Clinical THYROIDOLOGY FOR PATIENTS

AMERICAN THYROID ASSOCIATION
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VOLUME 4 • ISSUE 6 • JUNE 2011

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Clinical Thyroidology for Patients

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EDITOR'S COMMENTS

Welcome to Clinical Thyroidology for Patients. This publication is a collection of summaries of the top articles from the recent medical literature that cover the broad spectrum of thyroid disorders. *Clinical Thyroidology for Patients* is published on a monthly basis and includes summaries of research studies that were discussed in the previous month's issue of *Clinical Thyroidology*, a publication of the American Thyroid Association for physicians. This means that you, the patients, are getting the latest information on thyroid research and treatment almost as soon as your physicians. The Calendar of Events highlights educational forums and support groups that are organized around the country by members of the Alliance for Thyroid Patient Education. The *Alliance* member groups consist of: the *American Thyroid Association*, the *Graves' Disease Foundation*, the *Light of Life Foundation* and *ThyCa: Thyroid Cancer Survivors Association*.

In this issue, the studies ask the following questions:

- Do FDG-PET scans have a role in patients with thyroid nodules that have an indeterminate biopsy result?
- How accurate are tests for thyroglobulin antibodies?
- How accurate are thyroid fine needle aspiration biopsies?
- Do intraveneous bisphosphonates have a role in treating patients with thyroid cancer?
- Does the placenta have a role in making sure developing babies have adequate iodine during pregnancy?
- How common is cancer in nodules in patients with Hashimoto's thyroiditis?
- Do soy phytoestrogens affect thyroid function in patients with mild hypothyroidism?
- What is the best way to manage hypothyroidism in patients with pituitary tumors?

We welcome your feedback and suggestions. Let us know what you want to see in this publication. I hope you find these summaries interesting and informative.

— Alan P. Farwell, MD

HOW TO NAVIGATE THIS DOCUMENT: The Table of Contents and the Bookmarks are linked to the articles. To navigate, move your cursor over the article title you wish to see (either in the Contents or in the Bookmarks panel) and the hand will show a pointing finger, indicating a link. Left-click the title and the article will instantly appear. To return to the Contents, move the cursor to the bottom of the page and left-click Back to Table of Contents.

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THYROID CANCER

A negative FDG-PET scan excludes the diagnosis of cancer in thyroid nodules >15 mm diameter

BACKGROUND

Thyroid nodules are very common and raise the possibility of thyroid cancer. Fine needle aspiration biopsy is the best test to determine whether a thyroid nodule is cancerous outside of surgery. However, in 10-15% of biopsies, the cytology is unable to provide a definite answer, meaning that patients may need to undergo repeat biopsy or surgery to determine if the nodule is actually cancerous. 18F-2-fluoro-2-deoxy-d-glucose-positron emission tomography (FDG-PET) scanning, which is commonly used in the evaluation of cancer, has been studied by multiple authors with regard to its role in thyroid nodules. The authors of this study looked at existing studies to determine if FDG-PET scanning would be helpful in determining if patients with an indeterminate biopsy result have thyroid cancer.

THE FULL ARTICLE TITLE:

Vriens D et al. The role of [(18) F]-2-fluoro-2-deoxy-d-glucose-positron emission tomography in thyroid nodules with indeterminate fine-needle aspiration biopsy: Systematic review and meta-analysis of the literature. Cancer. March 22, 2011. [Epub ahead of print]. doi: 10.1002/cncr.26085.

SUMMARY OF THE STUDY

The authors searched the medical literature and found 6 studies comprising 225 patients that examined the role of FDG-PET scanning in thyroid nodules. The FDG-PET scan was positive in 63% of cases, but only 48% of these had a cancer, meaning that majority of the patients with a positive FDG-PET did not have thyroid cancer. When the authors limited the evaluation to thyroid nodules >15 mm, all of the cancers had a positive FDG-PET scan, but still the majority of patients with a positive test result did not have thyroid cancer. Thus, while a positive FDG-PET scan did not diagnose cancer, a negative FDG-PET ruled out cancer in the nodule.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that a negative FDG-PET scan in patients with thyroid nodules >15 mm with indeterminate thyroid biopsy results excludes the diagnosis of thyroid cancer. As the cost of FDG-PET scans is currently high, this test is unlikely to be routinely performed as part of the work-up of thyroid nodules. But as the cost comes down, there may be a role in for FDG-PET scanning in patients with a thyroid nodule greater than 15 mm with an indeterminate biopsy to rule out thyroid cancer and potentially avoid surgery for the purpose of making a diagnosis.

Also, as FDG-PET scan is commonly performed in patients with other types of cancer, finding a thyroid lesion that is positive is not diagnostic of thyroid cancer. Nonetheless, there is at least a 48% percent chance that such a thyroid lesion could be cancerous. It is important for a patient who has a thyroid mass identified by FDG-PET scan to be properly evaluated like any other nodule.

— Ronald Kuppersmith, MD

ATA THYROID BROCHURE LINKS

Thyroid cancer: http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html

Thyroid Nodules: http://thyroid.org/patients/patient_brochures/nodules.html

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THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

Thyroid fine needle aspiration biopsy (FNAB): a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

18F-2-fluoro-2-deoxy-d-glucose-positron emission tomography (FDG-PET): a nuclear medicine imaging test that uses a small amount of radiolabeled glucose to identify cancer. Since cancer cells are more active than normal cells, the cancer cells take up more of the radiolabeled glucose and show up on the FDG-PET scan. FDG-PET scans are frequently combined with CT scans to accurately identify where the cancer is located. Its role in thyroid cancer is still being studied.

Indeterminate thyroid biopsy: this happens usually when the diagnosis is a follicular or hurtle cell lesion. Follicular and hurtle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurtle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

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THYROID CANCER

Risk of persistent thyroid cancer in patients with negative thyroglobulin and thyroglobulin antibodies performed on some commercial tests

BACKGROUND

The initial treatment for patients with thyroid cancer is surgery to remove the thyroid gland and any abnormal lymph nodes. This is often followed by treatment with radioactive iodine to destroy any remaining thyroid cells, both cancerous and normal. This allows patients to be followed for a recurrence of the thyroid cancer with a blood test measuring the thyroid cell protein thyroglobulin which becomes a thyroid cancer marker in these patients. Thyroglobulin antibodies (TgAb) are usually measured along with the thyroglobulin test, because an elevated antibody level may interfere with thyroglobulin measurements. An elevated TgAb test may cause the thyroglobulin level to be lower than it really is while a negative TgAb test means that the thyroglobulin level is accurate. There are several companies that make tests for TgAb, often using different methods. In this study, the accuracy of 4 different tests to detect the TgAb in patients with thyroid cancer were compared.

THE FULL ARTICLE TITLE:

Spencer C et al. Current thyroglobulin autoantibody (TgAb) assays often fail to detect interfering TgAb that can result in the reporting of falsely low/undetectable serum thyroglobulin IMA values for patients with differentiated thyroid cancer. J Clin Endocrinol Metab. 2011;18:2010-2762.

SUMMARY OF THE STUDY

The blood from 785 thyroid cancer patients was used in this study. A total of 143 out of 785 thyroid cancer patients were TgAb positive by the most sensitive method. The other 3 tests failed to detect TgAb in 35%, 44.1% and 62.2% of these TgAb-positive patients.

Using the lowest level that can be measured by each test (instead of the recommended manufacture's reference), TgAb still was missed in 21.9% and 34.3% of patients while the 3rd test could detect TgAb in all TgAb-positive thyroid cancer patients.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This is an important report that shows that commercial TgAb tests can miss the presence of TgAb in TgAb-positive thyroid cancer patients. Using the manufacture's recommended reference ranges, commercial tests failed to detect TgAb in up to 2/3 of the TgAb-positive thyroid cancer patients. Even using lowest detection level of each test, TgAb was not detectable in 20-30% of TgAb-positive thyroid cancer patients.

This study shows that Tg alone may not be sufficient in all patients to detect persistent or recurrent thyroid cancer.

— Jamshid Farahiti, MD

ATA THYROID BROCHURE LINKS

Thyroid cancer: http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html

ABBREVIATIONS & DEFINITIONS

Thyroglobulin: a protein made only by thyroid cells, both normal and cancerous. When all normal thyroid tissue is destroyed after radioactive iodine therapy in patients with thyroid cancer, thyroglobulin can be used as a thyroid cancer marker in patients that do not have thyroglobulin antibodies.

Thyroglobulin Antibodies: antibodies are directed against foreign proteins that may interfere with hormone tests. Thyroglobulin-antibodies occur in approximately 25% of thyroid cancer patients and bind to thyroglobulin in serum and make the thyroglobulin measurement incorrect.

Cancer recurrence: this occurs when the cancer comes back after an initial treatment that was successful in destroying all detectable cancer at some point.

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THYROID CANCER

Implications of bisphosphonate use in thyroid cancer related bone metastatic disease

BACKGROUND

Bisphosphonates are a class of drugs that decrease bone breakdown. They are commonly prescribed for osteoporosis treatment to strengthen bones and prevent fractures. Zoledronic acid is also used in patients with cancers that spread to the bone, such as breast, prostate and lung cancers, as they decrease risk of complications related to bone metastasis itself. These complications include risk for spinal cord compression, need for radiation therapy, need for surgery and cancer-related fractures. Zoledronic acid is given more frequently in cancer patients than in patients with osteoporosis. While the bisphosphonate medications are generally well tolerated, a rare side effect, known as osteonecrosis of the jaw, may affect the teeth in patients treated with this higher does.

Thyroid cancer is the third most common cancer to spread to bone after breast and prostate cancers. To date, management of metastatic bone disease in thyroid cancer has been conservative, with use of surgery to decrease risk of impeding fracture and radiation therapy for pain control. In this study, the authors analyzed effect of monthly zoledronic acid infusion on development of bone complications in thyroid cancer patients with spread of the cancer to the bone.

THE FULL ARTICLE TITLE:

Orita Y et al Zoledronic acid in the treatment of bone metastases from differentiated thyroid carcinoma. Thyroid 2011;21:31-5. Epub November 8, 2010.

SUMMARY OF THE STUDY

A total of 50 thyroid cancer patients with spread of the cancer to the bone took part in the study. Of these, 22 patients were treated with monthly zoledronic acid for up to 2.75 years. All 50 patients received surgery and radiation therapy as needed. The development of cancer-related fractures or spinal cord compression occurred in 3 of 22 (13.4%) patients treated with zoledronic acid versus 14 of 28 (50%) untreated patients. Two (9.1%) zoledronic acid-treated patients developed osteonecrosis of the jaw despite regular dental follow-up.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

While this small study is limited, its results point toward beneficial effect of zoledronic acid in decreasing bone complications in patients with thyroid cancer spread to the bone. More studies are needed to better define 1) effect on bone complications, 2) the best frequency of administration and dose needed to achieve beneficial effect of zoledronic acid and 3) risk of long-term complications from such therapies. This is particularly important in patients with metastatic thyroid cancer with long life expectancies despite distant metastatic disease.

— Mona Sabra, MD

ATA THYROID BROCHURE LINKS

Thyroid cancer: http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html

ABBREVIATIONS & DEFINITIONS

Bisphosphonate medications: a class of drugs that are commonly prescribed for osteoporosis treatment to strengthen bones and prevent fractures. Commonly used bisphosphonates are Alendronate (Fosamax), Risedronate (Actonel), Zoledronic acid (Zometa, Reclast) and Ibandronate (Boniva). In addition, Zoledronic acid is used to prevent bone complications in cancer patients with spread of cancer to the bone.

Cancer metastasis: spread of the cancer from the initial organ where it developed to other organs, such as the lungs and bone.

Osteonecrosis of the jaw (ONJ): a condition where decreased blood supply occurs in part of the jaw bone, leading to pain and bone decay. ONJ can occur spontaneously or is associated with steroid use, radiation therapy and bisphosphonate therapy. Risk for ONJ in setting of bisphosphonate use is less than 1 in 100,000 person-years and is dependent on frequency, duration and mode of administration of the drug (intraveneous preparation, higher dose, longer duration are associated with increased risk). Avoidance of dental surgery while on bisphosphonate therapy decreases ONJ risk.

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THYROID NODULES

A review of the diagnostic accuracy of thyroid fine needle aspiration biopsy

BACKGROUND

Thyroid nodules are very common and often need to be evaluated for cancer. While most thyroid nodules are non-cancerous, ~5% are cancerous. Fine needle aspiration biopsy is the best test for diagnosing cancer outside of surgery. Although most of the time the thyroid biopsy provides an accurate diagnosis, sometimes the results can be inconclusive. Also, rarely a biopsy result may be incorrect and be read as cancerous when no cancer is present or read as benign when a cancer actually is present. This study examined the accuracy of the thyroid fine needle aspiration biopsy in diagnosing thyroid cancer. The authors compared the biopsy results with the pathology results after the surgical removal of thyroid nodules in their own patients and in other published studies. They also examined how often local pathologists and experts who also reviewed the specimens agreed on the diagnosis for the surgical specimens.

THE FULL ARTICLE TITLE

Wang CC et al. A large multicenter correlation study of thyroid nodule cytopathology and histopathology. Thyroid 2011;21:243-51.

SUMMARY OF THE STUDY

Four cytologic categories were used to report the biopsy results: benign, malignant (cancerous), indeterminate and non-diagnostic. The study included 753 biopsies: 80% were categorized as benign, 7% as malignant, 8% as indeterminate and 5% as non-diagnostic. Among the 112 thyroid nodules that were surgically removed, the following were diagnosed with cancer: 11% of the nodules with benign cytology on FNAB, 98% of the nodules with malignant cytology, 34% of the nodules with indeterminate cytology and none of the nodules with non-diagnostic cytology.

Similar results were obtained in the review of 11 other studies including a total of 17,059 patients who underwent thyroid biopsy. Among the 8,937 patients who proceeded with thyroid surgery based on the biopsy result, the cancer rate was 12% in the benign category, 97% in the malignant, 25-62% in the indeterminate and 12% in the non-diagnostic category.

Two expert pathologists reviewed the surgical specimens from 221 resected thyroid nodules in addition to the local pathologist to determine whether the specimens were benign or malignant. In 8-11% disagreement was noted between the diagnoses reported by experts compared to local pathologists when diagnosing the thyroid nodules as being benign or malignant.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Non-diagnostic and indeterminate thyroid biopsy results remain a challenge when evaluating patients with thyroid nodules. For example, most of the patients with biopsies in the indeterminate cytology results will undergo surgery for a definitive diagnosis, however, two thirds of these thyroid nodules are benign. Approximately 25% of the patients with biopsies that are indeterminate decide not to undergo thyroid surgery and thyroid cancer can be missed in this situation. Therefore, we need to further improve the biopsy diagnostic accuracy. Current research is looking into several areas to improve the diagnostic accuracy of biopsies. However, it is important to remember that the thyroid biopsy remains the best test to determine which patients will benefit the most from thyroid surgery.

— Alina Gavrila, MD

ATA THYROID BROCHURE LINKS

Thyroid Nodules: http://thyroid.org/patients/patient_brochures/nodules.html

Thyroid Cancer: http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html

Thyroid Surgery: http://thyroid.org/patients/patient_brochures/surgery.html

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THYROID NODULES, continued

ABBREVIATIONS & DEFINITIONS

Thyroid nodule: an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (benign), ~5% are cancerous (malignant).

Thyroid fine needle aspiration biopsy (FNAB): a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or malignant (cancer). The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

Non-diagnostic/Insufficient thyroid biopsy: this happens when not enough cells are obtained during the biopsy to provide a diagnosis and often results in the need to repeat the biopsy. This occurs in 5-10% of biopsies.

Indeterminate thyroid biopsy: this happens usually when the diagnosis is a follicular or Hurthle cell lesion. Follicular and Hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or Hurthle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule and have a definitive diagnosis.

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THYROID NODULES

A study about the risk of thyroid cancer in thyroid fine needle aspiration biopsy specimens read as suspicious

BACKGROUND

Thyroid nodules are very common and may be found in up to 50% of people over the age of 50. While most thyroid nodules are non-cancerous, ~5% are cancerous. The presence of cancer can be determined by performing a fine needle aspiration biopsy. One problem with fine needle aspiration biopsies is that 10-15% of results return with a diagnosis of "suspicious for cancer", also known as a follicular cell or hurthle cell neoplasm. While this diagnosis only carries a 10-15% risk of actual cancer, the diagnosis requires surgery to remove the nodule. Hurthle cells are common in Hashimoto's thyroiditis, a common cause of hypothyroidism, so a "suspicious" fine needle aspiration biopsy may have less of a risk for being a cancer in this setting. The purpose of this study was to determine how often the presence of a diagnosis of "suspicious of cancer, Hurthle cell type" predicted the presence of thyroid cancer in thyroid fine needle aspiration biopsy specimens.

THE FULL ARTICLE TITLE:

Roh MH et al. The predictive value of the fine-needle aspiration diagnosis "suspicious for a follicular neoplasm, hurthle cell type" in patients with hashimoto thyroiditis. Am J Clin Pathol 2011;135:139-45.

SUMMARY OF THE STUDY

The medical records of patients who had undergone thyroid fine needle aspiration biopsy during 1992-2007 at three institutions and whose biopsies were read as being suspicious for Hurthle cell neoplasm were analyzed. Of the 401 patients identified, 287 (72%) had thyroid surgery. Only 21 (7%) of these 287 patients had Hashimoto's thyroiditis. In 69 (24%) of the 287 patients, the thyroid nodule which was biopsied was proven to contain thyroid cancer. In patients whose biopsies were read as being suspicious for Hurthle cell neoplasm, the rate of thyroid cancer was 25% in patients without Hashmimoto's thyroiditis, whereas it was 9.5% in patients with Hashimoto's thyroiditis. While suggestive, these two rates were not significantly different.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The problem of "suspicious" results of fine needle aspiration biopsies is significant since this diagnosis usually results in surgery and the majority of these patients do not have cancer. The authors of this study suggest that in the case of patients with Hashimoto's thyroiditis whose thyroid biopsy findings are suspicious for Hurthle cell neoplasm, are less likely to have cancer. However, more research is needed to better understand the impact of a diagnosis of Hashimoto's thyroiditis on the ability of thyroid fine needle aspiration biopsy specimens to predict the presence of thyroid cancer, when biopsies are suspicious for Hurthle cell neoplasm.

— Anna Sawka, MD

ATA THYROID BROCHURE LINKS

Thyroid Nodules: http://thyroid.org/patients/patient_brochures/nodules.html

Thyroiditis: http://thyroid.org/patients/patient_brochures/thyroiditis.html

Thyroid Surgery: http://thyroid.org/patients/patient_brochures/surgery.html

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THYROID NODULES, continued

ABBREVIATIONS & DEFINITIONS

Thyroid fine needle aspiration biopsy (FNAB): a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

Hashimoto's thyroiditis: the most common cause of hypothyroidism in the United States. It is by antibodies that attack the thyroid and destroy the gland.

"Suspicious" thyroid biopsy: this happens usually when the diagnosis is a follicular or hurtle cell caused lesion. Follicular and hurtle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurtle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

Thyroid nodule: an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5% are cancerous.

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THYROID AND PREGNANCY

The placenta can store different amounts of iodine during pregnancy

BACKGROUND

Iodine is required for making thyroid hormones. The main source of iodine is the diet. If there is not enough iodine in the diet, as can be seen in iodine-deficient regions of the world, then hypothyroidism can develop. This is especially true during pregnancy where the demand for thyroid hormone increases and hypothyroidism can occur. Both iodine and thyroid hormone are very important for normal brain development of the baby during pregnancy. During pregnancy, the placenta forms both the barrier and the connection between the mother and the baby. This study was done to see if the placenta can store extra iodine in women who do not get enough iodine from their diets. The placental iodine levels of mothers in Ireland (where iodine intake is generally low) were compared to mothers in Iran (where iodine intake is generally adequate).

THE FULL ARTICLE TITLE:

Burns R et al. Is placental iodine content related to dietary iodine intake? Clin Endocrinol 2011. doi 0.1111/j.1365-2265.2011.04039.x

SUMMARY OF THE STUDY

Iodine levels in the placentas of 58 Irish women and 45 Iranian women were measured. The placentas were obtained after the deliveries of healthy single babies. The placental iodine level in each mother was compared to her urine iodine level, which is the best estimate of the amount of iodine in the diet. The placental iodine levels varied widely, particularly among the Iranian women. However, the Iranian mothers (adequate iodine in the diet) had about double the amount of placental iodine than the Irish mothers (low iodine in the diet).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Mothers who diets are higher in iodine may be able to store more placental iodine. This suggests a new role of the placenta that was not known. It may be a way for the body to make sure that the baby receives enough iodine to make thyroid hormone during an important time of brain development.

— Angela Leung, MD

ATA THYROID BROCHURE LINKS

Thyroid and Pregnancy: http://thyroid.org/patients/patient_brochures/pregnancy.html

Iodine deficiency: http://thyroid.org/patients/patient_brochures/iodine_deficiency.html

ABBREVIATIONS & DEFINITIONS

Iodine: an element found naturally in various foods that is important for making thyroid hormones and for normal thyroid function. Common foods high in iodine include iodized salt, dairy products, seafood and some breads.

Placenta: a part of the uterus that supplies blood and nutrients to the developing baby during pregnancy. It forms both a barrier and a connection between the mother and the baby.

Hypothyroidism: a condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. Treatment requires taking thyroid hormone pills.

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HYPOTHYROIDISM

High doses of soy phytoestrogen are a risk factor in the progression of subclinical to overt hypothyroidism

BACKGROUND

Soy foods are an important part of the diets of Asian people and are becoming increasingly popular in many non-Asian countries, including the United States. Soy foods are rich in phytoestrogens, which are thought to have many beneficial effects on cardiovascular health. Measures of cardiovascular health possibly affected by phytoestrogens include blood pressure, insulin sensitivity and markers of inflammation. Phytoestrogens also are though to have beneficial to bone health and are said to be protective also against breast and prostate cancer. Soy also has long been thought to interfere with absorption of thyroid hormone from the stomach. Because of this, there has been concern that soy may worsen thyroid function, particularly in people with pre-existing mild hypothyroidism (underactive thyroid). This study examined the effect of soy on thyroid function and markers of cardiovascular health in patients with mild hypothyroidism.

THE FULL ARTICLE TITLE:

Sathyapalan, T, et al. The effect of soy phytoestrogen supplementation on thyroid status and cardiovascular risk markers in patients with subclinical hypothyroidism: a randomized, double-blind, crossover study, J Clinical Endocrinol Metab 2011; 96 (5): 1442-49

SUMMARY OF THE STUDY

Sixty patients (age 44 to 70 years) with subclinical hypothyroidism (TSH between 5 and 15 mU/L and normal serum free thyroxine T_4) participated in the study. Patients were randomly assigned to low-dose phytoestrogen (30 grams of soy protein with 2 mg of phytoestrogens, typical of a Western diet) or high-dose phytoestrogen (30 grams of soy protein with 16 mg of phytoestrogens, representative of a vegetarian diet) for 8 weeks and then the groups were reversed after 8 weeks on a normal diet. Patients were followed and evaluated for development of overt hypothyroidism (serum TSH >10 mU/L and a low free T_4).

Six patients (10%) developed clinical hypothyroidism after high-dose phytoestrogen but none after low-dose phytoestrogen. These patients were started on levothyroxine and continued to receive this treatment after 6 months. All six patients were women and only one of them had positive TPO antibodies (a measure of autoimmune thyroid disease). Neither baseline thyroid function tests, nor thyroid antibody measurement were helpful to predict progression from subclinical to overt hypothyroidism in patients receiving high dose phytoestrogen supplementation.

After high dose phytoestrogen supplementation, there was an improvement in blood pressure and insulin sensitivity and a reduction in hsCRP (a marker of inflammation), all of which suggest improved cardiovascular health markers.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This is the first study to show that dietary supplementation with very high doses of soy phytoestrogen (at levels typical of a vegetarian diet), may result in a 3-fold increase in the risk of progression from subclinical to overt hypothyroidism, suggesting that vegetarian patients with mild subclinical hypothyroidism may need more careful monitoring of thyroid function. The mechanism for this effect is not well understood. On the other hand, high dose phytoestrogen also resulted in improvement in cardiovascular risk factors despite worsening of thyroid function and may be beneficial to patients with increased cardiovascular risk.

— M. Regina Castro, MD

ATA THYROID BROCHURE LINKS

Hypothyroidism: http://thyroid.org/patients/patient_brochures/hypothyroidism.html

Thyroid Function Tests: http://thyroid.org/patients/patient_brochures/function_tests.html

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HYPOTHYROIDISM, continued

ABBREVIATIONS & DEFINITIONS

Phytoestrogens: a group or compounds naturally found in some plants that have structural similarity to estradiol (the main female sex-hormone), are also called "dietary estrogens and can have some estrogen-like effects.

Hypothyroidism: a condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. Treatment requires taking thyroid hormone pills.

Subclinical Hypothyroidism: a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH. There is controversy as to whether this should be treated or not.

Overt Hypothyroidism: clear hypothyroidism an increased TSH and a decreased T_4 level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

TPO antibodies: these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

TSH: thyroid stimulating hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

Levothyroxine: the major hormone produced by the thyroid gland and available in pill form as Levoxyl™, Synthroid™, Levothroid™ and generic preparations.

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HYPOTHYROIDISM

Diagnosis and treatment of hypothyroidism in patients with pituitary tumors

BACKGROUND

The pituitary gland is an endocrine gland that sits at the base of the brain and secretes hormones that control thyroid and adrenal function, growth and reproduction. The pituitary gland secretes TSH to control thyroid function. The vast majority of hypothyroidism is caused by thyroid gland failure (primary hypothyroidism) and is associated with increased TSH levels. Hypothyroidism due to pituitary problems (central hypothyroidism) is associated with normal or low TSH levels in the setting of low thyroid hormone levels. The most common pituitary problems to cause central hypothyroidism are tumors of the pituitary gland. Treatment of hypothyroidism in these patients is complex because the TSH level cannot be used to help determine the correct dose. Common practice is to use the dose of Levothyroxine which results in a free T_4 blood level in the middle to upper part of the reference range. This practice may not result in an appropriate or safe level in all patients. This study was performed to determine if free T_4 levels in a group of treated patients with pituitary tumors were similar to the levels in patients with typical hypothyroidism or other thyroid disorders. The aim of the study was to reassess the proper range of free T_4 levels in patients with hypothyroidism who also have pituitary tumors.

THE FULL ARTICLE TITLE:

Koulouri O et al. Diagnosis and treatment of hypothyroidism in TSH deficiency compared to primary thyroid disease: pituitary patients are at risk of under-replacement with Levothyroxine. Clin Endocrinology. 2011 doi:10.1111/j.1365-2265.2011.03984.x.

SUMMARY OF THE STUDY

A total of 514 patients with pituitary tumors were studied. Some pituitary tumors were "low risk" with small tumors not requiring treatment and some were "high risk" with large tumors or had prior treatment with surgery and/or radiation to the pituitary. Their free T_4 blood levels were compared to levels in patients with typical primary hypothyroidism and other patients with thyroid disease. Approximately 38% of the "high risk" pituitary patients on thyroid hormone therapy had very low free T_4 levels, suggesting under-treatment in many of these patients. On the other hand, if all pituitary patients treated with thyroid hormone had free T_4 levels in the middle to upper normal range, 1/3 – ½ of them may be over-treated as compared to patients with primary hypothyroidism.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Patients with hypothyroidism from pituitary tumors should be treated on an individual basis using clinical signs. The goal of the free T_4 test should be close to the mid-normal range. Due to patient variables, an alternative treatment plan could be used by giving the Levothyroxine dose based on body weight (e.g. 1.3 mcg/kg weight). At present, there is no completely reliable method to restore the thyroid hormone levels to the exact level which is correct in every patient. Individual therapy is needed to avoid the consequences of over and under-treatment.

— Jerrold Stock, MD

ATA THYROID BROCHURE LINKS

Hypothyroidism: http://thyroid.org/patients/patient_brochures/hypothyroidism.html

Thyroid Hormone Treatment: http://thyroid.org/patients/patient_brochures/hormonetreatment.html

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HYPOTHYROIDISM, continued

ABBREVIATIONS & DEFINITIONS

Pituitary gland: this endocrine gland sits at the base of the brain and secretes hormones that control thyroid and adrenal function, growth and reproduction. The pituitary gland secretes TSH to control thyroid function.

Hypothyroidism: a condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. Treatment requires taking thyroid hormone pills.

Primary hypothyroidism: the most common cause of hypothyroidism cause by failure of the thyroid grand.

Central hypothyroidism: a rare cause of hypothyroidism where the thyroid gland is normal and the problem is inadequate TSH secretion from the pituitary gland.

TSH: thyroid stimulating hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

ATA Alliance for Thyroid Patient Education

GOAL

The goal of our organizations is to provide accurate and reliable information for patients about the diagnosis, evaluation and treatment of thyroid diseases.

WHO WE ARE

AMERICAN THYROID ASSOCIATION

www.thyroid.org
ATA Patient Resources: http://www.thyroid.org/patients/
Find a Thyroid Specialist: www.thyroid.org
Phone (toll-free): 1-800-THYROID
e-mail: thyroid@thyroid.org

ATA Mission: The ATA leads in promoting thyroid health and understanding thyroid biology.
ATA Vision: The ATA is the leading organization focused on thyroid biology and the prevention and treatment of thyroid disorders through excellence and innovation in research, clinical care, education, and public health.
ATA Values: The ATA values scientific inquiry, clinical excellence, public service, education, collaboration, and collegiality.

To further our mission, vision and values the ATA sponsors "Friends of the ATA" online to advance the information provided to patients and the public such as this publication, *Clinical Thyroidology for Patients*. We welcome your support.

GRAVES' DISEASE FOUNDATION

www.ngdf.org
Phone (toll-free): 1-877-NGDF-123 or 643-3123
e-mail: Gravesdiseasefd@gmail.com

Founded in 1990, the Graves' Disease Foundation offers support and resources to Graves' disease patients, their families, and health care professionals. Their mission is to find the cause of and the cure for Graves' thyroid disease through research, to improve the quality of life for persons with Graves' disease and their caregivers and to educate persons with Graves' disease, their caregivers, healthcare professionals, and the general public about Graves' disease and its treatment. The web site features a monitored bulletin board.

LIGHT OF LIFE FOUNDATION

www.checkyourneck.com
email: info@checkyourneck.com

The Light of Life Foundation, founded in 1997, is a nonprofit organization that strives to improve the quality of life for thyroid cancer patients, educate the public and professionals about thyroid cancer, and promote research and development to improve thyroid cancer care.

THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.

www.thyca.org
Phone (toll-free): 877 588-7904
e-mail: thyca@thyca.org

ThyCa: Thyroid Cancer Survivors' Association, Inc., founded in 1995, is an international nonprofit organization, guided by a medical advisory council of renowned thyroid cancer specialists, offering support and information to thyroid cancer survivors, families, and health care professionals worldwide.

AMERICAN THYROID ASSOCIATION FOUNDED 1923
Graves' Disease Foundation
Light of Life Foundation checkyourneck.com
ThyCa

AMERICAN THYROID ASSOCIATION®
FOUNDED 1923
www.thyroid.org

ATA Alliance for Thyroid Patient Education CALENDAR OF EVENTS

Educational forums, patient support groups and other patient-oriented meetings

ATA Conferences www.thyroid.org

Saturday, October 29, 2011
1:00 pm – 3:00 pm — Indian Wells, CA
FREE Public Health Forum — Thyroid Disease and You

Graves' Disease Conferences www.ngdf.org

Fall, 2011 — Boston, MA
Annual Patient & Family Conference

Light of Life Foundation www.checkyourneck.com

Ongoing — www.checkyourneck.com
Thyroid Cancer Awareness campaign with Cindy Crawford and Brooke Shields

June 12, 2010 — a previous symposium available online at:
http://www.checkyourneck.com/About-Thyroid-Cancer/Thyroid-Cancer-Symposium-Presentations

Thyroid Cancer Symposium Presentations: What's New in Thyroid Cancer?
A Day for Patients and Their Families

Please visit the Light of Life Foundation website to view the Patient Educational Symposium which took place in NYC in 2010. As part of the Patient Educational Program these online presentations provide valuable information in hopes that patients everywhere can gain further information and support about their disease.

ThyCa Conferences www.thyca.org

October 14–16, 2011 — Los Angeles, California
14th International Thyroid Cancer Survivors' Conference
(at the Hilton Los Angeles Airport Hotel, 5711 West Century Boulevard, Los Angeles, California)

September, 2011 — Worldwide
Thyroid Cancer Awareness Month

FREE Public Health Forum

AMERICAN THYROID ASSOCIATION®
FOUNDED 1923
www.thyroid.org

Thyroid Experts from the American Thyroid Association and thyroid patients join together to inform the general public, other thyroid patients, and their friends and families about:

Thyroid Disease and You

Have you experienced a significant change in:

- Energy?
- Memory?
- Fatigue level after a good night's sleep?
- Depression?
- Rapid heart beat?
- Restlessness?
- Infertility?
- Weight?
- Hair?
- A lump on your neck?

Could it be your thyroid?

Public Forum will be held on Saturday, October 29, 2011

1:00 pm – 3:00 pm • Indian Wells, California

Renaissance Esmeralda Resort and Spa, 44-400 Indian Wells Lane, Indian Wells CA 92210-8708
Phone: 760-773-4444 or toll free at 800-446-9875

Physician experts will discuss thyroid disorders. This program is free and all are welcome, including walk-in-attendees. Reservations are encouraged to ensure we have enough seating. For more information and to register, please e-mail ThyCa at thyca@thyca.org.

Who should attend? Anyone who has had an overactive or underactive thyroid, thyroiditis, a thyroid nodule, thyroid cancer, or a family history of thyroid problems or related disorders, including rheumatoid arthritis, juvenile diabetes, pernicious anemia, or prematurely gray hair (starting before age 30) Please come if you have questions, symptoms, or concerns about a thyroid problem. Receive free educational materials.

Reservations requested. Walk-ins welcome. E-mail thyca@thyca.org to RSVP
(Please indicate in your message the thyroid condition you are most concerned about.)

Online educational information for patients is provided by all members of the ATA Alliance for Patient Education co-sponsoring this forum: ThyCA: Thyroid Cancer Survivors' Association, Light of Life Foundation, and Graves' Disease Foundation. Go online to www.thyroid.org and click on "Patients and Public" to access the resources you need.