ORIGINAL RESEARCH PAPER

Medical Science

SERUM SELENIUM STATUS AND THYROID FUNCTION

KEY WORDS:

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ABSTRACT

Aim: The preliminary study is undertaken to evaluate the selenium status, glutathione (G.SH) levels and glutathione peroxidase activity (GPx) in hypothyroid patients. **Materials And Methods;** Among 200 cases a total of 62 study subjects, with hypothyroidism referred to one of the cardiology institute were taken for the present study. The serum fasting blood glucose (FBG), lipid profile, T3, T4 and Thyroid stimulating hormone (TSH) were measured by automated methods using electro chemiluminescence. Selenium was measured by using Graphite furnace Atomic absorption spectrophotometer, Shimadzu. GPx was determined by Enzyme linked immunoassay. **Results And Discussion:** There was a significant decrease in serum selenium levels in hypothyroid cases compared to the control subjects accompanied by a decrease in GPx activity in hypothyroid patients.G.SH levels did not show marked change in hypothyroid cases compared to control subjects. The levels of total cholesterol and LDL cholesterol were increased in hypothyroid cases with a non-significant increase in HDL cholesterol. Selenium dependent enzyme glutathione peroxidase shows a positive correlation between selenium status in hypothyroid patients.

INTRODUCION:

Thyroid hormone synthesis is dependent upon oxidative reactions. It is estimated that huge amount of reactive oxygen species (ROS), especially of H2O2, are produced in the thyroid under physiological conditions, justifying the statement that the thyroid gland is an organ of "oxidative nature". [1]

Hydrogen peroxide is an essential factor for thyroid hormone biosynthesis. It is produced in the thyroid gland by two isoform enzymes, dual oxidase 1 (DUOX1) and (DUOX2), belonging to NOX family, with the most convincing experimental evidence found for DUOX2 {2,3}.

Both DUOX enzymes are expressed in the apical plasma membrane of thyroid follicular cells (thyrocytes) [2,3]. In turn, NOX4 playing also an important role in the synthesis of H2O2 in the thyroid, acts intracellulary[4]. Hydrogen peroxide acts as an electron acceptor at each step of thyroid hormone synthesis, namely at iodide oxidation and, next, at its organification, as well as at coupling reaction of iodotyrosines [5]. It is essential for activity of thyroperoxidase (TPO) – the key enzyme for thyroid hormone synthesis.

Due to potential huge oxidative stress in the thyroid gland, effective protective mechanisms should have been developed. An antioxidative defence system in the thyroid gland comprises both antioxidative enzymes and free radical scavengers.

The presence of the following antioxidative enzymes in the thyroid gland has been documented: superoxide dismutase (SOD), glutathione (GSH), glutathione peroxidase (GPx) and catalase (CAT) [6].

One of the key enzymes GPx is selenium dependent. Therefore the selenium status of the patient may influence GPX activity and therefore thyroid function. It is shown that in hyperthyroidism there is increased production of reactive oxygen species(ROS) with a decrease in antioxidants and antioxidant enzymes including GPx. Hypothyroidism is considered to be a hypometabolic state but with a risk for coronary artery disease particularly in overt hypothyroidism. (7,8) Chinese herbal medicines are considered to have potential benefits in thyroid disorders including hypothyroidism.(9) Therefore the present preliminary study was carried out to evaluate serum selenium status along with G.SH and selenium dependent GPx activity and to devise further studies to assess the beneficial effects of Chinese herbs on hypothyroidism.

MATERIALS AND METHODS

Among total of 200 study subjects, referred by Department of Biochemistry, Institute of cardiology ,India 62 subjects with hypothyroidism were included in this study. 60 age-matched control subjects were taken for the study. Hypothyroidism had been present for 1 to 6 months prior to treatment in these subjects. These patients were not on any anti-thyroid treatment and were newly diagnosed on the basis of clinical symptoms and signs, serum hormone levels of T3, T4, TSH and ultrasonography. Subjects who were smokers, alcohol drinkers, diabetes mellitus, pregnancy, liver or kidney disorders, severe vascular diseases, other endocrine, immunological or inflammatory disorders, regular drug ingestion or antioxidant use were excluded from the study.

The study was approved by ethical committee and the written informed consent from each patient was obtained. And the whole project was designed and carried out by Institute of Cardiology, India and Capital Medical University, China.

Assessment Of Thyroid Function

At time of MRI, non-fasting blood samples were collected and put on ice immediately. Within 30 minutes serum was separated by centrifugation and stored at –80°C. Multiple biochemical markers were used to investigate thyroid function. TSH, free T4 (fT4) and T3 were all measured by chemoluminescence assays (Vitros ECI Immunodiagnostic System, Ortho-Clinical Diagnostics, Rochester, USA). Hypothyroidism was defined as a concentration of serum TSH above the upper limit of the reference range (0.4-4.3 U/dL) and fT4 or T3 concentrations below the reference range (0.85-1.94 ng/dL and 92.8-162.9 ng/dL respectively).

For all individuals, anthropometric parameters including weight and height were measured using standard protocols. From each patient, a detailed clinical history, covering dietary habits including smoking, alcohol consumption and family history was taken.

Biochemical Investigations:

The serum was used for the estimation of fasting blood glucose (FBG), Serum Cholesterol, HDL Cholesterol, LDL cholesterol and triglycerides by routine automated methods

using P-Modular 800 analyzer. Serum T3, T4 and TSH were measured based on the principle of antigen-antibody reaction by Electrochemiluminescence technology using Elecsys2010. Selenium was measured by using Graphite furnace Atomic absorption spectrophotometer, Shimadzu. GPx was determined by Enzyme linked assay.

Statistical Analysis

All statistical analysis were performed using the SPSS software (Statistical Package for the Social Sciences, version 13.0 SPSS Inc.) Quantitative variables were demonstrated as Mean±Standard deviation. Statistical analysis has been done using Kruskal-Wallis test and Mann-Whitney test. Relationship among the variables were analyzed using spearman's rank correlation.

RESULTS:

In the present study there was a marked decrease observed in the levels of serum selenium in hypothyroid cases compared to controls (TD)**. (Table.1).**

The difference in mean selenium between the groups was statistically significant (P<0.05).

There was a nonsignificant decrease in G.SH levels when compared to the control subjects (Table.2.)

There was a significant decrease in the level of Glutathione peroxidase activity in TD when compared to control subjects (Table.3).

There was no significant difference in fasting blood glucose level between control subjects and hypothyroid patients. There was a significant increase in total cholesterol compared to the control subjects with a fall in HDL cholesterol. There was a non-significant increase in LDL cholesterol in hypothyroid cases compared to the controls. There was no significant difference observed in serum triglyceride levels between the controls and hypothyroid patients. **(Table.4)**

There was a significant correlation between selenium and GPx activity as shown in Table.5 and 6.

Discussion:

The preliminary study is to evaluate selenium status as well as the levels of antioxidant G.SH and GPx a selenocysteine enzyme in hypothyroid patients. In the Nutritional Prevention of Cancer (NPC) Trial, a selenium level of 80ug. /L is considered the minimum level of plasma selenium necessary in the blood stream for maximum production of selenoproteins (glutathione peroxidase, thioredoxin reductase. [10]. The serum levels of selenium in our study is found to be comparatively lower than those reported by other workers described below. The differences observed in the values may be due to the method adopted, regional and racial differences along with the soil content of selenium in the respective areas.

Navarro M et al. [11] evaluated the serum selenium concentration in 130 healthy individuals living in Spain. The mean selenium concentration in serum was 74.9µg/L.

Cunha SD et al. [12] evaluated the serum level of selenium in healthy volunteers living in the city Rio de Janeiro. The mean serum selenium level was 73.18 ± 9.9 µg/L.

In India, there are some selected reports of serum selenium concentration of healthy adults. The mean serum selenium concentration reported by Mahalingum et al.[13] is 72 ± 4 µg/lit, Srikumar et al.[14] is 125 ± 19 µg/lit.,Yadav et al.[15] is 117 ± 16 µg/lit and by Gambhir et al. [16] is 133 ± 39 µg/L.

Safaralizadeh R et al. [17] evaluated the serum concentration of selenium in 184 healthy individuals living in Tehran by hydride generator flame atomic absorption spectrometry. In adults the mean serum selenium was 100.6 ± 13 µg/L.

Navarro M et al [11] found that the mean serum selenium concentration in healthy individuals did not vary significantly in relation to the sex of the subject. Significant reductions in selenium levels are indicators of metabolic response to oxidative stress in patients with diabetes.

The thyroid gland is characterized by relatively high level of selenium [10,11]. Selenoproteins seem to be crucial for antioxidative protection in the thyroid, for thyroid hormone synthesis and for the global integrity of thyrocytes, as they are present in antioxidative enzymes such as GSH-Px, thioredoxin reductases, and also in deiodinases [10,11].

It is known that at least two selenium dependent enzymes are involved in the metabolism of thyroid hormones. GPx protects thyrocyte from high H_2O_2 levels that are required for iodination of prohormones to form T4 in thyroid cell. Type I iodothyronine 5′-deiodinase (5′-D) catalyzes the deiodination of L-thyroxin (T4) to the biologically active thyroid hormone 3,3′-5-triiodothyronine (T3) in liver, in kidney and in thyroid tissues. Correlation studies between plasma Se level and both GPx activities were carried out to verify the hypothesis of a marginal Se deficiency in patients whether it will affect thyroid function.[18,19]

In the present study serum selenium did show significant correlation between T3 levels and GPx activity in TD patients while there was no significant correlation between selenium, thyroid hormones and GPx activity excepting with serum cholesterol levels.

T4→T3

Deiodinase

Deiodinase a selenium dependent enzyme is required for conversion of T4 to T3. The fall in T3 fall in the patients studied may be due to reduced activity of deiodinase required for the formation of T3 from T 4 because of selenium deficiency.

The fall in serum T3 levels coupled with a fall in GPx activity in TD subjects clearly show that a fall in selenium level will affect thyroid function.[20,21].

There was no significant difference in the fasting blood glucose levels in normal and hypothyroid cases. The increase in serum total cholesterol with an elevation in LDL cholesterol was observed in the present hypothyroid cases may be due to decreased LDL receptors which may cause such an elevation in total cholesterol.(22). A slight increase in HDL cholesterol observed in these cases may be due to decrease in cholesterol ester transfer protein (CETP) for which further studies may be needed. In this preliminary study serum selenium levels were markedly decreased in the hypothyroid cases. There was a marked decrease in GPX activity in the hypothyroid cases compared to the control subjects as reported by other workers (23,24) .

This difference may be due to decreased selenium levels which may affect GPx activity. (25)

Table.1. Serum Selenium Levels In Hypothyroid Cases And Normal Subjects:

Group	N	Mean µg/L	S.D.	SE of Mean	95% CI for Mean		Min	Max	P-Value
					Lower Bound	Upper Bound			
Normal	62	61.12	13.67	1.74	57.65	64.59	40.00	89.00	0.009
TD	60	45.60	14.64	2.21	40.15	51.05	37.50	102.00	

Table.2. Serum Glutathione (G.SH) Levels In Patients With Periodontitis Without And With Diabetes And

Normal Subjects

Group	N	Mean mg/dL	SD of Mean	SE of Mean	95% CI for Mean		Min	Max	P-Value
					Lower Bound	Upper Bound			
Normal	62	14.54	5.25	1.14	8.55	16.20	11	17	0.648
TD	60	18.50	7.04	1.60	11.20	21.40	8.0	22	

Table.3. Serum Glutathione Peroxidase (GPx) Activity In Hypothyroid Cases And Normal Subjects :

Group	n	Mean	SD of Mean	SE of Mean	95% CI for Mean		Min	Max	P-Value
					Lower Bound	Upper Bound			
Normal	62	236.92	56.25	7.14	222.64	251.20	156	399	0.019*
TD	60	261.64	57.04	8.60	244.29	278.98	178	399	

*Denotes significant difference

Table.4. Comparison Of Various Parameters Between Normal Subjects And Hypothyroid Patientse: Statistical Test Used: Mann-whitney Test

Parameter	Normal (Mean± SD)	Hypothyroid (Mean ±SD)	Mean difference	Z	P-Value
Age (years)	53.40±10.14	49.68±10.20	3.717	-2.625	0.009*
FBS mg/dL	97.54±45.99	104.93±50.22	2.615	-0.684	0.494
Cholesterol-mg/dL	159.54±42.34	178.99±42.79	-19.444	-3.686	<0.001*
HDL-mg/dL	33.73±6.911	42.78±9.560	-9.054	-7.134	<0.001*
LDL-mg/dL	93.92±36.44	109.86±36.70	-15.936	-3.140	0.002*
TGL-mg/dL	152.58±80.48	143.31±77.66	9.275	-1.154	0.248

*denotes significant difference

Table.5. Correlation Between Selenium And Other Parameters In TD group: (Spearman's Rank Correlation)

Parameter	ρ	P-Value
Age	0.089	0.489
FBS	0.116	0.370
Cholesterol	-0.191	0.137
HDL	-0.046	0.722
LDL	-0.224	0.080
TGL	-0.099	0.444
T3	-0.262	0.040*
T4	-0.032	0.802
TSH	0.070	0.586
GPX	0.441	<0.001*

*denotes significant correlation

Table.6. Correlation Between GPX And Other Parameters In TD Group: (Spearman's Rank Correlation)

Parameter	ρ	P-Value
Age	0.059	0.648
FBS	0.071	0.582
Cholesterol	0.010	0.941
HDL	0.102	0.432
LDL	-0.039	0.761
TGL	0.009	0.945
T3	-0.141	0.275
T4	0.062	0.631
TSH	0.130	0.315
Selenium	0.441	<0.001*

*denotes significant correlation

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