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THYROTOXICOSIS IN PREGNANCY

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Abstract : Thyrotoxicosis in Pregnancy.

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Thyrotoxicosis in pregnacy is very interesting not only in pathogenesis but also in diagnosis and management. Its incidence is about 0.2 percent. Graves' disease is the most common cause of thyrotoxicosis in pregnancy which tends to have remission during pregnancy and exacerbation during postpartum period. The reason is due to immunologic process occurring during pregnancy. Fetal and neonatal hyperthyroidism are also the interesting topics deserved to be discussed here.

เรื่องย่อ : ภาวะ thyrotoxicosis ในสตรีมีครรภ์น่าสนใจทั้งในแง่พยาธิสภาพกำเนิด การวินิจฉัยและการรักษา อุบัติการพบร้อยละ 0.2 สาเหตุที่พบบ่อยที่สุดเกิดจากโรค Graves' ซึ่งเป็นโรคทางภูมิคุ้มกันของต่อมธัยรอยด์ในขณะตั้งครรภ์ พบว่าความรุนแรงของโรคลดลง แต่จะกลับรุนแรงขึ้นอีกได้ในช่วงภายหลังการคลอดบุตร สำหรับภาวะ hyperthyroid ของเด็กในครรภ์และเด็กแรกเกิด นับเป็นอีกหัวข้อหนึ่งที่น่าสนใจซึ่งได้กล่าวไว้ ณ ที่นี้ด้วย

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Introduction

Pregnancy mimics many aspects of clinical thyroid disease especially thyrotoxicosis. Therefore it is the problem of making diagnosis clinically in a pregnant woman. Its incidence of thyrotoxicosis in pregnancy is about 0.2 percent.[1] Maternal complications of untreated hyperthyroidism now occur rarely but may still be life threatening in the severe case. It has been estimated that in untreated hyperthyroidism early fetal loss of 5 percent is similar to the general population but late fetal loss may be four times greater if the mother is untreated.[2] So careful management with consideration to physiologic principles is essential for the avoidance of maternal and fetal morbidity and mortality.

Causes of Hyperthyroidism in Pregnancy

The causes of hyperthyroidism are not different in pregnant women from those identified in non-pregnant women. Graves'disease is the most common cause of hyperthyroidism in pregnancy. Other causes of hyperthyroidism in pregnancy include toxic adenoma, Hashimoto's thyroiditis (Hashitoxicosis) and trophoblastic tumours such as choriocarcinoma and hydatidiform mole. But toxic multinodular goiter is the rare cause of thyrotoxicosis in pregnancy.

Graves'disease is aggravated in early pregnancy.[3] An amelioration of thyrotoxicosis commonly occurs in the second half of pregnancy. Relapse frequently occurs in the postpartum period. The fact that normal immune surveilliance is diminished in pregnancy, has been well documented. Since Graves'disease is an autoimmune in etiology, its severity can decrease.[4]

Diminished immune function may be partially related to the changes in cortisol levels, HCG or other circulation factors in pregnancy and to the transfer of immune suppressor factors from the fetus to the maternal circulation.[5] In the postpartum state, reversal of this phenomenon may reduce rebound activiation of autoimmune disease, with marked increases in thyroid antibody titers. This will occur 3-5 months of postpartum period.

Diagnosis of Hyperthyroidism in Pregnancy

Clinical manifestations of hyperthyroidism are widely variable and there are problems in diagnosis of hyperthyroidism in pregnancy. Systemic symptoms such as fatigue, heat intolerance, emotional lability and hyperhidrosis are often part of normal pregnancy accompanied by tachycardia and hyperdynamic systolic murmurs.[7] Failure to gain weight adequately may be one of the more helpful clinical signs. The size of the thyroid in pregnancy may increase but a visible goiter is likely to be an indication of thyroid dysfunction in most patients. The syndrome of Graves'disease is composed of thyroid dysfunction, ophthalmic involvement and dermatological manifestation usually referred to as pretibial myxedema. Hyperemesis gravidarum is one of thyrotoxicosis symptoms in pregnancy.[8]

Thyroid function test abnormality includes an increased serum T_3 in all patients with hyperthyroidism. The T_4 concentration generally increases. The resin T_3 uptake may return toward the midnormal range. FT_4 is useful because it will reflect the real metabolic status in pregnancy. T_4 and T_3 in pregnancy are always elevated because of the increment of thyroid binding glubulin due to estrogen effect.[9,10] Thyroid stimulating immunoglobulins are elevated and may be measured to establish a diagnosis of Graves'disease in difficult cases.[11] Detection of elevated maternal thyroid stimulating immunoglobulins in the third trimester predicts neonatal hyperthyroidism.[12]

Treatment of Hyperthyroidism in Pregnancy

An antithyroid drug regimen is the appropriate treatment for most cases of hyperthyroidism in pregnancy. Radioactive iodine is contraindicated. Surgical intervention in second trimester is reserved for those patients with significant drug intolerance.

Antithyroid Drugs

Propylthiouracil (PTU) and methimazole are thionamide drugs which block thyroid hormone synthesis at the stage of organification and iodotyrosine coupling. Inhibition of peripheral deiodination by PTU has been found.[13] PTU crosses the placenta and is excreated in milk in less amout than methimazole and PTU can enhance placental tranfer of T_4 and T_3 from a mother to the fetus by blocking deiodinase in placenta. Methimazole has been associated with congenital scalp defects such as aplasia cutis. Therefore PTU may be preferable for use in pregnancy.[13] It is important to adjust the dosage of PTU during treatment of Graves'

disease in pregnancy because the severity of Graves' disease decreases and also to avoid fetal complication of excessive PTU dosage.[14] Therapy should begin with as low dose as possible e.g. 100 to 150 mg/d every 8 hrs. Patients will has euthyroidism from 3 weeks to 3 months. The dosage of PTU can reach 450 mg/d if hyperthyroidism can not be controlled and the dosage must be reduced immediately when patients are in euthyroid stage.[15] The maintenance dosage of PTU is 50 to 100 mg/d. But if the maintenance dosage is greater than 300 mg/d, it is advisable to have surgical intervention in the second trimester.[16] It is not recomendable to use thyroid hormone with antithyroid drug in pregnancy in order to prevent hypothyroidism in fetus because thyroid hormone slightly passes the placenta.[17] Hyperthyroidism in fetus and neonatal hyperthyroidism can occur when a pregnant woman has Graves'disease. It is the fact that thyroid-stimulating immunoglobulins (TSI) from mothers can cross the placenta to the fetus and stimulate fetal thyroid gland to have over function.[18] However, hyperthyroidism in the fetus and neonatal hyperthyroidism are independent from status of maternal thyroid function and they will be diagnosed if fetal heart rate is greater than 160 bpm and maternal TSI leval is high.[15] Incidence of neonatal hyperthyroidism is about 1 percent.[19] Neonatal hyperthyroidism is mostly transient because newborns can not produce TSI themselves. The onset of neonatal hyperthyroidism may delay a week after delivering in a pregnant woman who was given thionamides. The dosage of PTU (less than 150 mg/d) is safe for breast feeding but newborns should be closely observed.[20,21] Agranulocytosis should be considered as a potential complication of PTU therapy, although it is a rare complication.[22]

Beta-blocking Agent

Beta-blocking agent can reduce sympathetic activity via beta-receptor and reduce peripheral tissue conversion of T_4 to T_3. The function of thyroid gland is not effected by beta blocker. Beta blocker is relatively contraindicated in pregnancy. It can cause premature labor, the small size placenta, intrauterine growth retardation, fetal bradycardia, neonatal jaundice and neonatal hypoglycemia.[23,24] Beta blocker reportedly can be used in long-term treatment in pregnancy in dosage of 60 mg/d.[25]

Iodine

Iodine can inhibit combination of iodide and thyroglobulin and inhibit release of thyroid hormone. Fetal thyroid gland may be so enlarged that it can obstruct airway by using this drug. So the only indication of iodine in pregnancy is thyroid crisis.[26,27]

Surgery

In the case of pregnant hyperthyroid patient who sustains major drug toxicity, surgery may be the means of success. Subtotal thyroidectomy in the nonpregnant patient results in a cure rate of over 80 percent, with hypothyroidism occurring in about 15 percent and recurrent disease in approximately 5 percent depending upon the experience of the surgical teams. Subtotal thyroidectomy should be done in the second trimester.[28]

Management of Labor in Graves'Disease

A euthyroid patient seems to sustain no increased risk of labor complications and exacerbated hyperthyroidism. The poorly prepared patient should be started with antithyroid drugs at the onset of labor and begin intravenous sodium iodide therapy to block the release of preformed thyroid hormone from thyroid gland.[29] The beta blocker may be used cautiously in the event of tachycardia and circulatory distress. Oral or parenteral corticosteroid e.g. dexamethasone 2 mg qid for 24 hrs should be added since there is an evidence that they repidly decrease circulating T_3 levels and may reduce the morbidity of thyroid storm.[30]

Thyroid Storm, Thyroid Crisis

Thyroid storm is the rare complication in pregnancy. The classical symptoms of thyroid crisis are the symptoms of severe hyperthyroidism, high-graded fever (greater than 41°c), tachycardia and severe dehydration. Immediate treatment with thionamides, beta blocker, iodide and corticosteroid should be given in these patients.

Postpartum Thyroiditis

Graves'disease will exacerbate during postpartum period. Incidence of postpartum thyroiditis is about 5.5 percent in Japan.[31] The onset of postpartum thyroiditis occurs in the third to sixth month postpartum period. Postpartum thyroiditis is composed of 2 phases : hyperthyroid phase and hypothyroid phase, the former usually preceding the latter.[7,8]

Recovery to the euthyroid state may take 3 to 5 months. Beta blockers should be used in these patients but thionamides should not be used because the etiology of postpartum thyroiditis is not due to overfunction of thyroid gland but is due to destruction of thyroid cell to release excessive thyroid hormone.[32]

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