



## HYPERTHYROIDISM

# Should the approach to management of Graves' hyperthyroidism in women of child-bearing age be revised?

### BACKGROUND

Graves' disease is the most common cause of hyperthyroidism in the United States and often occurs in women of child-bearing age. Because of this, Graves' disease can be diagnosed in women during pregnancy. Untreated hyperthyroidism during pregnancy can result in complications to both the baby and the mother. These complications include heart failure, preterm delivery, low weight at birth and even fetal death. The antithyroid drugs (ATDs) propylthiouracil (PTU) and methimazole (MMI) have been successfully used to treat hyperthyroidism during pregnancy and prevent these complications. In Europe, carbimazole (CMZ), which is converted to MMI in the body, is often used. While antithyroid drugs are usually well tolerated, several rare birth defects have been reported during use of MMI and CMZ. Since the risk of birth defects in prior studies is extremely rare with PTU, this is currently considered the medication of choice during early pregnancy. Indeed, it is recommended that women who got pregnant while on MMI or CMZ be switched to PTU as soon as possible. However, PTU has its own side effects. The aim of this study using the Danish National Register is to evaluate the frequency of birth defects in children exposed to ATDs in early pregnancy compared to children not exposed to these drugs.

### THE FULL ARTICLE TITLE

Andersen L et al. Birth defects after early pregnancy use of antithyroid drugs: a Danish nationwide study. *J Clin Endocrinol Metab* 2013;98:4373-81. Epub October 22, 2013.

### SUMMARY OF THE STUDY

The study included 817,093 children born in Denmark between 1996 and 2008. Among these children, 1820 children were born to mothers who took ATDs in early

pregnancy, 3542 children were born to mothers who took ATDs before and after but not during pregnancy and 811,730 children were born to mothers never exposed to this treatment. Among the children exposed to ATDs, 564 were exposed to PTU, 1097 were exposed to MMI or CMZ and 159 were exposed to both MMI or CMZ and PTU, these medications being changed in early pregnancy. The frequency of birth defects was higher in babies exposed to ATDs in early pregnancy compared to non-exposed babies (PTU, 8.0%; MMI or CMZ, 9.1%; MMI or CMZ and PTU, 10.1%; babies never exposed to ATD, 5.7%). These birth defects were usually mild and affected the skin and GI tract. Maternal ATD treatment before or after pregnancy was not associated with an increased risk of birth defects. Interestingly, 16 out of 149 babies born to mothers who changed from MMI or CMZ to PTU during early pregnancy, had birth defects.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Surprisingly, PTU use during pregnancy had an increased risk of birth defects, although this risk was slightly less than exposure to either MMI or CMZ. Importantly, a significant proportion of the babies born of mothers who switched from MMI or CMZ to PTU in early pregnancy still developed birth defects. Further studies are needed to confirm these results, as this study is at odds with prior studies. In any event, physicians should discuss the potential risk of congenital malformations associated with antithyroid drug use in early pregnancy with all women of child-bearing age diagnosed with Graves' disease.

— Alina Gavriila, MD, MMSC

### ATA THYROID BROCHURE LINKS

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

### ABBREVIATIONS & DEFINITIONS

**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.

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



## **HYPERTHYROIDISM**, continued

**Preterm delivery:** the birth of a human offspring occurs too early prior to 37 weeks of pregnancy.

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

**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.

**Carbimazole (CMZ):** an antithyroid medication that is transformed to methimazole in the body and blocks the thyroid from making thyroid hormone. This medication is not available in the United States.

**Birth defects:** Abnormal development of a body part that exists at birth.

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