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HYPERTHYROIDISM

Substituting potassium iodide for methimazole in first-trimester pregnant women with Graves' disease may unpredictably worsen hyperthyroidism

BACKGROUND

Graves' disease is the most common cause of hyperthyroidism (overactive thyroid) in the United States. Women are affected 7-8 times more frequently than men and many are in the pre-menopausal age group. This results in Graves' disease being the most common cause of hyperthyroidism during pregnancy. Treatment of Graves' disease includes anti-thyroid medications, surgery and radioactive iodine therapy. During pregnancy, radioactive iodine therapy is contraindicated and surgery is only safe to be performed during the second trimester. This leaves anti-thyroid medications as the main treatment option for Graves' disease during pregnancy. Both of the available anti-thyroid medications, propylthiouracil (PTU) and methimazole, can affect the baby, although the risk is very low. Methimazole is the safer medication during pregnancy, since the risk is less than PTU and can be limited by maintaining the lowest possible dose during pregnancy. However, the possibility of identifying an alternative medical therapy for Graves' disease in early pregnancy without side effects in the baby is highly appealing.

Potassium iodide (KI) has been used to prepare patients with Graves' disease for surgery and has occasionally been used to control hyperthyroidism by itself. The major drawback to KI as a treatment option is that it can occasionally make the hyperthyroidism worse and more difficult to treat. A prior study by the current research group suggests that the risk of side effects on the baby is less with KI than with methimazole. However, in some patients, the switch from methimazole to KI did indeed make the hyperthyroidism worse. This study aimed to identify predictors of both clinical improvement and worsening hyperthyroidism following the switch from methimazole to KI treatment in hyperthyroid pregnant women.

THE FULL ARTICLE TITLE

Yoshihara A et al 2020 The characteristics of patients with Graves' disease whose thyroid hormone level increases after substituting potassium iodide for methimazole in the first trimester of pregnancy. Thyroid. Epub 2020 Jan 13. PMID: 31928169.

SUMMARY OF THE STUDY

This study was conducted at Ito Hospital in Tokyo. Pregnant women with Graves' disease whose treatment was switched from methimazole to KI during the first trimester and who gave birth between 2005 and 2018 were included. The switch from methimazole to KI was made at the first visit following confirmation of the pregnancy. KI was given from 10 to 30 mg/day in a solution or in the form of 38-mg tablets.

Level of serum TSH, free T_3, free T_4 levels and TSH receptor antibodies (the cause of Graves' disease) were measured during the first trimester both before and then 2 to 4 weeks after changing from methimazole to KI treatment. After the change of therapy, the KI dose was decreased if the free T_4 was low or increased if the free T_4 was elevated. If hyperthyroidism persisted in the second trimester of pregnancy, an anti-thyroid drug was either added to the KI or substituted for it.

The average age of the 240 women at the time of delivery was 33 years. The switch from methimazole to KI treatment occurred at an average of 6 weeks of pregnancy. Of the 133 (55%) patients who were able to taper off of all medication during pregnancy, 4 became hypothyroid and needed levothyroxine by the time of delivery. Women who were able to discontinue therapy required lower methimazole doses prior to the switch to KI, had lower antibody and higher serum TSH levels and were on lower KI doses as compared with women who needed treatment for hyperthyroidism throughout the pregnancy. The only significant predictor of the ability to discontinue therapy was the level of the TSH receptor antibody. A continued high level of thyroid receptor antibody predicted a need to continue medication. Worsened hyperthyroidism

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occurred in 22 patients (9.2%) following the switch to KI, requiring higher methimazole doses by the third trimester than before the medication switch. There was no clinical sign or level of thyroid hormone or antibody level that predicted which patient would get worse with KI therapy.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that ~9% of pregnant women with Graves' disease who were switched from methimazole to KI in the first trimester of pregnancy are at risk for worsening hyperthyroidism during the pregnancy. No clear predictors for this observation could be identified. Thus, while KI may have a lower risk of developing rare side effects in the baby, the increased risk of worsening hyperthyroidism supports the current American Thyroid Association guideline that recommends that KI treatment for Graves' disease in pregnancy is not recommended outside Japan until more evidence on safety and efficacy is available. Therefore, staying with methimazole in pregnant women with Graves' disease continues to be the safer option for both the mother and the developing baby.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

Hyperthyroidism (Overactive): https://www.thyroid.org/hyperthyroidism/

Graves' Disease: https://www.thyroid.org/graves-disease/

Thyroid Disease in Pregnancy: https://www.thyroid.org/thyroid-disease-pregnancy/

Thyroid Function Tests: https://www.thyroid.org/thyroid-function-tests/

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.

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.

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.

TSH receptor antibodies: antibodies often present in the serum of patients with Graves disease that are directed against the TSH receptor, often causing stimulation of this receptor with resulting hyperthyroidism.

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.

Thyroxine (T_4): the major hormone produced by the thyroid gland. T_4 gets converted to the active hormone T_3 in various tissues in the body.

Triiodothyronine (T_3): the active thyroid hormone, usually produced from thyroxine.

Levothyroxine (T_4): the major hormone produced by the thyroid gland and available in pill form as Synthroid™, Levoxyl™, Tirosint™ and generic preparations.