

Research Article

Idiopathic Hypogonadotropic Hypogonadism: Erythrocyte Indices in Naive Male Patients

 Zafer Pekkolay

Department of Adult Endocrinology and Metabolism, Dicle University Faculty of Medicine, Diyarbakir, Turkey

Abstract

Objectives: The aim of this study was to determine the erythrocyte indices in patients with naive male idiopathic hypogonadotropic hypogonadism.

Methods: In our retrospective cross-sectional study, patients who were admitted to the university hospital adult endocrinology outpatient clinic naive male idiopathic hypogonadotropic hypogonadism between 1 January 2010 and 30 September 2018 were included. The patient group consisted of naive male patients diagnosed as hypogonadotropic hypogonadism who had no anatomic or functional hypothalamo-hypophyseal disease between the ages of 18-40. Healthy men in the same age range were taken as control group. In patients with naive idiopathic hypogonadotropic hypogonadism, LH, FSH and Testosterone values in serum were measured. All patients erythrocyte indices (Hb, Htc, MCV, RDW) and platelets were measured. Student's t test was used to compare groups.

Results: The study included 145 male patients (78 patients and 67 control group). There was no difference in age between the groups ($p > 0.05$). Hb levels, Htc levels and MCV levels of the patient group were lower and statistically significant than the control group. Respectively ($p < 0.01$), ($p < 0.05$), ($p < 0.01$). RDW levels and platelet levels of the patient group were higher and statistically more significant than the control group. Respectively ($p < 0.001$), ($p < 0.01$).

Conclusion: Erythrocyte indices may predict anemia in patients with naive idiopathic hypogonadotropic hypogonadism. In men with reproductive period, androgen deficiency should be considered in the differential diagnosis in anemia etiology. Recovery is expected after androgen replacement.

Keywords: Idiopathic hypogonadotropic hypogonadism, male, erythrocyte indices

Cite This Article: Pekkolay Z. Idiopathic Hypogonadotropic Hypogonadism: Erythrocyte Indices in Naive Male Patients. EJMI 2019;3(1):74–76.

Idiopathic hypogonadotropic hypogonadism (IHH) is characterized by inappropriate gonadotropin and sex steroid levels in the absence of delayed or absent sexual development disorder in the absence of anatomical or functional abnormalities of the hypothalamus-pituitary-gonadal axis. The main underlying cause is the inability, inadequate release, or ineffectiveness of gonadotropin-releasing hormone (GnRH), which is an important hormone for puberty and fertility in humans. Gonadotropin (LH, FSH) deficiency negatively affects gonadal maturation. Other anterior pituitary hormones are normal. It is observed 3-5

times more frequently in males than females. The diagnosis is Kallmann's syndrome if the disease is accompanied by the absence or lack of smell. Most patients are diagnosed in adolescence or in young adulthood.^[1, 2]

Testosterone is a hormone that is critical to the development of the male reproductive system and the maintain sexual functions. It also has important roles in muscle-bone health, body composition and erythropoiesis. LH deficiency in IHH leads to testosterone deficiency. Excessive testosterone treatment in patients with hypogonadism leads to erythrocytosis. This situation is more common in

Address for correspondence: Zafer Pekkolay, Asist. Prof. Dicle Universitesi Tip Fakultesi, Eriskin Endokrinoloji ve Metabolizma Bilim Dalı, Diyarbakir, Turkey

Phone: +90 412 248 80 01 **E-mail:** drpekkolay@gmail.com

Submitted Date: November 24, 2018 **Accepted Date:** December 29, 2018 **Available Online Date:** January 18, 2019

©Copyright 2019 by Eurasian Journal of Medicine and Investigation - Available online at www.ejmi.org



elderly patients than in young people.^[3-5]

Androgens increase erythropoiesis with several mechanisms. Increases erythropoietin release, activates erythroid precursors in the bone marrow, facilitates the entry of iron into erythrocyte, enhances hemoglobin synthesis.^[6]

Testosterone suppresses hepcidin, an important hormone in iron regulation. Thus, iron transport becomes easier. Hemoglobin production increases in erythrocytes.^[7]

We did not find any study on erythrocyte indices in patients with naive male idiopathic hypogonadism.

In patients with testosterone deficiency, expected erythrocyte markers are adversely affected.

The aim of this study was to determine erythrocyte indices in patients with naive male idiopathic hypogonadotropic hypogonadism.

Methods

In our retrospective cross-sectional study, patients who were admitted to the university hospital adult endocrinology out-patient clinic with symptoms of hypogonadism between 1 January 2010 and 30 September 2018 were included.

The study group consisted of naive male patients diagnosed as hypogonadotropic hypogonadism who had no anatomic or functional hypothalamohypophyseal disease between the ages of 18-40. Healthy men in the same age range were taken as control group.

Female patients, patients with primary hypogonadism, patients with hemochromatosis, those with systemic disease and other pituitary hormone deficiency were excluded from the study.

The files of all subjects included in the study were evaluated retrospectively.

Erythrocyte indices (Hb, Htc, MCV, RDW) and platelets were measured by an automated hematology analyzer (Abbott Cell-Dyn Ruby).

In patients with idiopathic hypogonadotropic hypogonadism LH, FSH and Testosterone values in serum were measured by Roche-cobas 6001 device by electrochemiluminescence method.

Statistical analyses were performed using the SPSS software version 22. The variables were investigated using visual and analytical methods to determine whether or not they are normally distributed. Descriptive analyses were presented using means and standard deviations for normally distributed variables. Since the values were normally distributed; Student's t test was used to compare groups. A p value of less than 0.05 was considered to show a statistically significant result.

Results

The study included 145 male patients (78 patients and 67 control group). The mean age in the patient group was 25.98±6.26 (18-40) years and the mean age in the control group was 26.11±6.54 (18-40) years. There was no difference in age between the groups (p>0.05).

Hormonal profile in the patient group LH (0.36±0.25) (0.1-1.96) mIU/ml FSH (0.64±0.44) (0.1-1.81) mIU/ml Testosterone (0.36±0.32) (0.2-1.91) ng/ml (Table 1).

Hb levels, Htc levels and MCV levels of the patient group were lower and statistically significant than the control group. Respectively (p<0.01), (p<0.05), (p<0.01) (Table 2).

RDW levels and platelet levels of the patient group were higher and statistically more significant than the control group. Respectively (p<0.001) (p<0.01) (Table 2).

Discussion

In this study, we found that erythrocyte indices hemoglobin, hematocrit and mean corpuscular volume (MCV) were lower in patients with idiopathic hypogonadotropic hypogonadism compared to the control group. We also found that red cell distribution width (RDW) and platelet levels were higher and statistically significant in the patient group. These findings indicate that androgen deficiency leads to anemia due to mechanisms such as lack of stimulation in erythroid series, erythropoietin deficiency and inability to use iron. The platelet count in the patient group was higher and statistically significant than the control group. This finding indicates that increase in thrombocyte count secondary to anemia.

Red blood cell distribution width (RDW) is a measure of the variation of erythrocyte size. RDW increases when there is a size difference (anisocytosis). RDW increases in iron deficiency anemia.^[8] In androgen deficiency, the use of iron is

Table 1. Patient group hormonal profile

	Mean±SD (min-max)
LH (1.7-8.6)mIU/ml	0.36±0.25 (0.1-1.96)
FSH (1.5-12.4) mIU/ml	0.64±0.44 (0.1-1.81)
Testosteron (2.18-9.05) ng/ml	0.36±0.32 (0.2-1.91)

Table 2. Erythrocyte indices and platelet

	Patient group	Control group	p
Hb	14.53±1.38	15.70±0.99	<0.01
Htc	42.65±3.79	43.97±2.74	<0.05
MCV	81.90±3.87	84.97±4.87	<0.01
RDW	13.53±1.76	10.97±0.78	<0.001
Platelet	254404.22±41854.55	222185.71±51714.38	<0.01

adversely affected and RDW increases. In our study, RDW was higher in our patient group due to androgen deficiency.

Testosterone is the main androgen in men. Testosterone directly stimulates bone marrow with dehydrotestosterone form, suppresses hepcidin, accelerates iron turnover, changes erythropoietin setpoint.^[9-11]

Paustian et al.^[12] found that significant improvement in erythropoiesis in studies of androgen use in fanconi anemia.

Roy et al.^[13] found that testosterone treatment significantly increased hemoglobin levels compared to placebo in patients with unexplained anemia in older men.

Hicks et al.^[14] found that ,in a study involving more than thirty thousand patients, anemia in patients with prostate cancer with androgen deprivation 3 times more frequently than patients who did not receive this treatment. After discontinuation of this treatment, the anemia was reversed. This study clearly describes the relationship between androgen deficiency and anemia.

Retrospective analysis and the limited number of patients are the limitations of the study.

Conclusion

In conclusion, erythrocyte indices may predict anemia in patients with naive idiopathic hypogonadotropic hypogonadism. In men with reproductive period, androgen deficiency should be considered in the differential diagnosis in anemia etiology. Recovery is expected after androgen replacement.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The author declares that there is no conflict of interest.

References

- Boehm U, Bouloux PM, Dattani MT, de Roux N, Dodé C, Dunkel L, et al. Consensus document: European Consensus Statement on congenital hypogonadotropic hypogonadism-pathogenesis, diagnosis and treatment. *Nat Rev Endocrinol* 2015;11:547–64. [\[CrossRef\]](#)
- Bianco SD, Kaiser UB. The genetic and molecular basis of idiopathic hypogonadotropic hypogonadism. *Nat Rev Endocrinol* 2009;569–76. [\[CrossRef\]](#)
- Coviello AD, Kaplan B, Lakshman KM, Chen T, Singh AB, et al. Effects of graded doses of testosterone on erythropoiesis in healthy young and older men. *J Clin Endocrinol Metab* 2008;93:914–9. [\[CrossRef\]](#)
- Bhasin S, Brito JP, Cunningham GR, Hayes FJ, Hodis HN, Matsumoto AM, et al. Testosterone Therapy in Men With Hypogonadism: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2018;103:1715–44. [\[CrossRef\]](#)
- Haddad RM, Kennedy CC, Caples SM, Tracz MJ, Boloña ER, Sideras K, et al. Testosterone and cardiovascular risk in men: a systematic review and meta-analysis of randomized placebo-controlled trials. *Mayo Clin Proc* 2007;82:29–39. [\[CrossRef\]](#)
- Shahani S, Braga-Basaria M, Maggio M, Basaria S. Androgens and erythropoiesis: past and present. *J Endocrinol Invest* 2009;32:704–16. [\[CrossRef\]](#)
- Guo W, Bachman E, Li M, et al. Testosterone administration inhibits hepcidin transcription and is associated with increased iron incorporation into red blood cells. *Aging Cell* 2013;12:280–91. [\[CrossRef\]](#)
- Andrews NC. Disorders of iron metabolism. *N Engl J Med* 1999;23;341:1986–95. [\[CrossRef\]](#)
- Ohlander SJ, Varghese B, Pastuszak AW. Erythrocytosis Following Testosterone Therapy. *Sex Med Rev* 2018;6:77–85. [\[CrossRef\]](#)
- Bachman E, Travison TG, Basaria S, Davda MN, Guo W, Li M, et al. Testosterone induces erythrocytosis via increased erythropoietin and suppressed hepcidin: evidence for a new erythropoietin/hemoglobin set point. *J Gerontol A Biol Sci Med Sci* 2014;69:725–35. [\[CrossRef\]](#)
- Lenzi A, Balercia G, Bellastella A, Colao A, Fabbri A, Foresta C, et al. Epidemiology, diagnosis, and treatment of male hypogonadotropic hypogonadism. *J Endocrinol Invest* 2009;32:934–8. [\[CrossRef\]](#)
- Paustian L, Chao MM, Hanenberg H, Schindler D, Neitzel H, Kratz CP, Ebell W. Androgen therapy in Fanconi anemia: A retrospective analysis of 30 years in Germany. *Pediatr Hematol Oncol* 2016;33:5–12. [\[CrossRef\]](#)
- Roy CN, Snyder PJ, Stephens-Shields AJ, Artz AS, Bhasin S, Cohen HJ, et al. Association of Testosterone Levels With Anemia in Older Men: A Controlled Clinical Trial. *JAMA Intern Med* 2017;177:480–90. [\[CrossRef\]](#)
- Hicks BM, Klii-Drori AJ, Yin H, Campeau L, Azoulay L. Androgen Deprivation Therapy and the Risk of Anemia in Men with Prostate Cancer. *Epidemiology* 2017;28:712–8. [\[CrossRef\]](#)