



HYPERTHYROIDISM

Does a break in antithyroid drug treatment of hyperthyroidism lead to an increased risk of agranulocytosis?

BACKGROUND

The antithyroid drugs methimazole (MMI) and propylthiouracil (PTU) are used as one option to treat patients with hyperthyroidism, especially those with Graves' disease. The goal of antithyroid drug treatment is to treat for a defined period of time then stop to determine if the Graves' disease has gone into remission. If the hyperthyroidism returns, the antithyroid drugs are re-started. Agranulocytosis, a marked decrease in white blood cells which increases the risk for infection, is a rare complication of treatment with the antithyroid drugs. Most cases of agranulocytosis occur within 3 months of beginning therapy with these drugs. There has been speculation that re-starting therapy with these drugs in patients who have relapsed after the first course of antithyroid drug treatment may increase the risk or accelerate the onset of agranulocytosis. This study was designed to exam whether agranulocytosis is likely to occur faster in a patient who stops antithyroid drug therapy and then resumes at a later time in contrast to a patient who stays on the drug continuously.

THE FULL ARTICLE TITLE

Kobayashi S et al. Characteristics of Agranulocytosis as an Adverse Effect of Antithyroid Drugs in the Second or Later Course of Treatment. *Thyroid*. December 16, 2013 [Epub ahead of print]. Available at <http://online.liebertpub.com/doi/abs/10.1089/thy.2013.0476>.

SUMMARY OF THE STUDY

A total of 87 patients seen at the Ito Hospital in Tokyo between 1983 and 2012 were found to have agranulocytosis. After excluding patients with other possible causes, 67 patients were identified as having MMI or PTU-induced agranulocytosis. Of these, 35 developed it while on a

continuous course of the drug, while 22 had gaps in therapy that ranged from 5 months to 22 years. On closer inspection, several of the latter patients were excluded because they did not fit the criteria for the study, leaving 14 patients with interrupted treatment.

There was no significant difference in the time to onset of agranulocytosis between the continuous or the interrupted groups. No agranulocytosis occurred in patients with 1-5 months of a "gap". None of the patients in the continuous treatment group who were exposed to the other drug developed side effects, whereas 9 of 10 patients in the "gap" group exposed to the other drug developed minor side effects. Thus, short term gaps (<5 months) did not appear to increase the rapidity of occurrence of agranulocytosis.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

After re-starting MMI or PTU therapy following a 5 or month gap, patients should be observed for agranulocytosis for the first 3 months, similarly to those who start these drugs for the first time. Patients should be aware of the signs and symptoms of agranulocytosis which include fever, fatigue or sore throat. If these occur they should notify their physician and have a white blood cell count measured before resuming MMI or PTU.

— Glenn Braunstein, MD

ATA THYROID BROCHURE LINKS

Hyperthyroidism: <http://www.thyroid.org/what-is-hyperthyroidism>

Graves' disease: <http://www.thyroid.org/what-is-graves-disease>

ABBREVIATIONS & DEFINITIONS

Hyperthyroidism: a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

Methimazole (MMI): an antithyroid medication that blocks the thyroid from making thyroid hormone. Methimazole is used to treat hyperthyroidism, especially when it is caused by Graves' disease.



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Propylthiouracil (PTU): an antithyroid medication that blocks the thyroid from making thyroid hormone. Propylthiouracil is used to treat hyperthyroidism, especially in women during pregnancy.

Agranulocytosis: a marked decrease in the white blood cell count that causes a patient to be more likely to

develop an infection. This is commonly associated with a fever and/or a sore throat.

White blood cells: the infection-fighting cells of the blood.