The Association Between Hypothyroidism and Anemia: a Clinical Study

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Abstract

Introduction: Hypothyroidism is diagnosed by elevated thyroid stimulating hormone (TSH) and normal or decreased serum levels of T4 or T3, and is associated with a wide range of metabolic abnormalities, including anemia. This clinical study aimed to assess the improvement of anemia in patients with primary hypothyroidism following administration of levothyroxine in Iranian population.

Materials & Methods: The effect of levothyroxine in 70 patients with hypothyroidism was examined and the improvement of anemia in patients who had a poor or good response to levothyroxine was assessed during a 3 month follow-up.

Results: Three months after treatment, the levels of TSH in 64 patients with hypothyroidism (91.4%) significantly decreased to a normal limit (TSH< 2.5 IU/ml). Forty three out of 70 patients (61.4%) had a concurrent anemia. A significant difference was found in the levels of hematologic parameters between those who had a good response (TSH< 2.5 IU/ml) and those with poor responses to the treatment (TSH≥2.5 IU/ml) (p< 0.05).

Conclusions: Current study showed a high rate of association between anemia and hypothyroidism in Iranian population. Improvement in hypothyroidism and its associated anemia was observed in majority of patients (more than 90%), indicating a dual benefit for hypothyroidism treatment. Less than 10% of patients poorly responded to levothyroxine, with no clear reasons.

Keywords: Anemia, Hypothyroidism, Iran, Levothyroxine

Introduction

Hypothyroidism is a clinical syndrome resulting from deficiency of thyroid hormones, leading to generalized slowing of all metabolic processes.(1) Hypothyroidism in infants and children results in growth and mental development retardation.(2, 3) The prevalence of hypothyroidism has been shown to be varied from 2-5% depending on the study, increasing to 15% by age 75 years, with a higher incidence in females.(4) In iodine deficient areas such as India the incidence can reach as higher as 10-20 times more than non-iodine areas like U.S.A.(5-7)

Metabolic abnormalities associated with hypothyroidism include anemia, dilutional hyponatremia, hyperlipidemia, and reversible increase in creatinine.(8) The prevalence of anemia in patients with hypothyroidism has been shown to be 20-60% .(9) Thyroid hormones involve in hemoglobin synthesis in adults and maturation of hemoglobin in fetus (3, 10) and by affecting hematopoietic process, hypothyroidism results in anemia through slowing the oxygen metabolism.(11)

Hypocoaglupathies, hemorrhages, malabsorbtion of iron, vitamin B12 and folic acid, reduced erythropoietin and bone marrow hematopoietic cells hypoplasia are known as the reasons for anemia.(12)

Table- 1. Frequency of anemia in patients with hypothyroidism

Anemia	Male (n= 11, 25.6%)	Female (n= 32, 74.4%)
Microcytic	1 (14.3%)	6 (85.7%)
Normocytic	10 (32.3%)	21 (67.7%)
Macrocytic	0 (0%)	5 (100%)

Table- 2. Hematological parameters in patients who had a good or poor response to treatment before and after administration of levothyroxine

Blood parameters	Good response (Mean± SD, n= 64)			Poor response (Mean± SD, n= 6)		
	BT	AT	*p*- value	BT	AT	*p*- value
Hb, g/dL	11.5± 1.3	13.4± 1.1	0.001*	10.5± 0.52	11.3± 1.13	0.06
HCT, %	34.8± 2.7	37.7± 4.5	0.001*	33.4± 2.6	34.9± 2.7	0.34
MCH, pg	24.09± 3.1	28.5± 2.9	0.001*	21.9± 3.2	24.1± 3.4	0.48
MCHC, g/dL	33.04± 1.72	35.9± 1.3	0.001*	31.4± 2.2	30.7± 2.7	0.15
MCV, *f*L	82.5± 4.2	84.1± 3.9	0.001*	80.1± 3.06	80.3± 2.3	0.80
PLT, ×10^3/mL	254± 620	235± 814	0.300	239± 110	244± 68	0.90
RBC, ×10^{12}/L	4.2± 0.78	4.7± 0.88	0.001*	4.13± 0.49	4.41± 0.58	0.48
WBC, ×10^3/mm^3	6.3± 1565	6.2± 1.3	0.060	6.3± 0.8	6.0± 0.6	0.10

*The parameters that had a significant difference between the two groups.
AT: After treatment with levothyroxine; BT: Before treatment with levothyroxine; Hb: Hemoglobin; HCT: Hematocrit; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; MCV: Mean corpuscular volume; PLT: Platelet; RBC: Red blood cells; WBC: White blood cells.

Table- 3. Hematological parameters in the patient who had a good or poor response to levothyroxine administration

Blood parameters	Mean ± SD after treatment in patients with		*p* value
	Good response (n = 64)	Poor response (n = 6)	
Hb, g/dL	13.4 ± 1.1	11.3 ± 1.13	0.030*
HCT, %	37.7 ± 4.5	34.9 ± 2.7	0.040*
MCH, pg	28.5 ± 2,9	24.1 ± 3.4	0.001*
MCHC, g/dL	35.9 ± 1.3	30.7 ± 2.7	0.003*
MCV, *f*L	84.1 ± 3.9	80.3 ± 2.3	0.020*
PLT, x10^3/mL	235 ± 814	244 ± 68	0.700
RBC, x10^{12}/L	4.7 ± 0.88	4.41 ± 0.58	0.400
WBC, x10^3/mm^3	6.2 ± 1.3	6.0 ± 0.6	0.650

*, the parameters that had a significant difference between the two groups.
Hb: Hemoglobin; HCT: Hematocrit; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; MCV: Mean corpuscular volume; PLT: Platelet; RBC: Red blood cells; WBC: White blood cells.

Autoimmune reactions are the most common causes of hypothyroidisms than non-autoimmune type and it has been shown that the increased frequency of chronic anemia in patients with autoimmune thyroid disease (ATD) can be caused by concurrent autoimmune gastrointestinal diseases.(13)
This study aimed to assess the prevalence of anemia associated with hypothyroidism and the effect of current hypothyroidism treatment in reducing frequency of anemia in Iranian population, which can provide further insight to better understanding of disease management and epidemiology.

Materials & Methods
Patients: In a clinical trial, 70 patients with clinical and laboratory signs of hypothyroidism admitted in Endocrine clinic of Rasul Akram Hospital from March 2006 to March 2009 were selected. Patients with a normal range of ferritin, vitamin B12 and reticulocyte count that had no known diseases and

did not take drugs affecting hematopoiesis and thyroid functions were considered eligible for this study. The levels of TSH, T3, T4 were measured to determined the hypothyroidism. Blood parameters, including red blood cells (RBC) and white blood cells (WBC) count, hemoglobin (Hb) concentration, mean corpuscular hemoglobin concentration (MCHC), mean corpuscular haemoglobin (MCH) and mean corpuscular volume (MCV), platelets (PLT), hematocrit (HCT), levels were measured, peripheral blood morphology and reticular cell count, including platelets (PLT), hematocrit (HCT), hemoglobin were assessed before and 3 months after treatment with levothyroxine. Other common causes of anemia, including iron deficiency and megaloblastic anemia were ruled out.

On the basis of hematological criteria, patients were categorised into non-anemic patients, patient with macrocytic anemia, patients with normochromic-normocytic anemia, and patients with hypochromic-

mictocystic anemia, as described previously.(14) This study was approved by institutional ethics committee and the patient's information was kept confidential.

Protocol of treatment of hypothyroidism: Levothyroxine was administrated according to protocol described previously.(15, 16)

Statistical analysis: Quantitative variables were statistically analysed using independent *t*-test and Mann-Whitney *U* test, and qualitative variables were statistically analysed using Chi-square test and Fisher test (SPSS version 16) and differences with *p*-values less than 0.05 were considered significant. Data are expressed as mean ± standard deviation (SD).

Results

In this study, blood parameters of 70 patients with hypothyroidism were investigated. The mean age of patients was 45.3 ± 13.7 years and varied between 18 to 75 years. Fifty-six out of 70 patients (80%) were women and 14 were male (20%). Thirty-two out of 56 women (57.14%) and 11 out of 14 men (78.5%) were anemic with a total prevalence rate of 61.4%. The Hb level for defining the anemia in female and male were < 12 g/dl and < 13 g/dl, respectively. Anemia was morphologically classified and the frequency of microcytic, normocytic and macrocytic anemia for each male and female patient was determined (Table- 1).

Three months after levothyroxine administration, 64 patients (91.4%) showed a decrease in TSH level (less than 2.5 IU/ml) and 6 patients (8.6%) did not (TSH ≥ 2.5 IU/ml). In the group with good response to treatment, most of the blood parameters, including MCV, Hb, HCT, MCH, MCHC, RBC, were significantly increased to a normal range, but no change was seen in WBC and PLT values. No significant increase was observed in the group with poor response to the treatment after 3 months. The levels of blood parameters in both groups who had a good or poor response to treatment are listed in Table- 2. The significant differences between the levels of blood parameters between two groups after 3 months are also summarised in Table- 3.

Discussion

The anemia in patients with hypothyroidism varies between 20 and 65 % (9, 17) and in this current study it was found to be 61.4% (43 out of 70), indicating a high correlation between hypothyroidism and anemia in Iran.

While little is known about the frequency of hypothyroidism and its associated symptoms, including anemia, endemic goiter, hypothyroidism, cretinism, decreased fertility rate, increased infant mortality and mental retardation , there are a body of evidences showing a dramatic decrease in hypothyroidism incidence in Iran following adopting universal salt iodization strategies and iodine deficiency disorders (IDD) prevention over two decades, and meeting WHO/UNICEF/ICCIDD criteria for the sustainable elimination of iodine deficiency since 1996.(18) In a cross-sectional survey from January 2006 through April 2006 in Isfahan, Iran, the overall prevalence of hypothyroidism was 4.8 in men and 12.8% in women. Over 37% of patients had positive anti-thyroperoxidase and/or anti-thyroglobulin antibodies and only 19.3% were euthyroid, suggesting an autoimmune-derived hypothyroidism, with no correlation to iodine intake.(19)

The results from the current study showed that 64 out of 70 patients (91.4%) had a significant improvement in mean values of MCV, HCT, Hb, MCHC and MCH after treatment with levothyroxine (TSH less than 2.5 IU/ml, p<0.001). Similar results were shown by another study (17), investigating the effect of treatment of hypothyroidism on the frequency of anemia.

In the current study, 85.7% of women were anemic, compared to 14.3% in men. The greater percentage of anemia in women with hypothyroidism may be linked to menorrhagia, as it proposed previously.(9)

It has been shown that in concurrent hypocoaglupathies, hypothyroidism is associated with increased risk of bleeding and hematologic parameters, including MCH, MCV, MCHC, HCT and Hb significantly improve in patients with significant response to levothyroxine, compared to patients who had poor response to the treatment, suggesting that standard administration of levothyroxine is able to reduce TSH level and improve concurrent anemia.(12)

Autoimmune hypothyroidism is the most common organ-specific autoimmune disorder. The prevalence of hypothyroidism with autoimmune etiology is not known in Iran. Besides to the primary tests for TSH, T3, and T4 levels to diagnose hypothyroidism, it might be helpful to confirm autoimmune-derived hypothyroidism by examining for thyroid antibodies.

In conclusion, this study showed that hypothyroidism is highly associated with anemia, especially in women, and proper treatment of hypothyroidism can obviate treatment of concurrent

anemia, with an emphasis on using more efficient therapeutic replacements or options for those patients who had a poor response to the levothyroxine therapy.

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