithyroid drug plus T₄ for about 18 months. Persons with Graves' disease who did not have a goiter or had a small goiter had a significantly lower relapse rate compared with persons with Graves' disease who had a medium- or large-size goiter. Persons with multinodular goiter had a relapse within the first year after stopping medication.

Author disclosure: Nothing to disclose.

EDITOR'S NOTE In the United States, carbimazole is not available, thiamazole is called methimazole, and thyrotropin is only available in the injectable form.

SEARCH DATE: April 2006

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