CLINICAL **THYROIDOLOGY** FOR THE **PUBLIC**

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HYPERTHYROIDISM

Antithyroid drug side effects in patients of child-bearing age and during pregnancy

BACKGROUND

Hyperthyroidism is defined as any condition in which there is too much hormone produced in the thyroid gland. The most common cause is Graves' Disease, which tends to run in families, and affects more commonly younger women. Another cause of hyperthyroidism is the presence of thyroid nodules that grow and increase activity (toxic nodular goiter). Currently, there are three types of treatment for hyperthyroidism: antithyroid medications (ATD), surgery and radioactive iodine. A physician will recommend one treatment over another, taking into account factors such as the age of the patient, pregnancy status, other illnesses and also physician/patient preference.

Antithyroid medications are very useful in both the long term treatment of hyperthyroidism as well as in the short term to prepare a patient for surgery or radioactive iodine therapy. Indeed, ATDs are the preferred therapy during pregnancy. In the US, there are two ATD available for use: propylthiouracil (PTU) and methimazole (MMI). In Europe, carbimazole (CMZ) is also an option (this drug is converted to MMI in the body). In general, PTU is used only during pregnancy or if there is an adverse reaction to MMI or CMZ. While generally well tolerated, all ATDs have been reported to cause adverse side effects such as agranulocytosis and birth defects and, rarely, liver failure.

Untreated or inadequately treated hyperthyroidism during pregnancy may poorly affect the mother and the developing baby, so treatment of hyperthyroidism in pregnancy is always recommended. The goal of this study was determine the frequency of side effects of ATDs in a large segment of the Danish population of child-bearing age.

THE FULL ARTICLE TITLE

Andersen SL et al. Antithyroid drug side effects in the population and in pregnancy. J Clin Endocrinol Metab. January 27, 2016

SUMMARY OF THE STUDY

The Danish Medical Birth Register database, including ~2.3 million parents of babies born in Denmark between 1973 and 2008. This database was matched with data from the Danish National Prescription Register, which provided information regarding ATD use. The Danish Hospital Register was accessed for information regarding outcomes (liver failure, agranulocytosis and birth defects).

Of approximately 2.3 million persons, 28,998 filled prescriptions for ATD, of which 23,103 were for MMI or CMZ, 1,717 were for PTU alone and the rest for both at one time or another. Of this group, 2115 patients were pregnant women. In the total population there were 45 cases of agranulocytosis (0.16%) and 10 cases of liver failure (0.03%). The frequency of both agranulocytosis and liver failure was higher among persons treated with PTU than with MMI and the onset of these adverse effects was shorter in patients on MMI those on PTU.

When looking at the 2115 pregnant women, the frequency of liver failure and agranulocytosis was lower than in the non-pregnant population. Over all, the frequency of birth defects was 3.4% higher than those birth defects reported in the general population.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This data reinforces that ATD therapy is generally safe, with a very low frequency of severe side effects. Compared to PTU, the risk of agranulocytosis with MMI treatment seems lower and the period of greatest risk shorter in a population of individuals of child-bearing age. Interestingly, it appears that pregnant women had a lower risk of severe side effects than non-pregnant women. However, there was a significant increase in birth defects in children who were exposed to ATD during pregnancy. This study also supports the recent American Thyroid Association guidelines for treating hyperthyroidism during pregnancy in that PTU is preferable to MMI because of the lower frequency of severe side effects.

— Jessie Block-Galarza, MD

ATA THYROID BROCHURE LINKS

Thyroid Disease and Pregnancy: http://www.thyroid.org/thyroid-disease-pregnancy/

Hyperthyroidism: http://www.thyroid.org/hyperthyroidism/

HYPERTHYROIDISM, continued

ABBREVIATIONS AND 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.

Graves' disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Toxic nodular goiter: characterized by one or more nodules or lumps in the thyroid that may gradually grow and increase their activity so that the total output of thyroid hormone in the blood is greater than normal.

Methimazole: 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.

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

Carbimazole (CMZ): an antithyroid medication that blocks the thyroid from making thyroid hormone, used primarily in Europe. Carbimazole is converted into methimazole in the body.

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 a sore throat.