

A Study on the Relationship between Thyroid Hormones and Adenosine Deaminase Enzyme Activity in Patients with Auto- Immune Hyperthyroid Disease

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ABSTRACT :

BACKGROUND :

Adenosine deaminase ADA catalyzes the deamination of adenosine in purine metabolism . Adenosine deaminase deficiency is an inborn error resulting in immunodeficiency condition . clinical interest in this enzyme has been revived by the discovery of a syndrome of severe humoral and cellular immunodeficiency associated with deficiency of ADA in somatic erythrocyte cell .

AIM OF STUDY:

The aim of present study is conducted to find the relationship between human hyperthyroid activities and immune etiology in graves disease.

MATERIALS AND METHODS :

Forty individuals with hyperthyroidism autoimmune state were included in this study in comparison with forty normal persons .

Thyroid hormones levels were estimated by HPLC and serum ADA specific activity was estimated using spectrophotometric method at 265 nm . Serum protein value was determined by Bradford method .

RESULTS :

Serum ADA activity was measured for 40 hyperthyroid patients as well as 40 normal individuals . The mean activity of ADA in patients was higher than in the controls . A significant increase in T3 / T4 ratio and level of TSH were noticed .

CONCLUSION :

A positive correlation between thyroid level and ADA enzyme activity was noticed .

KEY WORDS : grave's disease , hyperthyroid activity adenosine deaminase .

INTRODUCTION :

Adenosine aminohydrolase { adenosine deaminase (ADA) (EC. 3.5 , 4.4) } which catalyses the deamination of adenosine to inosine in purine metabolism (purine catabolism) is a polymorphic enzyme that is found in most human tissues ⁽¹⁾. Adenosine deaminase deficiency is an inborn error resulting in immunodeficiency conditions . Clinical interest in this enzyme has been revived by the discovery of a syndrome of sever humeral and cellular immunodeficiency associated with deficiency of ADA in somatic erythrocyte cells ⁽²⁾ . It is reported that the deficiency of ADA represent the first association of a specific enzyme defect with an inherited disorder of both T- and B-

lymphocyte functions ⁽³⁾ .

The focusing is on the relationship between DNA damage and DNA precursor pools in cultures of deoxyadenosine treated , ADA inhibited resting lymphocyte ⁽⁴⁾ .One of the immune diseases in the human was graves disease and hashimoto's thyroiditis which are associated with impairment of natural killer cell activity of peripheral blood lymphocytes against human tumor cell targets . These two conditions have abnormalities of thyroid hormone secretion , although an effect of the underlying autoimmune reaction had not been excluded ⁽⁵⁾ .

Also there an autoimmune thyroid disease and presumably to maternal thyroid stimulating hormone (TSH) receptor blocking antibody , that is associating much higher prevalence of transient congenital hypothyroidism than suspected because of maternal thyroid dysfunction , thus assessment of thyroid function in such women and their babies thyroid hormones function must be available routinely ⁽⁶⁾

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Several studies investigated the participation of thyroxin in the regulation of energy metabolism blood leukocytes elements and their bone marrow precursors . it were also reported that the administration of 4 resulted in preferential stimulation of oxidative stages of carbohydrate catabolism in myelokaryocyte while the activity of glycolytic enzymes in these cells was less affected ⁽⁷⁾ . his work is conducted to study the relationship between human hyperthyroid activity and immune aetiology in graves disease by using DNA enzyme as a principle parameter .

MATERIALS AND METHODS :

Case control study was carried out to evaluate the relation between serum thyroid hormone level which were estimated by PHLC technique (high power liquid chromatography) ⁽⁸⁾ and serum ADA specific activity that is estimated by spectrophotometer ⁽⁹⁾ . Serum protein value was determined by Bradford method ⁽¹⁰⁾ .

RESULTS :

The patients selected for this study were suffering from graves disease (autoimmune hyperthyroidism) and had abnormal thyroid hormone . Data presented in table 1 showed that those patients have a significant increase in T3/T4 ratio and an increase in TSH levels .

Serum T3 and T4 hormone levels were 1.212 (I.U.) and 44.97 (I.U.) respectively these were significantly lower than those of the controls (table 1) hormone which 1.212 (I.U.) . Though the T3/T4 ratio was increased (0.026) which is accompanied by increasing TSH level (47.75 I.U.) ADA enzyme is one of the most essential immune enzyme ; it's function gives a clear picture of immune state of the body . The result in table 2 show that patients with lower T3/T4 ratio and higher TSH level had higher specific activity of serum ADA than normal individual .

There was a positive correlation ($r = 0.98$, 0.6) between ADA specific activity and T3/T4 ratio and also with increased TSH level , respectively (table 3) .

The mean activity of ADA in patients was (0.496 ± 0.014) v/gm) and 0.291 ± 0.021 v/gm in the controls . The difference was statistically significant ($p < 0.05$) .

Simultaneously thyroid hormones T3 , T4 as well as TSH hormone in the sera of the same patients were also determined significant increase in T3/T4 ratio and level of TSH were also noticed , a positive correlation between thyroid hormone level and ADA enzyme activity was noticed .

DISCUSSION :

Hyperthyroidism is a clinical condition results from over production of T3 and T4 . When the over production is confined to T3 the condition is called T3 toxicosis ⁽⁹⁾ .

The thyroid gland secretes predominantly thyroxin (T4) and only small amount of triiodothyronine (T3) , approximately 85% of T3 is produced by mono deiodination of T4 in other tissues such as liver muscles and kidneys . T4 is probably not metabolically active unit converted to T3 and may be regarded as a prohormone . T3 and T4 circulate in plasma almost entirely ($> 99.9\%$) bound to transport proteins . it is the minute fraction of unbound or free hormone that diffuses into tissues and exerts its metabolic action ⁽¹⁰⁾ .

Production of T3 and T4 in thyroid is stimulated by thyrotropin (thyroid stimulating hormone TSH) . There is a negative feedback of thyroid hormone on the thyrotropin such as in hyperthyroidism .

When plasma concentration of T3 and T4 are raised , TSH secretion is suppressed in hyperthyroidism due to disease of thyroid gland . Low T3 and T4 are associated with high circulating TSH levels . The combination of normal T3 and T4 and suppressed or raised TSH is known as hyperthyroidism and sub clinical hyperthyroidism respectively . The cause of hyperthyroidism is not completely understood but is probably immunologic patients with this disease have circulating thyroid stimulation in their serum known as thyroid stimulating immunoglobulins (antibodies) .

These antibodies are directed against the TSH receptors and specifically stimulate the activity of the thyroid . The present study showed that there is a significant reduction in T4 hormone levels in patients with graves disease in compare with control (table 1) . T3/T4 ratio is increased which is accompanied by increasing TSH levels .

ADA enzyme is one of the most essential immune enzymes ; its function gives a clear picture of immune states of the body . The results in table 2 show that patients with lower T3/T4 ratio and higher TSH level had specific activity of serum ADA than normal individual .

It is also found that there is a positive correlation ($r = 0.98$, 0.6) between ADA specific activity and T3/T4 ratio and also with increasing TSH level , respectively (table 3) there is a proportionally greater increase in the serum T3 and T4 concentration in patients with hyperthyroidism , and that serum T3 and T4 ratio is a single and

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useful predictor of the outcome anti thyroid drug therapy in patients with hyperthyroidism state ⁽¹¹⁾ . A previous study⁽¹²⁾ showed that there was a significant reduction in the mean level of T3 after treatment with propranolol while there was no significant change in T4 level . Thyroid hormone may effect bone metabolism and turnover including a loss of bone mass among hyperthyroid and in hyperthyroid patients under hormone replacement treatment via change in the dynamic of calcitonin in secretion ⁽¹³⁾ .

CONCLUSION:

The lower T3/T4 ratio and higher TSH level had specific activity of serum ADA than normal individual .

Difference was statistically significant ($p < 0.05$) simultaneously thyroid hormone T3,T4 well as TSH hormone in the sera of the same patients were also determined significant increase in T3/T4 ratio and level of TSH were also enzyme activity was noticed .

Table (1): The relationship between thyroid hormones levels of patients with hyperthyroidism and normal individual.

Estimated hormones (I.U.)	Cases X ⁻ ± SE N=40	controls X ⁻ ± SE N=40	P value	significant
T3	1.21 ± 0.04	1.8 ± 0.06	> 0.05	N.S.
T4	44.97 ± 3.45	80.0 ± 4.4	<0.05	S.
T3/T4 ratio	0.03	0.02	<0.05	S.
TSH	47.75 ± 1.04	2.4 ± 0.03	<0.05	S.

Table (2): Specific activity of serum ADA enzyme of with hyperthyroidism and normal individual.

Parameter of ADA	Cases X ⁻ ± SE N=40	controls X ⁻ ± SE N=40	P value	significant
Volume activity (U/L)	3.66 ± 0.01	1.93 ± 0.03	<0.05	S.
Protein (gm/dl)	7.37 ± 0.13	6.62 ± 0.15	<0.05	S.
Specific activity (U/gm)	0.45 ± 0.01	0.29 ± 0.02	<0.05	S.

Table (3): The correlation between ADA and thyroid

Y	X	R	P
T3/T4 ratio	ADA spec. activity	0.98	<0.05 S.
TSH level	ADA spec. activity	0.60	<0.05 S.

Table (4) : Thyroid hormones level and serum activity ADA in females with Grave's disease.

NO	Age(years)	T3 (I.U.)	T4(I.U.)	TSH(I.U.)	ADA(U/gm)
1.	19	2	57.3	1.95	0.306
2.	17	1.3	33.0	32.0	0.187
3.	45	1.7	49.6	27.7	0.403
4.	45	1.7	56.6	100.3	0.852
5.	28	1.6	51.5	69.4	0.353
6.	25	0.8	15.6	22.8	0.544
7.	48	0.9	31.2	76.8	0.420
8.	48	0.9	39.6	56.8	0.214
9.	35	1.8	58.1	1.5	0.673
10.	24	1.4	30.2	47.7	0.766
11.	24	1	56.8	1.4	0.300
12.	48	1.1	48.0	80.0	0.175
13.	50	1.6	58.4	82.0	0.190
14.	18	1.1	32.4	80.0	0.400
15.	40	0.8	29.4	1.3	0.850
16.	18	1.1	55.7	92.0	0.552
17.	42	0.2	17.8	181.0	0.341
18.	36	0.6	36.7	83.2	0.424
19.	27	0.2	26.8	89.8	0.211
20.	28	1.7	54.5	3.2	0.678
21.	28	1.1	47.4	90.2	0.698
22.	26	1.1	38.3	95.5	0.698

Table(5): Thyroid hormones level and serum activity ADA in males with Grave's disease

NO	Age(years)	T3 (I.U.)	T4(I.U.)	TSH(I.U.)	ADA(U/gm)
1.	20	1.1	49.9	163.3	0.719
2.	20	1.1	4.8	84.0	0.810
3.	41	1.2	49.3	3.8	0.732
4.	38	0.9	13.8	3.01	0.750
5.	25	0.9	25.7	146.2	0.300
6.	38	0.8	9.8	10.6	0.540
7.	38	1.9	31.8	8.9	0.451
8.	22	0.2	1.0	90.0	0.123
9.	23	0.1	1.0	6.0	0.078
10.	18	2.1	40.0	3.7	0.111
11.	42	1.0	59.4	105.6	0.244
12.	37	2.0	25.0	100.1	0.640
13.	28	1.0	52.2	90.7	0.432
14.	24	1.0	46.1	18.0	0.458
15.	34	1.1	15.1	1.2	0.229
16.	34	1.0	53.0	96.2	0.069
17.	24	0.9	22.3	79.1	0.054
18.	26	1.1	54.6	66.5	0.410

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