Assessment of Maternal Health and Thyroid Activity by Determination of TSH, fT3 and fT4 in Pregnant Women Taking a Vitamin Supplement Containing Iodine

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Abstract: *Background*: During pregnancy, important changes occur in maternal thyroid function. The thyrotropic activity of human chorionic gonadotropin (hCG) has been studied by many authors. This hormone has similarities to thyroid-stimulating hormone (TSH). This has led to the supposition that hCG is indirectly involved in thyroid stimulation.

In pregnancy, TSH is inhibited, with low levels of fT3 and fT4; in recent years, some authors have found a relationship between raised thyroid hormones and the onset of hyperemesis gravidarum. Thus, increasing or starting levothyroxine therapy is not indicated in the first trimester of pregnancy. Nutritional supplements may have an important role; in fact, iodine may encourage more physiological thyroid function and could affect the onset or absence of hyperemesis gravidarum.

Materials and Methods: To identify the incidence of hyperemesis gravidarum in two groups of women treated with multivitamin supplementation with or without iodine, we analysed TSH, fT3 and fT4 levels and the severity of symptoms in pregnant women with nausea and vomiting.

Results: TSH levels were significantly reduced in the group treated with iodine. fT3 and fT4 showed a significant decrease in the group treated with the multivitamin supplement containing iodine.

Conclusions: Our results also show that the multivitamin supplement containing iodine was more effective in controlling the onset of hyperemesis gravidarum, improving TSH, fT3 and fT4 levels.

Keywords: Pregnancy, thyroid, hyperemesis, multivitamins, iodine.

INTRODUCTION

Nausea and vomiting are common symptoms in pregnancy, affecting 70 % of women in the first trimester, but in only 1-2% of these cases are symptoms so severe as to require hospitalisation due to fluid loss, electrolytic disturbances and ketoacidosis.

During pregnancy, important changes occur in maternal thyroid function. High oestrogens levels induce increased hepatic synthesis of thyroxine-binding globulin (TBG) leading to reduced availability of iodine. Other factors include human chorionic gonadotropin (hCG), human chorionic thyrotropin (hCT) and placental factors [1-3].

The thyrotropic activity of hCG has been studied by many authors. This hormone has similarities to thyroid-stimulating hormone (TSH) which has the same α-subunit and a similar β-subunit. This has led to the supposition that hCG is indirectly involved in the thyroid stimulation [4, 5]. In rat cells, hCG appears to activate the signal transduction system, iodine uptake and increased cyclic adenosine monophosphate (cAMP). A higher prevalence of hyperthyroidism has been reported in cases of hydatidiform mole, hyperemesis gravidarum and choriocarcinoma, which is probably related to a higher plasma hCG concentration.

Because of changes in metabolism during early pregnancy and their correlation with foetal growth and maternal health [6-9], gynaecologists now routinely prescribe multivitamins for pregnant women. In recent years, the number of supplements available has grown exponentially, and it is therefore the task and responsibility of specialists to choose those supplements whose content and number of vitamins satisfy the nutritional requirement of pregnant women.

In pregnancy, TSH is inhibited, with low levels of fT3 and fT4 [10-12]; in recent years, some authors have found a relationship between raised thyroid hormones and the onset of hyperemesis gravidarum [13]. Thus, increasing or starting levothyroxine therapy is not indicated in the first trimester of pregnancy. Nutritional supplements may have an important role, with it being important to distinguish between those that contain

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E-ISSN: 2309-4400/13

iodine and those that do not. Iodine may encourage more physiological thyroid function and could affect the onset or absence of hyperemesis gravidarum [14, 15].

With the aim of identifying the incidence of hyperemesis gravidarum in two groups of women treated with multivitamin supplementation with or without iodine, we analysed the levels of TSH, fT3 and fT4 and the severity of symptoms in pregnant women with nausea and vomiting.

MATERIALS AND METHODS

The study population consisted of 40 pregnant women, aged between 24 and 36 years, body mass index (BMI) between 20 and 24 kg/m^2, without endocrine disorders, who planned to become pregnant for the first time (Table **1**). Informed consent was obtained from all patients before participation in the study, and the Clinical Research Ethics Committee approved the study.

Table 1: Values of age, BMI and parity in the two study groups. Group I treated with a multivitamin supplement containing iodine 150 µg and group NI treated with a multivitamin supplement without iodine

Group	Age (years)	BMI (kg/m^2)	Parity
I	28±3	23±1	0000
NI	26±2	22±1.5	0000

Upon enrolment, all patients underwent a basic workup, including the completion of a referral status form that covered demographic characteristics, basic medical and gynaecological history and comprehensive physical examination, including BMI. Moreover, blood was taken from all patients for TSH, fT3 and fT4 to ascertain that the women were euthyroid.

Eligible women were randomly assigned to two groups:

- Group I (n=20) treated with one tablet/day of a multivitamin (Forgest, Rottapharm/Madaus) containing docosahexaenoic acid (DHA) 0.2 g, folic acid 400 µg, biotin 75 mcg, iodine 150 mcg, iron bisglycinate 30 mg, lutein 2 mg, niacin 16.2 mg, selenium 55 µg, beta-carotene 1.8 mg, vitamins B (B1 0.7 µg, B2 1.6 mcg, B5 3 µg, B6 2 µg, B12 2 µg), vitamin C 30 mg, vitamin D3 10 µg, vitamin K 35 µg, vitamin E 5 mg, copper 600 µg and zinc 7 µg.
- Group NI (n=20) treated with one tablet/day of a multivitamin without iodine containing folic acid 400 µg, vitamins B (B1 1 mg, B2 1.6 mg, B3 14 mg, B5 6 mg, B6 1.3 mg, B12 2.2 µg) vitamin C 70 mg, vitamin D 10 µg, vitamin E 8 mg, vitamin K1 35 µg, biotin 100 µg, iron 30 mg, zinc 7 µg.

All data groups are summarized in Table **2**.

During treatment with the multivitamin supplement, the women became pregnant within two to six months.

Their stage of pregnancy was assessed based on the first day of their last menstrual period, transvaginal pelvic ultrasound examination (which showed a single embryo with cardiac activity) and a blood test to measure hCG.

Clinical symptoms such as nausea (mild and moderate) and vomiting during the first trimester and TSH, fT3 and fT4 levels were evaluated at 10 weeks' gestation.

All samples were tested by the central laboratory at the Santa Maria alle Scotte Hospital, Siena, Italy. Plasma TSH, fT3 and fT4 were measured by double antibody radioimmunoassay using Immunotech kits (Marseille, France) for fT3 and fT4, and Radim kits (Rome, Italy) for TSH.

Plasma hCG concentrations were measured by immunoradiometric assay using Bioclone Australia kits

Table 2: Thyroid profiles of the two study group, before and following the treatment. Group I treated with a multivitamin supplement containing iodine 150 µg and group NI treated with a multivitamin supplement without iodine. Data are presented as mean (M) ± standard deviation (SD). P values are significant if p<0.05

	GROUP I			GROUP NI		
	BASAL	AFTER	P	BASAL	AFTER	P
TSH (mlU/ml)	2.04±0.36	1.38±0.26	0.001	2.18±0.41	1.72±0.35	0.002
fT3 (pg/ml)	3.29±0.36	2.61±0.23	0.001	3.27±0.34	3.05±0.31	0.002
fT4 (ng/ml)	12.86±1.45	8.69±1.26	0.001	11.5±1.51	11.03±1.16	0.053

(Marrickville, Australia). Samples were analysed at two diluitions. Samples from each subject were analysed together.

Statistical Analysis

Statistical analysis was performed by SPSS statistical software version 17 (SPSS I Chicago, IL, USA), with Wilcoxon and Mann-Whitney tests, as appropriate. Results are presented as means ± standard deviations; $p< 0.05$ was considered significant.

RESULTS

All women accepted the multivitamin products and none reported side effects linked to the introduction of the tablets.

Patients did not know the contents of the multivitamin tablets. They were very happy to take this kind of product that can let positively on going pregnancy.

The baseline clinical and hormone parameters were comparable between the two study groups. Following multivitamin supplement treatment, among women in group I (treated with the iodine-containing supplement) there were 3 cases of mild hyperemesis and 2 cases of moderate hyperemesis compared with group NI (treated with supplementation without iodine) where in 7 cases there was mild hyperemesis and in 4 cases moderate hyperemesis.

In no case did the pregnant women have to be hospitalised because of their symptomatology.

TSH levels were significantly reduced in both groups with the reduction being more significant in the group treated with iodine; moreover, patients treated with iodine showed a significant improvement in TSH compared with the group treated without iodine (Figure **1**).

fT3 (Figure **2**) and fT4 (Figure **3**) showed a significant decrease in group I in patients treated with iodine compared with patients treated with the supplementation without iodine, where the reduction was slight significant.

DISCUSSION

Many aspects of thyroid gland function during pregnancy and in particular at the beginning of

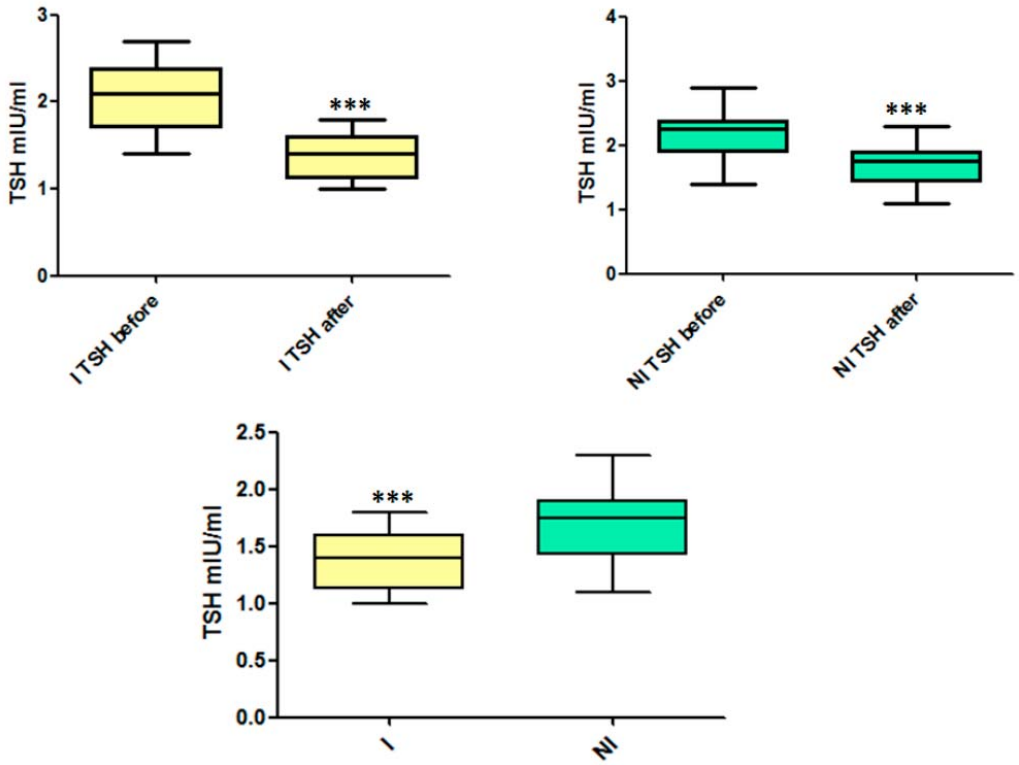

Figure 1: Values of TSH before and after treatment with a multivitamin complex. Group I treated with a multivitamin supplement containing iodine 150 µg and group NI treated with a multivitamin 14 supplement without iodine. Values are presented as mean and standard deviation. *=p<0.05, **=p<0.005, ***=p<0.001.

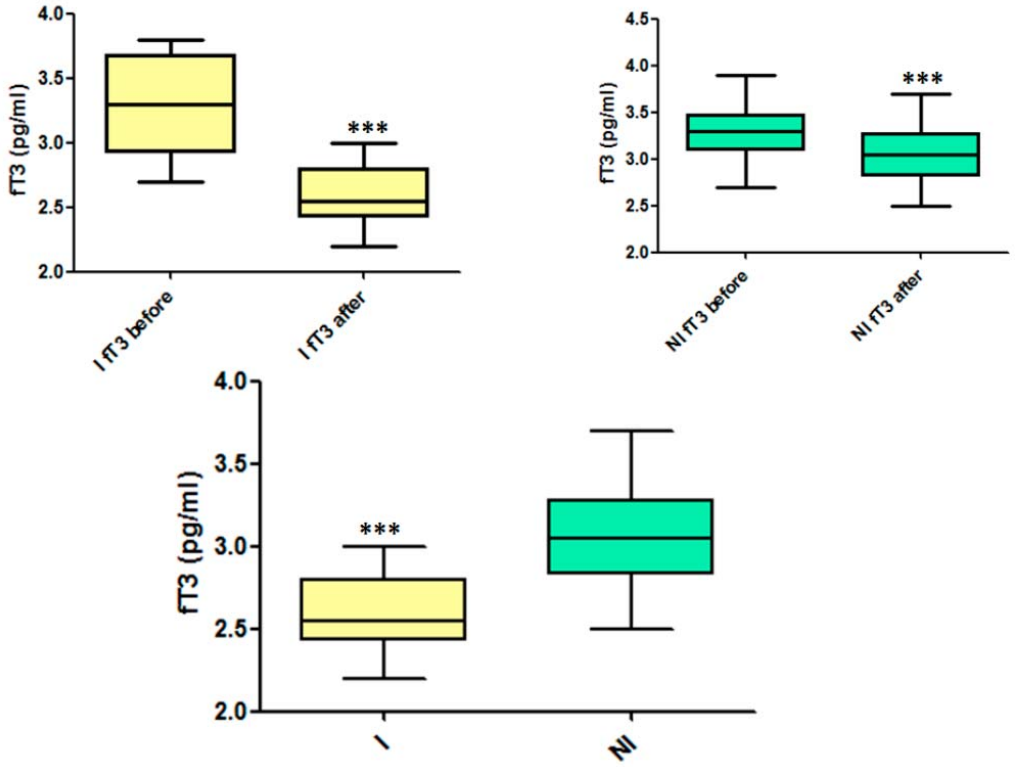

Figure 2: Values of fT3 before and after treatment with a multivitamin complex. Group I treated with a multivitamin supplement containing iodine 150 µg and group NI treated with a multivitamin supplement without iodine. Values are presented as mean and standard deviation. *=p<0.05, **=p<0.005, ***=p<0.001.

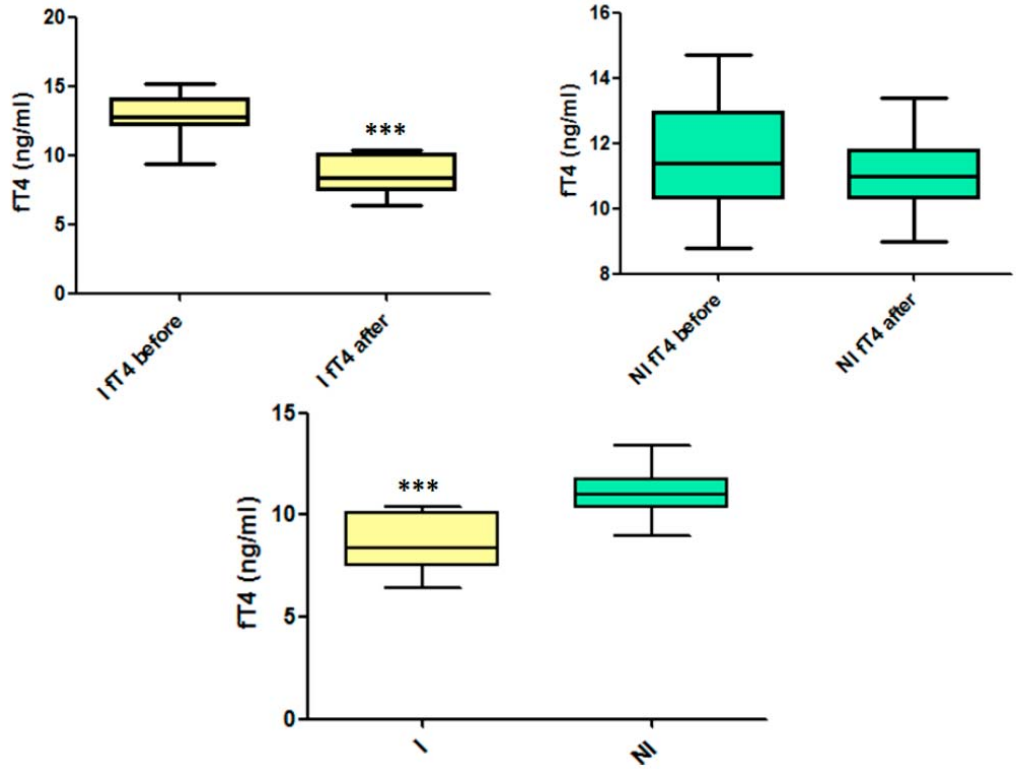

Figure 3: Values of fT4 before and after treatment with a multivitamin complex. Group I treated with a multivitamin supplement containing iodine 150 µg and group NI treated with a multivitamin without iodine. Values are presented as mean and standard deviation. *=p<0.05, **=p<0.005, ***=p<0.001.

pregnancy remain un clear. In our previous study, we reported TSH regulation during pregnancy and showed a reduction in thyroid activity [4, 16].

In the present study, we mainly focused on the clinical symptoms of hyperemesis gravidarum in pregnant women. The results suggest that the obstetrician should recommend an appropriate multivitamin supplement able to provide the daily requirement of the recommended individual components to stop women choosing products that may be more heavily advertised but whose contents are inappropriate.

From a clinical point of view, our results also show that the multivitamin supplement with iodine was more effective in controlling the onset of hyperemesis gravidarum, improving levels of TSH, fT3 and fT4. Women treated with the iodine-containing supplement had a lower incidence of hyperemesis and, when it did occur, it was less severe. Moreover, in this group of women (Group I), the TSH, fT3 and fT4 levels were indicative of more physiological thyroid function in comparison to women treated with supplementation without iodine.

Iodine is a necessary element in the synthesis of thyroid hormones in general, and in particular in conditions such as pregnancy when the requirement for these hormones is increased. For good health in pregnant women, the aim is to achieve euthyroidism even when TSH levels are suppressed [17-19]. The presence of exogenous iodine contributes to physiological thyroid function without any risk of causing the hyperthyroidism frequently observed in women during the first trimester of pregnancy [20, 21]. This condition is the result of a compensatory mechanism where beta-hCG takes over the role of the suppressed TSH in the thyroid. Iodine concentrations in excess of the physiological level may oppose this action and restrict functional hyperthyroidism with high levels of fT3 and fT4 [22].

A complete multivitamin supplement containing folic acid and iodine is an appropriate supplement for pregnant women who want to protect the products of conception and experience fewer symptoms of hyperemesis gravidarum [23]. Taking this type of supplement even before conception encourages more physiological thyroid hormone secretion, and this could improve quality of life during pregnancy.

The literature shows that folic acid taken during the three months preceding conception can reduce the risk of preterm delivery [24]. It is therefore recommended that all women who wish to become pregnant should start taking multivitamin supplements, and that they should choose food supplements that contain iodine as well as folic acid; in this context is very important that the gynaecologist knows which multivitamin components to prescribe with the best combination of vitamins and minerals.

CONCLUSIONS

The present study shows that the multivitamin supplement containing iodine was more effective in controlling the onset of hyperemesis gravidarum, modifying TSH, fT3 and fT4 plasma levels.

DECLARATION OF INTERESTS

Claudio Benvenuti is a consultant for Rottapharm/ Madaus.

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Received on 24-09-2013 Accepted on 09-10-2013 Published on 31-12-2013

DOI: http://dx.doi.org/10.14205/2309-4400.2013.01.02.5