Original Article

Study of Glutathione peroxidase as an indirect biochemical index of enzymatic deiodination of thyroid hormones in hypothyroidism

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Abstract

Introduction: Glutathione peroxidase (GSHPx) enzyme is the first seleno enzyme to be identified and is the most abundant selenoprotein in most cells. **Aims and Objectives:** To Study Glutathione peroxidase as an indirect biochemical index of enzymatic deiodination of thyroid hormones in hypothyroidism. **Methodology:** The study was carried out in patients attending the special investigation laboratory, department of Biochemistry, Medical College, Trivandrum, for assessment of their thyroid function. The present study was conducted on three groups, based on the thyroid function tests. Group 1 (n-40) consisted of healthy euthyroid controls. Group II (n-30) included hypothyroid patients. In erythrocytes- Glutathione peroxidase enzyme, Serum -Thyroid function tests T3, T4, TSH .Statistical analysis done by Un-paired t-test. **Result:** The Mean value of T4 is significantly more in Control i.e. 8.25±0.30 µg /dL as compared to Hypothyroid i.e. 5.42±0.60 µg /dL(t = 4.95, p value <. 0005). The Mean value of T3 is significantly more in Control i.e. 113.93±3.40 ng/dL and in Hypothyroid 100.80±3.60 ng/dL (t= 2.478, p value .01). The Mean value of TSH is significantly more in Hypothyroid i.e. 27.35±2.8 µ IU/ml as compared to Control 2.49±0.20 µ IU/ml. The Mean value of GSH Px is significantly more in Control i.e. 6.117±0.133µmole/ L and in Hypothyroid 4.831±0.136 (t = 6.64; p<. 0005). **Conclusion:** Glutathione peroxidase enzyme is a Selenoprotein. Erythrocyte GSHPx activity is significantly decreased in Hypothyroidism, thus indirectly correlating to deficient peripheral deiodination of thyroid hormones and selenium status. A significantly elevated serum TSH level is the key diagnostic laboratory finding of Hypothyroidism. Serum TSH assay is the single best marker for detection of Hypothyroidism.

Key words: Glutathione peroxidase (GSHPx), T3, T4, TSH, Enzymatic deiodination.

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INTRODUCTION

Glutathione peroxidase (GSHPx) enzyme is the first seleno enzyme to be identified and is the most abundant selenoprotein in most cells. Primary hypothyroidism is a common disease worldwide. Most striking features are the high prevalence; the marked female preponderance and the increasing occurrence with advancing age.[1] The vast majority of patients have primary hypothyroidism. Hypothyroidism is a graded phenomenon that ranges from subclinical hypothyroidism to myxedema coma, the most severe manifestations of the syndrome.[2] The ideal diagnostic test for hypothyroidism would be one that accurately measures the effect of thyroid hormone deficiency in target tissues. Without a doubt, serum TSH is the single best assay for detection of hypothyroidism.[3] Selenium is one of the most beneficial elements for man and animals. Since Schwartz and Folts defined Se as an essential trace element, many of its functions and structures have been demonstrated.[4] Apart from the essential trace element iodine, which is the central constituent of thyroid hormones, a second essential trace element, selenium is required for appropriate thyroid hormone synthesis, activation and metabolism. The

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human thyroid gland has the highest selenium content per gram of tissue among all organs. [5]

Glutathione Peroxidase: It was in 1973 that, selenium was known to have a biochemical role as a component of glutathione peroxidase. It was then that J.T. Rotruck et al. presented a paper titled, "Selenium; biochemical role as a component of glutathione peroxidase". The paper presented an over view of selenium's importance in the structure of glutathione peroxidase in that it contains one selenium residue per subunit.[6]

There have been studies done in which Vit E and Selenium work synergistically. The basis for this interaction is likely to be the ability of GPX-4 to remove phospholipid hydroperoxides, which have the potential to cause damage in the membrane. GPX-1 cannot react directly with such hydroperoxides, unless first metabolized by phospholipase A2.[7,8]

Selenium deficiency triggers hypothyroidism because selenium is an essential part of the deiodinase enzyme. Selenocysteine is necessary for the maximal enzyme activity and conversion of T_4 to T_3 for thyroid regulation. This explains why conversion of T_4 to $T_3$is impaired in experimental selenium deficiency and identifies an essential role for selenium in thyroid hormone action [9,10].

Many research studies conclude that the preferred indexes of human selenium status are blood, or plasma and/ or serum, concentrations of the element and the level of activity of the selenium – dependent enzyme glutathione peroxidase in erythrocytes or in plasma [11]. Studies were performed to assess the role of selenium in hypothyroidism. One effect of selenium deficiency may be to lower glutathione peroxidase activity. In another study, glutathione peroxidase enzyme was significantly correlated with selenoprotein P, indicating that both glutathione peroxidase and selenoprotein P were functional indicators of selenium status.[12]

METHODOLOGY

The study was carried out in patients attending the special investigation laboratory, department of Biochemistry, Medical College, Trivandrum, for assessment of their thyroid function.

The present study was conducted on three groups, based on the thyroid function tests. Group 1 (n-40) consisted of healthy euthyroid controls. Group II (n-30) included hypothyroid patients. In erythrocytes-Glutathione peroxidase enzyme, Serum -Thyroid function tests T3, T4, TSH .Commercially procured kits were used for the determination of these parameters- T3, T4, and TSH, A detailed history of each subject which includes personal history, family history, past history, and treatment history was taken.

GSHPx estimations was done in semi auto analyzer (RA 50) manufactured by Bayer. Thyroid function was assessed by ELISA technique. Glutathione peroxidase (GSH Px)(GSH: H_2O_2oxidoreductase, E.C.1.11.1.9) Glutathione peroxidase activity was assayed in erythrocytes, using cumenehydroperoxide as substrate. The method followed is as described by O' Brien and Little [13] which is a modification of the method described by Paglia and Valentine [14] Reagents: TrisHCl buffer, reduced glutathione, NADPH, EDTA, Cumenehydroperoxide and saponin. All the reagents were purchased from sigma. Deionized water was used for making all solutions.[13]

Thyroid Function Tests: T_3, T_4 and TSH were determined using ELISA (Enzyme Linked Immuno Sorbent Assay) technique. Statistical analysis done by Un-paired t-test.

RESULT

Table 1: Comparison of mean values of T4 between control group and hypothyroid group

Group	Control	Hypothyroid
N	40	30
Mean value of T4	8.25±0.30	5.42±0.60
µg /Dl	µg /dL	µg /dL

t = 4.95, p value <. 0005 Statistically very significant

The Mean value of T4 is significantly more in Control i.e. 8.25±0.30 µg /dL as compared to Hypothyroid i.e. 5.42±0.60 µg /dL(t = 4.95, p value <. 0005)

Table 2: Comparison of mean values of T3 between control group and hypothyroid group

Group	Control	Hypothyroid
N	40	30
Mean value of T3	113.9±3.40	100.80±3.60
ng/dL	ng/Dl	ng/dL

t= 2.478, p value .01 statistically significant

The Mean value of T3 is significantly more in Control i.e. 113.93±3.40 ng/dL and in Hypothyroid 100.80±3.60 ng/dL (t= 2.478, p value .01)

Table 3: Comparison of mean values of TSH between control group and hypothyroid group

Group	Control	Hypothyroid
N	40	30
Mean Value of TSH µ IU/ml	2.49±0.20	27.35±2.8

t= 10.26, p value <. 0005 statistically very significant

The Mean value of TSH is significantly more in Hypothyroid i.e. 27.35±2.8 µ IU/ml as compared to Control 2.49±0.20 µ IU/ml.

Table 4: Comparison of mean values of GSH Px between control groups and hypothyroid group

Group	Control	Hypothyroid
N	40	30
Mean µmole/ L	6.117±0.133	4.831± 0.136

t = 6.64; p<. 0005 statistically very significant

The Mean value of GSH Px is significantly more in Control i.e. 6.117±0.133µmole/ L and in Hypothyroid 4.831±0.136 (t = 6.64; p<. 0005)

DISCUSSION

In this study, the hypothyroid group showed statistically significant (p<.0005) decrease in the GSHPx levels when compared with that of control group . A study has indicated that, GSH Px is an enzyme which is clearly influenced by intake of dietary supplements, life style and environmental factors. [15]

In another study, the effect of iron supplementation on GSH Px levels was studied. It was found that, iron supplementation increases GSHPx levels 15. In this present study, 2 subjects in the control group who were taking iron supplements showed increase in the GSHPx levels.

The effects of a low selenium diet on thyroid hormone metabolism was investigated in growing kittens. Twelve specific – pathogen – free kittens with ages ranging from 16-18 wks were divided into two groups of equal number, with equal sex distribution in each group. One group was fed a yeast – based low selenium diet (0.02 mg Se/kg diet) while the other group was fed the same diet supplemented with Na_2SeO_3 at o.4 mg Se/kg diet for 8 weeks. The kittens given the low – Se diet had significantly reduced plasma selenium concentration and glutathione peroxidase activity.

Total T3 decreased significantly in kittens fed the low Se diet, at the end of the study. These results suggest that type I deiodinase and GSHPx are selenoprotiens or selenium dependent enzymes. [16]

Selenium deficiency for periods of 5 or 6 weeks in rats produced, an inhibition of T3 production from added thyroxine in brain, liver and kidney homogenate. This was reflected in plasma T3 concentrations, which was decreased in selenium deficient rats. Selenium deficiency was confirmed in the animals by decreased selenium dependent glutathione peroxidase activity in all tissues. Administration of selenium as (Na_2SeO_3)/kg body weight, completely reversed the effect of selenium deficiency on thyroid hormone metabolism, and partly restored the activity of Se GSH Px. These data are consistent with the view that type I deiodinase enzyme and GSHPx enzyme are selenoenzymes. [17] Another study, similar to this, also concluded that imbalances in thyroid hormone metabolism are an early consequence of selenium deficiency [18] A study by the dept. of clinical chemistry, Royal Infirmary, Edinburgh, suggested that Se deficiency produces inhibition of 5' deiodination. The mechanism of inhibition appears not be mediated by changes in thiol levels, but a direct role of Se in the activity of the deiodinase complex cannot be excluded [19].

To examine the relationship between Se deficiency and thyroid hormone metabolic disturbance, especially, 5' deiodinase type I activity, Serum T3, GSHPx and lipid peroxides were observed in the peripheral tissues of (liver, kidney and blood) of wister rats maintained on Se deficient artificial semisynthetic diet for 8 weeks. Results were compared with the Se supplemented rats. Deiodinase D1 activities, serum levels of T3 and GSHPx activities were reduced in the selenium deficient rats.[20]

CONCLUSION

Glutathione peroxidase enzyme is a Selenoprotein. Erythrocyte GSHPx activity is significantly decreased in Hypothyroidism, thus indirectly correlating to deficient peripheral deiodination of thyroid hormones and selenium status.A significantly elevated serum TSH level is the key diagnostic laboratory finding of Hypothyroidism. Serum TSH assay is the single best marker for detection of Hypothyroidism.

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