IODINE IN EARLY PREGNANCY – IS THERE ENOUGH?

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Aims: To evaluate the iodine status of patients in early pregnancy and its dependence on level of thyroid-stimulating hormone (TSH).

Methods: Between June 2005 and December 2006, 168 patients with a confirmed vital pregnancy (up to 10th week of pregnancy) were included in the study. The entry criteria were no prior thyroid disease, did not take any other medication, had not undergone radio-iodine therapy and did not take multivitamins containing iodine. The iodine status was measured as the amount of iodine in urine over 24 hours. The TSH level was determined from the blood using chemiluminescence.

Results: The average ioduria value in patients was found to be 3.04 $\mu\text{mol}/24\text{ hr}$, with the norm 0.6–2.4 $\mu\text{mol}/24\text{ hr}$, median 2.9, SD 1.5. None of the patients had a value lower than 0.9 $\mu\text{mol}/24\text{ hr}$. The average TSH value was 1.98 mIU/l, median was 1.31, SD 0.98. The laboratory limits were set to 0.25–3 mIU/l for pregnant women in the first trimester. Three pregnancies ended in miscarriage by week 12, 1 miscarriage occurred in week 22 and the other pregnancies concluded in delivery between weeks 38–41. Fourteen patients had TSH levels above 3 mIU/l with normal levels of free thyroxine (T₄): 10.3–25 pmol/l.

Conclusions: The results of this study did not reveal any iodine deficit in any of the patients. However 14 patients had elevated TSH levels signalling subclinical or incipiently clinical hypothyroidism. These patients underwent levothyroxine therapy after endocrinologist's consultations.

INTRODUCTION

A female organism undergoes many anatomical and functional changes during pregnancy. These changes also occur in the thyroid gland, whose function is closely associated with the metabolism of iodine. Iodine is a part of thyroxine (T₄) and triiodothyronine (T₃) – hormones of the thyroid gland. In the blood, iodine is in the form of an iodine anion. In the thyroid gland, iodine, regulated by thyroid-stimulating hormone (TSH), is actively taken up, oxidized by peroxidase to elementary iodine and then bound to thyroid-binding globulin (TBG) (ref.¹).

Only 20 % of the T₃ found in serum originates from the thyroid gland (and only in cases of iodine deficit), the rest is formed by peripheral deiodization of T₄.

Thyroid gland activity is regulated by negative feedback. The tripeptide thyroliberin (TRH) is produced in the hypothalamus and stimulates the production of the glycoprotein TSH from the pituitary gland. The level of T₄, as well as T₃, also regulates the level of TSH.

Under normal conditions, hormones of the thyroid gland exude a metabolic, calorogenic, differentiating effect and regulate cell growth, contribute to the development of the CNS, somatic growth, puberty, regulate the synthesis of proteins important for proper liver, heart, nervous system and muscle function and regulate oxygen consumption and saccharide entry into cells^{2,3}.

The aim of our work was to determine the iodine status in the period of early pregnancy (up to the 10th week

of pregnancy) while monitoring TSH. The result may determine whether it is beneficial to routinely test iodine quantity during pregnancy or not⁴.

PATIENTS AND METHODS

Between June 2005 and December 2006, 168 patients with a confirmed pregnancy (up to 10th week of pregnancy) and an average age of 23 years (17–41 years of age) were included in this prospective longitudinal study. The patients fulfilled the following entry criteria: no previous illness or use of medication for thyroid gland function, did not use any other medication (amiodarone, lithium, interferon α , tamoxifen, metoclopramide, phenothiazine, antidepressives, medication containing iron, multivitamins containing iodine, rifampicin, phenytoin), had not undergone radioiodine therapy.

The iodine level in urine is indicative of iodine balance in the organism. A 24-hour urine sample was tested by an in-house methodology using a photometric detector MAX 002 (Diagnostic Products Corporation, Los Angeles, USA), where the physiological range was 0.6–2.4 $\mu\text{mol}/24\text{ hr}$ (80–300 mg/24 hr). The TSH level in the blood was measured by the Immulite 2000 immunoassay system using chemoluminescent DPC testing on 3-generation TSH (Diagnostic Products Corporation, Los Angeles, USA), where physiological values range from 0.32–5 mIU/l for non pregnant women.

RESULTS

The average ioduria value in our patients was 3.04 $\mu\text{mol}/24\text{ hr}$, the norm was 0.6–2.4 $\mu\text{mol}/24\text{ hr}$, median was 2.9, SD 1.5.

The average TSH value was 1.98 mIU/l. The median was 1.31, SD 0.98. Three pregnancies terminated in spontaneous abortion before week 12. There was 1 spontaneous abortion in week 22 of pregnancy. The other pregnancies concluded with delivery within the 38th–41st week of pregnancy. Four patients had a TSH level above 3 mIU/l and ten patients had levels above 5 mIU/l. All of them had a free T4 level in normal range 10.3–25 pmol/l, what gives evidence about subclinical hypothyreosis. All fourteen mothers were immediately referred to endocrinologist and they received levothyroxine therapy.

DISCUSSION

Daily iodine intake should be 150–200 $\mu\text{g}/\text{day}$ and this requirement is increased to 250 $\mu\text{g}/\text{day}$ during breast-feeding. Iodine excretion slightly increases during pregnancy due to increased renal clearance from increased glomerular filtration. The ability of the thyroid gland to accumulate iodine is reduced and this results in hypertrophy of the gland. A 24-hour ioduria value informs us of the amount of iodine in the organism and a value of excreted iodine above 150 μg ensures a sufficient amount of iodine in the body⁵. 10 μg of iodine are excreted into the stool daily. The amount of iodine in the organism ranges between 15–20 mg, the majority of which is found in the thyroid gland⁶.

Iodine deficiency disorders (IDD) include hypothyroidism and structural changes in the thyroid gland- goiter. A goiter develops due to stimulation by increased levels of TSH and may be associated with normal or impaired thyroid gland function. Uncontrolled iodine intake may lead to both hypo- and hyperthyroidism⁷.

In addition, iodine insufficiency leads to the impairment of somatic, sexual and psychological development and difficulties during pregnancy and breast-feeding. A euthyroid state of the mother during early pregnancy is very important for proper development and differentiation of the fetal brain. Fetal thyroid gland begins to produce thyroidal hormones after the 12th week of pregnancy⁸.

The thyroid gland has internal regulatory mechanisms, which allow normal function despite excess iodine

and this prevents subsequent overproduction of thyroid hormones. Inhibition of iodine organification occurs and this phenomenon is termed the Wolff- Chaikoff effect. It is believed that iodopeptides in the thyroid gland temporarily inhibit thyroideal peroxidases and thus also the iodination of thyroglobulin⁹. Another way of self-regulation is by suppressing the sodium-iodide symporter, which results in a decrease in intrathyroid iodine concentration. This may lead to hypothyroidism. During pregnancy, hypothyroidism carries a higher risk of placental abruption, preeclampsia, mental retardation and impaired development of the central nervous system of the fetus or repeated miscarriages¹⁰⁻¹².

Excessive iodine intake may also lead to hyperthyroidism, especially in patients with autonomous nodules in the goiter, or in populations with a prior iodine deficiency. In iodine-deficient locations, a sudden increase in iodine intake may induce the development of Graves' disease. This phenomenon is known as the Jod-Basedow phenomenon. Hyperthyroidism during pregnancy increases the risk of premature delivery, delivery of a fetus with low birth weight, risk of congenital birth defects and it affects the heart activity of the mother and fetus¹³.

CONCLUSIONS

This study did not confirm a deficit of iodine in patients in early pregnancy in our region. Overall, the need for routine ioduria examinations for women in early pregnancy was not confirmed in our sample. The level of TSH is a sensitive marker of functional thyroid disorders which may be the results of a thyroid autoimmune disorder or (rarely) a deficit of iodine¹⁴.

REFERENCES

- Berghout A, Wiersinga W. Thyroid size and thyroid function during pregnancy: an analysis. *Eur J Endocrinol* 1998; 138:536-542.
- Gao F, Apperly J, Raff M. Cell-intrinsic timers and thyroid hormone regulate the probability of cell-cycle withdrawal and differentiation of oligodendrocyte precursor cells. *Dev Biol* 1998; 22:64-71.
- Glinioer D. Potential Consequences of Maternal Hypothyroidism on the Offspring: Evidence and Implications. *Hum Res* 2001; 55:109-114.
- Vitti P, Rago T, Aghini-Lombardi F, Pinchera A. et al Iodine deficiency disorders in Europe. *Pub Health Nutrition* 4:529-535.
- Delange F. Optimal iodine nutrition during pregnancy, lactation and the neonatal period. *Int J Endocrinol Metab* 2004; 2:1-12.
- Soldin OP. Thyroid Function Testing in Pregnancy and Thyroid Disease. *Trimester-specific Reference Intervals The Drug Monit* 2006; 1:8-11.
- Delange F. Iodine deficiency in Europe and its consequences: an update. *Eur J Nucl Med* 2002; 29(Suppl.2):404-416.
- Pemberton HN, Franklyn JA, Kilby D. Thyroid hormones and fetal brain development. *Minerva Ginecol* 2005; 57:367-378.
- Markou K, Georgopoulos N, Kyriazopoulos V, Vagenakis A G. Iodine - Induced Hypothyroidism. *Thyroid* 2001; 5:501-510.
- Basbug M, Aygen E, Tayyar M, Tutus A, Kaya E, Oktem O. Correlation between maternal thyroid function tests and endothelin in preeclampsia-eclampsia. *Obstet Gynecol* 1999; 94:551-555.

Table 1. Ioduria and TSH in patients n = 168.

n = 168	Average	Median	SD
Ioduria $\mu\text{mol}/24\text{ hr}$	3.04	2.9	1.5
TSH mIU/l	1.98	1.31	0.98

11. Pop VJ, Vulsma T. Maternal hypothyroxinaemia during (early) gestation. *The Lancet* 2005 Vol 365 Issue 9471:1604-1606.
12. Nava-Ocampo A A, Soldin O P, Koren G. Hypothyroidism during pregnancy. *Canadian Family Physician* 2004; 50:549-551.
13. Dunn JT, Semigran MJ, Delange F. The prevention and management of iodine-induced hyperthyroidism and its cardiac features. *Thyroid* 1998; 1:101-106.
14. Springer D, Horacek J, Hauerova D, Limanova Z. Thyroid Malfunction in pregnancy. *Ces. Gynek* 2007; 6:375-381.