

The influence of thyroid hormones on hemoglobin α_2 and F expression

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Abstract

Background: To evaluate the effect of thyroid hormones on the production of hemoglobin A_2 and F (Hb A_2 and F).

Patients and methods: Sixty three patients were enrolled in this study including new cases of hyperthyroidism, hypothyroidism and thalassemia minor; 28 healthy subjects were used as control group. Assessment of Hb A_2 , Hb F levels as well as measurement of thyroid hormones were performed for each of them.

Results: Hb A_2 was significantly higher in hyperthyroid patients than in control group ($P=0.002$), while Hb F was significantly higher in hypothyroid group in comparison with the control ($P=0.012$).

Conclusion: Hemoglobin A_2 levels are increased in hyperthyroidism and decreased in hypothyroidism, unlike hemoglobin F. This may clarify the effect of thyroid hormones on globin chain synthesis.

Key words: Thyroid hormones, thyroxine, tri-iodothyronine, hemapoiesis, erythropoiesis, hemoglobin structure, globin chains, anemia.

Introduction

The thyroid gland produces thyroxine (T_4) and tri-iodothyronine (T_3) hormones that play critical role in cell differentiation, maintenance of thermogenic and metabolic homeostasis. In thyroid disorders, a slight elevation of Hb A_2 & F had been found occasionally, raising the question of thyroid hormones effect on globins chain synthesis and/or globins gene expression. The percent of Hb A_2 is increased in beta thalassemia minor, but usually decreased in other cases like α -thalassemia trait, iron deficiency [1- 6].

Normal and variant hemoglobins can be detected and quantified by standard clinical laboratory techniques. Standard cellulose acetate electrophoresis performed at alkaline pH or isoelectric focusing can detect most of the common variants [7, 8]. High performance liquid chromatography (HPLC), which can be a relatively fast and reproducible method, had been used for the determination of various hemoglobin including Hb A_2 and F [9, 10]. The aim of this study was to evaluate the effect of thyroid hormones (T_3 & T_4) on the production of hemoglobin A_2 and hemoglobin F.

Patients and methods

From November 2006 to May 2007, sixty three patients were included in this study and divided into 3 groups:

Group 1; thirty patients who are newly diagnosed cases of hyperthyroidism. Group 2; twenty one patients who proved to have hypothyroidism recently. Group 3; twelve patients known to have thalassemia minor. After thorough medical interview and physical examination to confirm the diagnoses, laboratory investigations were performed to prove the diagnoses of these selected cases.

Additional 28 healthy people were taken as a control group. (Group 4).

Venous blood samples were withdrawn from all 4 groups and divided into 2 parts: first, in (Ethylenediaminetetraacetic acid) EDTA plastic tube for Hb A₂ & Hb F estimation by variant β thalassemia short program (Bio-Rad-France) depending on the principal of cation exchange high performance liquid chromatography (HPLC); the rest of blood sample was used for thyroid function assessment via minividas technique (Bio-Merieux-France).

Statistical analysis was performed with the SPSS 10.01 (statistical Package for social sciences). Data analysis was done using student t-test to estimate the difference between groups; a p value <0.05 was considered significant. All values were expressed as mean \pm standard error (M \pm SEM).

Results

The mean age of hyperthyroid patients was 42 ± 9 years (range 24-55), and for hypothyroid patients was 22 ± 17 years (range 1-50), while the mean age of

thalassemic patients was (15 ± 11) years (range 2-31) as shown in. table-1.

Groups	No	Mean age (years)	Range (years)	SEM
Hyperthyroid	30	42	24-55	9
Hypothyroid	21	22	1-50	17
Thalassemia minor	12	15	2-31	11
Controls	28	28	16-60	12

Table (1): Age distribution in different groups (P value <0.05)

The fourth group was the 28 normal adult controls, 21 of them were females; their mean age was 28 ± 12 years (range 16-60). The mean HbA₂ percent was 2.39 ± 0.007 in control group, 2.77 ± 0.008 in hyperthyroid group, 2.25 ± 0.176 in hypothyroid and 5.78 ± 0.148 in thalassemia minor group (Table 2). Hb A₂ was significantly higher in the hyperthyroid group of patients than in control group ($p=0.002$), while there was no significant difference between the hypothyroid group of patients in comparison with control group ($p=0.432$). HbA₂ was significantly higher in thalassemia minor group with respect the other 3 groups as shown in table-2.

The mean HbF percent was 0.18 ± 0.00 in control group, 0.68 ± 0.27 in hyperthyroid group, 0.71 ± 0.18 in hypothyroid group, and 6.65 ± 2.86 in thalassemia minor group (Table 3). There was no significant difference in HbF percent between the hyperthyroid group and the control group ($p=0.093$), However there was a significant difference in HbF percent between the hypothyroid group of patients in comparison with control group ($p=0.012$). HbF was significantly higher in thalassemia minor group than in control group ($p=0.002$).

Groups	No	Mean	SEM	P- value	Interpretation
Hyperthyroid/ control	30/28	2.77/2.39	0.008/0.007	0.002	Significant
Hypothyroid/ control	21/28	2.25/2.39	0.176/0.007	0.432	Non-significant
Thalassemia minor/control	12/28	5.78/2.39	0.148/0.007	<0.001	Highly significant
Hyperthyroid/Hypothyroid	30/21	2.77/2.25	0.008/0.176	0.007	Significant
Hyperthyroid/ Thalassemia-minor	30/12	2.77/5.78	0.008/0.148	<0.001	Highly significant
Hypothyroid/ Thalassemia- minor	21/12	2.25/5.78	0.176/0.148	<0.001	Highly significant

Table (2) Comparison of HbA₂% between different groups of patients (P value <0.05)

Groups	No.	Mean	SEM	P- value	Interpretation
Hyperthyroid/control	30/28	0.68/0.18	0.277/0.004	0.093	Non-significant
Hypothyroid/control	21/28	0.71/0.18	0.186/0.004	0.012	Significant
Thalassemia- minor/control	12/28	6.65/0.18	2.861/0.004	<0.001	Highly Significant
Thalassemia minor/hyperthyroid	12/30	6.65/0.68	2.861/0.277	0.002	Significant

Table (3) Comparison of HbF% in different groups of patients (P value <0.05)

Discussion

Hemoglobin A₂ was significantly elevated in hyperthyroid group of patients than normal controls, and was also significantly elevated than hypothyroid group of patients & this result is similar to that obtained by Kendall AG, Bastomsky CH[12] and Kuhn JM, Rieu M. Hemoglobin A₂ was significantly elevated in thalassemia minor group as compared with that of hyperthyroidism group which is similar to results of Kuhn JM, Rieu M. Hemoglobin A₂ levels were reduced slightly in hypothyroid group of patients than the control group [13].

Thyroid hormone can specifically increase expression of delta globin, which is consistent with clinical observations that hemoglobin A₂ levels

are increased in hyperthyroidism and decreased in hypothyroidism according to conclusion of Benjamin L. et al [2].

There was no significant difference in HbF between the hyperthyroid group of patients and the control group, however HbF was significantly higher in the hypothyroid group of patients than control group, and these results were in disagreement with that obtained by Kendall AG, Bastomsky CH [12] and Kuhn JM, Rieu M [13]. which could be explained by small sample size enrolled in this study and the use of different techniques in hemoglobin qualification? Meanwhile HbF was significantly higher in thalassemia minor group than control group which clearly explained on the basis of ineffective erythropoiesis due to defective β globin chain synthesis that is replaced partially with γ chain synthesis [10, 11, 13, 14, 15].

Conclusion

The thyroid hormones have a possible correlation with the expression of hemoglobin A₂ percent in the blood. Its production is enhanced in hyperthyroidism and decreased in hypothyroidism. Differentiating between hyperthyroid patients and thalassemia trait cases is easy as the increase in the percentage of HbA₂ in blood of thalassemia minor group is rather high levels in addition to the specific clinical manifestation seen in hyperthyroid status. An inhibitory effect of the thyroid hormones on Hb F is evident which may explain the high Hb F percentage in cases of hypothyroidism.

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