Hyperthyroidism, Antithyroid Medications, and Pregnancy: Overall Risks Announced by the American Thyroid Association and the North European Registries

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Abstract

Hyperthyroidism during pregnancy is rare, but has adverse effects both on the mother and fetus. Besides, antithyroid medications (ATMs), methimazole (MMI) and propylthiouracil (PTU), are known to have potential teratogenic effects, as well. The present mini-review aims to attract the attention of all clinicians involved in the health care of pregnant women, relying on the most recent recommendations of both American Thyroid Association and European Registries.

Keywords: Hyperthyroidism; Antithyroid; Pregnancy; Antithyroid Medications (ATMs); Methimazole (MMI); Propylthiouracil (PTU)

Introduction

Hyperthyroidism in pregnant women is a rare entity (1/500), but it should be treated, since it is associated with preterm birth, congenital anomalies and pre-eclampsia [1,2]. However, the antithyroid medications (ATMs) has well-known side effects such as agranulocytosis and liver failure [3]. Furthermore, a potential risk of birth defects is added to this concern.

Mini-Review

To evaluate the association of hyperthyroidism (most often Graves’ disease), and ATMs either propylthiouracil (PTU) or methimazole (MMI) during pregnancy, a quick Medline, PubMed and Cochrane Library search was performed, and the recent knowledge on this subject has been reviewed. Pregnant women with hyperthyroidism need careful treatment, because if they remain untreated, an increased risk of fetal loss, pre-eclampsia, heart failure, premature labour, and having a low birthweight baby can be inevitable [1,3]. On the other hand, the ATMs have their own risks. First of all, recently revised (2017) guidelines of the American Thyroid Association (ATA) recommend the use of PTU in early pregnancy, but also address the possibility of ATMs withdrawal in appropriately selected patients [4].

In a recently published Swedish study (2017), MMI was associated with an increased incidence of septal heart defects [3]. PTU was associated with ear and obstructive urinary system malformations. A case of choanal atresia was observed after exposure to both MMI and PTU. The incidence of birth defects in children born to mothers who received ATM before or after, but not in pregnancy, was 8.8% and not significantly different from non-exposed, MMI exposed or PTU exposed. MMI and PTU were associated with subtypes of birth

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defects previously reported, but the frequency of ATD exposure in early pregnancy was low and severe malformations described in the MMI embryopathy were rarely observed.

The study of Li., et al revealed an increased risk of birth defects among the group of pregnant women with hyperthyroidism treated with MMI compared with the control group or the non-exposed group [2]. A maternal shift between MMI and PTU was associated with an increased odds ratio of birth defects. An equal risk of birth defects was observed between the group of pregnant women with hyperthyroidism treated with PTU and the non-exposed group. There was only a slight trend towards an increased risk of congenital malformations in infants whose mothers were treated with PTU compared with in infants whose mothers were healthy controls. The children of women receiving MMI treatment showed an increased risk of adverse fetal outcomes relative to those of mothers receiving PTU treatment. Therefore, the authors suggested that PTU was a safer choice for treating pregnant women with hyperthyroidism according to the risk of birth defects but that a shift between MMI and PTU failed to provide protection against birth defects.

The ATA and the Endocrine Society guidelines recommend using PTU in the first half of pregnancy if drug treatment is needed, due to a greater frequency of birth defects with MMI [4,5]. This increased risk of birth defects with MMI is very small as a Food and Drug Administration (FDA) review of all pregnancies between 1969-2009 found 29 reports of birth defects associated with MMI use in the first trimester of pregnancy as compared to 9 reports of PTU-associated birth defects [5]. Two more recent studies have found a higher rate of birth defects (2-4%) in children exposed to MMI during the first trimester of pregnancy and one of these also reported some cases of PTU-associated birth defects. However, four other recent studies have not found an association between the use of ATMs during pregnancy and the development of birth defects.

Conclusion

Guidelines recommend the use of PTU for the treatment of maternal hyperthyroidism in early pregnancy, and also suggest the possibility of ATMs withdrawal if the risk of relapse or worsening of hyperthyroidism is considered low. The recommendation on ATMs withdrawal is classified as a weak recommendation based on low-quality evidence and the risk of relapse after ATM withdrawal in pregnancy specifically has not been determined.

Bibliography


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