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DAGNOSIS AND TREATMENT OF THYROID GLAND DISEASES IN PREGNANCY – GUIDELINE AND RECOMMENDATIONS

The field referred to thyroid gland diseases and pregnancy has recorded the fast progress in past twenty years, but left few controversies also. That is the complicated field because it includes both, the mother and the fetus and all their interactions; the knowledge about all specific changes linked to physiology of pregnancy is necessary; also, the cooperation of few specialist is necessary, primarily gynecologists and endocrinologists.

The few present guidelines aimed to equalize diagnostics and therapy of pregnant women suffered of thyroid gland diseases are published by the European, American - international Societies (1) (2). National guidelines are also published, and the Thyroid Society of Serbia are one of the national societies offered the recommendations in the field of thyroid diseases, included the thyroid diseases in pregnancy also (3). The Serbian Society for fetal and prenatal medicine at the Congress in April 2017 was dealing with pregnancy complicated by chronic illness, and by thyroid diseases as the part of this pathology and are actually in preparation of guidelines came out from this discussions (4).

1.

Screening of thyroid dysfunction in early pregnancy or before pregnancy

The universal screening in all women planning pregnancy is not recommended. The selective screening is recommended for high risk population in group of women planning pregnancy or in early pregnancy between 6th and 8th

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week of pregnancy.

Screening covers TSH (thyroid stimulating hormone) and anti TPO (thyroid peroxidases) and TRAB (TSH receptor antibodies).

1.1 The groups of women recommended for selective screening are:

- Older than 34 years of life
- Family history of thyroid diseases
- Goiter
- The presence of antithyroid antibodies, above all anti TPO and TRAK
- Clinical signs of thyroid dysfunction
- Women suffered from diabetes type 1 or other autoimmune illness
- Women with infertility problems
- Premature delivery or spontaneous abortion in family history
- Previous radiation therapy of neck or thyroid gland operations
- Women taking levothyroxine therapy
- Women from regions insufficient for iodine

1.2 If high normal TSH concentrations are recognized in non pregnant women, repeat the assay. There is no evidence based data that the pregnancy outcomes are better if low dose T4 are given to bring TSH below 2, 5 mIU/ml before pregnancy, but some experts recommend this kind of therapy. If no therapy is added before pregnancy, than it is necessary to measure TSH concentrations in early pregnancy (6 to 8 week), in the time of HCG (human chorionic gonadotrophin) measurement and after that in intervals of 6 to 8 weeks.

1.3 Women with elevated TSH concentrations are at increased risk for bad outcomes of pregnancy, so if identified such women should be screened for serum TSH when concerned pregnancy, and in each trimester of pregnancy

1.4 If hypothyroidism has been diagnosed before pregnancy, TSH concentrations should not be higher than 2, 5 IU/ml. Women should be informed that pregnancy has to be planned and realized only if thyroid hormones are normal

1.5 These women should be counseled to contact the doctor immediately when pregnancy is diagnosed to check their TSH level. These women have to be informed that the increment of levothyroxine dose should be done at early pregnancy by about

30%.

2. Iodine nutrition before and during the pregnancy

Women in reproductive age should take the 150 micrograms of iodine daily. During pregnancy and breastfeeding, the daily intake of iodine should be higher, 250 micrograms of iodine daily.

3. Thyroid nodules and cancer

3.1 If thyroid nodule discovered in pregnancy is solid and 1 cm and larger, cytology should be obtained by FNA (fine needle aspiration).

3.2 If nodule is found to be malignant, women should be presented to the Consilium for pregnancy and Cancer

The nodules found in the first and early second trimester if malignant, highly suspicious or exhibit rapid growth or are accompanied by pathological adenopathy, surgery should be recommended in the second trimester. Women in latter period of pregnancy with papillary or follicular thyroid carcinoma without evidence of advanced disease can wait for definitive surgery until soon after delivery

4.0 Hyperthyreosis in pregnancy

4.1 Maternal aspects

4.1.1. Because of harmful effects for mother and fetus, hyperthyreosis should be treated in pregnancy- therapy should be started for newly diagnosed illness or adopt the dosage of medication if therapy has been started before pregnancy. Endocrinologist should take care about antithyroid medication dosage.

4.1.2. Propylthiouracil (PTU) is the first line therapy for the treatment of hyperthyroidism in the first trimester of pregnancy, because there is the specific association between methimazole (MMI) and congenital anomalies of the fetal skin. The responsibility of gynecologist is to recommend the change of the therapy to the lower risk medication i.e. PTU for women planning the reproduction or in the early pregnancy if no change were done previously. American association for

endocrinology recommends change of treatment from PTU to MMI after the first trimester because the therapy with PTU may rarely be associated with severe liver toxicity. Not all associations recommends that change and our association, taking into account good experiences with PTU, is at the point of view that therapy may not be changed to MMI. If patient stay with the PTU therapy after the first trimester, it is reasonable to assess the liver function in pregnant women in PTU every 4 week.

4.2. Fetal aspects

4.2.1. Thyroid receptor antibodies (TRAK) freely cross the placenta, TRAK should be assessed in 18th week of pregnancy in pregnant women if: 1. there is current M Graves Basedow 2. Previous M Graves Basedow threated with I 131 or thyroidectomy 3. Previous neonatal M Graves Basedow 4. Previously elevated TRAK

4.2.2. Pregnant women with elevated TRAK in 18th week of pregnancy should be referred to tertiary center for Gynecology and Obstetrics and thyroid hormones, antithyroid antibodies and fetal morphology should be assessed periodically, in periods of 4 to 6 weeks, because maternal antithyroid antibodies can influence fetal thyroid function

The signs of fetal thyroid dysfunction are: enlargement of fetal thyroid gland, fetal goiter, intrauterine growth restriction, changed bone maturity, fetal tachycardia, fetal cordial insufficiency and fetal hydrops.

4.2.3. Umbilical cord sampling should be considered if the diagnosis of thyroid dysfunction of the fetus is not reasonably certain from the clinical and sonographic data but some signs are present, or if there is the signs of serious fetal compromise and information gained would change the treatment.

4.2.4. If fetal hyperthyreosis is diagnosed, than the introduction or the adjustment of the antithyroid medication should be considered, accompanied with periodical sonographic controls.

4.2.5. Fetal diagnostics and therapy belongs to tertiary centers for Gynecology and Obstetrics, with possibilities for coordinated work of different subspecialists (gynecologist- endocrinologist), with experienced staff and all necessary equipment for this kind of work and concentration of rare and complicated patients that permits analysis of the results and making the conclusions which will influence

the next work in the field.

4.2.6. All newborns of the mothers with Graves' disease and present TRAB, should be evaluated by the medical care provider for thyroid dysfunction and treated if necessary.

5.0 Gestational hyperemesis and hyperthyroidism

5.1. If pregnant women suffer from hyperemesis gravidarum (5% weight loss, dehydration and ketonuria) , than thyroid function tests should be done (TSH, fT4, TRAK).

5.2. The most pregnant women with hyperemesis do not demand anti thyroid therapy, in spite of elevated T4 or suppressed TSH. Clinical judgement should be followed if women appear significantly thyrotoxic and in that case the temporary anti thyroid therapy should be initiated.

5.3. Women with positive TRAK have M Graves Basedow and should initiate continuous therapy according to the fT4 concentration.

6.0 Management of hypothyroidism in pregnancy- maternal and fetal aspects

6.1. Overt maternal hypothyroidism is known to have serious adverse effects on the fetus, and should be avoided because of that.

Overt or subclinical hypothyreosis diagnosed before pregnancy should be treated and the aim is to lower TSH concentration below of 2, 5 IU/ml before conception. Hypothyreosis for the first diagnosed in pregnancy should be treated promptly, the aim is to lower TSH concentrations to 2,5 and lower in first and second trimester of pregnancy and below 3 IU/ml in third trimester.

6.2 The antithyroid antibodies concentrations should be measured about 18th to 20th weeks of gestation; if present, the protocol is the same as for hyperthyroidism in pregnancy with positive auto antibodies.

7.0 The general aspects

7.1 The careful interpretation of serum free T4 values is recommended in pregnancy and each laboratory should establish trimester specific values.

7.2 If maternal thyroid hormone concentrations are not in normal reference values in early pregnancy, the pregnancy termination is not recommended, but

mother should be informed about the risks and should be directed to the tertiary center of Gynecology and obstetrics for further observation.

7.3 In mothers with thyroid disease, the glycemic control should be assessed in 28th week gestation, by postprandial glycaemia or OGTT using 75 gr of oral glucose.

7.4 The fetal thyroid assessment by ultrasound examination after 24th weeks of gestation is good parameter to uncover fetal thyroid dysfunction. If the fetal thyroid gland is enlarged in mother with present antithyroid antibodies, the probability for fetal thyroid dysfunction is about 75%. If fetal thyroid gland is not enlarged, the probability for fetal thyroid dysfunction in mothers with positive antithyroid antibodies is about 35%. This data are useful when considering if fetal thyroid hormones should be measured.

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