

Evaluation Inhibin B, FSH, and LH in Male with Thalassemia

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Abstract

Background : - Hypogonadism is the most frequently reported endocrine problem, affecting 70–80% of patients with thalassemia. **Aim of study:** -The current study is aimed to found correlation among inhibin-B, FSH, LH and testosterone in male with thalassemia. **Material and Subject:** The study carried out 40 healthy volunteer male, age range between (18-30) years, and enrolled 40 patients with thalassemia major age range between 18-30 years. The concentrations serum inhibin-B was estimated by two-side enzyme-linked immunosorbent assays (ELISA), While FSH, and LH estimated by using Cobas e analyzers. **Results:** LH reduce significantly in thalassemia patients when compared with healthy individuals, while FSH and testosterone decrease significantly in thalassemia patients when compared with healthy. Inhibin B was reduced significantly in thalassemia patients when compared with healthy individuals. **Conclusion:** Infertility common in thalassemia patients, that correlation with decrease inhibin B.

Key Words: -Inhibin B, FSH, LH and thalassemia

Introduction

Beta-thalassemia is 'a genetic blood disorder characterized by absent or β globin chains synthesis, resulting in decrease hemoglobin in red blood cells, reduced RBCs production and anemia^[1].

The direct effect is an imbalance of the α and β globin chain synthesis that results in anemia from ineffective erythropoiesis and hemolysis^[2].

The severity and prevalence of hypogonadism in thalassemia major differs among studies, dependent on the genotype of thalassemia and age group studied^[3] ^[4]^[5]^[6]^[7]. Dysfunction of the sexual and infertility due to hypogonadism are well-recognized disorders of the hypothalamic pituitary gonadal axis^[8].

Hypogonadism is the most frequently reported endocrine problem, affecting 70–80% of patients with thalassemia. Luteinizing hormone (LH) and Follicle stimulating hormone (FSH) are involved in the regulation and activation of the reproductive axis. Hormones produced via the gonads control LH and FSH synthesis and excretion in a feedback loop ^[9]. Inhibin-B exhibit a physiological role in the feedback regulate of FSH secretion, and reflects FSH-stimulated Sertoli cell to be the function^[10]. Testicular functions can be evaluated via the basal hormonal FSH and LH^[3].

Inhibin's are presently predictable as paracrine testicular controllers and have many paracrine effects representing a promising marker for infertility in male^[11].

Aim of study: -The current study is aimed to found correlation among inhibin-B, FSH, LH and testosterone in male with thalassemia.

Patients and Method

The study carried out 40 healthy volunteer male, age range between 18-30 years, and enrolled 40 patients with thalassemia major age range between 18-30 years. All patients received blood transfusion every 4–5 weeks.

The concentrations inhibin-B was estimated via two-side enzyme-linked immunosorbent assays (ELISA), While FSH, and LH estimated by using Cobas e analyzers.

All data are stated as mean \pm standard error. The comparisons among groups were completed via using t test.

The relationship between inhibin B, testosterone, FSH, and LH were determined using a Pearson correlation coefficient. P less 0.05 was measured significant. The SPSS software for windows, version 20 were achieved to all analyses.

Findings

Table 1 illustrated fertility parameters and inhibin B in male with thalassemia, the result showed LH within normal range (1.7-8.6mIU/ml) in thalassemia patients (3.37±0.62 mIU/ml) but reduce significantly when compared with healthy individuals (8.60±0.26 mIU/ml) $p < 0.000$, while FSH and testosterone decrease than the normal range (0.5-4.3 ml/mL, and 3-10 ng/mL)

respectively in thalassemia patients (3.07±0.31mIU/mL, and 2.20±0.28ng/mL) respectively, as well as decrease significantly when compared with healthy individuals (6.52±0.34mIU/ml, and 7.08±0.29ng/mL) respectively $p < 0.000$. Inhibin B was within the normal rang (25-325pg/mL) in thalassemia patients (45.61±4.69pg/mL), and also reduce significantly when compared with healthy individuals (102.14±3.10/mL) respectively $p < 0.000$.

Table:1 Inhibin B, Testosterone, FSH, and LH

Parameters	Normal range	Healthy Individuals (N=30)M±SE	Thalassemia Patients (N=60)M±SE	T-test P value
Inhibin B	25-325pg/mL	102.14±3.10	45.61±4.69	<0.000
Testosterone	3-10ng/mL	7.08±0.29	2.20±0.28	<0.000
FSH	0.5-4.3mIU/mL	6.52±0.34	3.07±0.31	<0.000
LH	1.7-8.6 mIU/mL	8.60± 0.26	3.37± 0.62	<0.000

M Mean, SE Stander error, LH Luteinizing Hormone, FSF Follicular Stimulating Hormone

Table illustrated relationship among the changes in inhibin B with testosterone, FSH and LH, The mean inhibin-B was significantly positive correlation with mean testosterone, FSH and LH ($r=0.497$, $p=0.001$, $r=0.333$, $p=0.036$), and ($r=0.447$, $p=0.004$) respectively in thalassemia patients Table (2).

Table: 2 Correlation among Inhibin B, Testosterone, FSH, and LH

Inhibin B		
Parameters	Pearson Correlation	P-value
Testosterone	0.497	0.001
FSH	0.333	0.036
LH	0.447	0.004

Discussion

Physiological inhibin-B production via the adult testis needs a normal population of Sertoli cells, Spermatogenesis and FSH stimulation, to be existing and it displays an significant role in feedback hormone regulation between the gonads and the pituitary gland^{[12][11]}. Current results show a significant positive

correlation among inhibin-B, FSH and LH in male with thalassemia. Bergada *et al.* 2002 report a significant positive correlation of men inhibin-B with men LH^[13]. These results then funding the inhibin-B has a role in the physiological regulation of LH and FSH excretion in male and inhibin-B is the testicular feedback signal for FSH^[14]. Testosterone and inhibin-B

and originate from different forms of cells in the testis [15]. In our results we found positive correlation among inhibin-B and testosterone concentrations. that inhibin excretion from Sertoli cells is controlled via interaction with germ cells and expression of α - and β -subunit mRNA is maximal at stages of spermatogenesis which are greatly sensitive to FSH [16][17][18]. The mean values of inhibin B, LH, FSH and testosterone, in this study, there was highly significant decrease in thalassemia patients when compared with healthy individuals. An earlier study displayed that histological investigation of the testicular tissue in patients with thalassemia proved variable degrees of fibrosis in testicular interstitial with small deeply pigmented undifferentiated seminiferous tubules, hyalinized, and an absence of Leydig cells [19]. Because of developments in the current medical care systems, males with β -thalassemia major who receive life-long blood transfusions now live longer. Therefore, the fertility and reproductive endocrinology requirements for such men are becoming more significant. The results of this study showed a significant decrease in the level of pituitary and testicular hormones, and this may afford additional strong evidence to suggest that iron overload is at high risk of being related with reduced function of gonad [20].

Serum Inhibin concentration have been stated useful to evaluate testicular function in many conditions [21]. In this study, they were lower than the healthy controls. This suggested that Sertoli cell function is abnormal in thalassemia patients and regular blood transfusions [22].

Serum testosterone levels, FSH and LH in patients with major were different significantly when compared with healthy controls suggested that the hypothalamic-pituitary-gonadal axis is defect. In addition, serum testosterone levels in thalassemia patients were lesser than in controls. This suggested that testicular function is weakened [23]. Other causes of these abnormalities may be related to the catabolic iron catalyzes the production of free radicals, resulting in oxidative stress in lipid membranes, lysosomes, mitochondria, DNA, proteins. This is maybe induced oxidative stress and direct effect in many organs, like, pituitary gland, hypothalamus, and female reproductive organs, other organs indirectly effected such as, pancreas and liver, and this will be contributing to the impaired the processes of metabolism of serum antioxidants and hormones [24]. Oxidative stress modulates the age-related decline the infertility in patients suffer from β -thalassemia [25].

Conclusion

Infertility common in thalassemia patients, that correlation with decrease inhibin B.

Conflict of Interest: Non

Source of Findings: Self findings.

Ethical Clearance: Non

References

- [1] M. Asif *et al.*, "Correlation between serum ferritin level and liver function tests in thalassemic patients receiving multiple blood transfusions, *Int J Res Med Sci.* 2014; vol. 2, no. 3, pp. 988–994.
- [2] S. Srisukh, B. Ongphiphadhanakul, and P. Bunnag, "Hypogonadism in thalassemia major patients," *J. Clin. Transl. Endocrinol.*, 2016; vol. 5, pp. 42–45.
- [3] S. Siripunthana, T. Sahakitrungruang, S. Wacharasindhu, D. Sosothikul, and V. Supornsilchai, "Testicular function in patients with regular blood transfusion for thalassemia major," *Asian Biomed.*, 2015; vol. 9, no. 2, pp. 185–191.
- [4] J. P. S. Chern *et al.*, "Hypogonadotropic hypogonadism and hematologic phenotype in patients with transfusion-dependent beta-thalassemia," *J. Pediatr. Hematol. Oncol.*, 2003; vol. 25, no. 11, pp. 880–884.
- [5] M. Delvecchio and L. Cavallo, "Growth and endocrine function in thalassemia major in childhood and adolescence," *J. Endocrinol. Invest.* 2010; vol. 33, no. 1, pp. 61–68.
- [6] V. De Sanctis *et al.*, "Growth and endocrine disorders in thalassemia: The international network on endocrine complications in thalassemia (I-CET) position statement and guidelines," *Indian J. Endocrinol. Metab.*, 2013; vol. 17, no. 1, p. 8.
- [7] N. Skordis *et al.*, "The impact of genotype on endocrine complications in thalassaemia major," *Eur. J. Haematol.*, vol. 2006; 77, no. 2, pp. 150–156.
- [8] P. Roussou, N. J. Tsagarakis, D. Kountouras, S. Livadas, and E. Diamanti-Kandarakis, "Beta-thalassemia major and female fertility: the role of iron and iron-induced oxidative stress," *Anemia*, 2013; vol. 2013.
- [9] M. Chada, R. Prusa, J. Bronsky, M. Pechova, and L. Lisa, "Inhibin B, follicle stimulating hormone,

- luteinizing hormone, and estradiol and their relationship to the regulation of follicle development in girls during childhood and puberty,” *Physiol. Res.*, 2003;vol. 52, no. 3, pp. 341–346.
- [10] R. A. Anderson, E. M. Wallace, N. P. Groome, A. J. Bellis, and F. C. Wu, “Physiological relationships between inhibin B, follicle stimulating hormone secretion and spermatogenesis in normal men and response to gonadotrophin suppression by exogenous testosterone.,” *Hum. Reprod.*, 1997;vol. 12, no. 4, pp. 746–751.
- [11] S. Luisi, P. Florio, F. M. Reis, and F. Petraglia, “Inhibins in female and male reproductive physiology: role in gametogenesis, conception, implantation and early pregnancy,” *Hum. Reprod. Update*, 2005;vol. 11, no. 2, pp. 123–135.
- [12] M. Chada *et al.*, “Inhibin B, follicle stimulating hormone, luteinizing hormone and testosterone during childhood and puberty in males: changes in serum concentrations in relation to age and stage of puberty,” *Physiol. Res.*, 2003;vol. 52, no. 1, pp. 45–52.
- [13] I. Bergadá, G. M. Ballerini, S. Ayuso, N. P. Groome, C. Bergadá, and S. Campo, “High serum concentrations of dimeric inhibins A and B in normal newborn girls,” *Fertil. Steril.*, 2002; vol. 77, no. 2, pp. 363–365.
- [14] M. L. Uhler, M. J. Zinaman, C. C. Brown, and E. D. Clegg, “Relationship between sperm characteristics and hormonal parameters in normal couples,” *Fertil. Steril.*, 2003; vol. 79, pp. 1535–1542.
- [15] P. Kumanov, K. Nandipati, A. Tomova, and A. Agarwal, “Inhibin B is a better marker of spermatogenesis than other hormones in the evaluation of male factor infertility,” *Fertil. Steril.*, 2006; vol. 86, no. 2, pp. 332–338.
- [16] C. Pineau, R. M. Sharpe, P. T. K. Saunders, N. Gerard, and B. Jegou, “Regulation of Sertoli cell inhibin production and of inhibin α -subunit mRNA levels by specific germ cell types,” *Mol. Cell. Endocrinol.*, 1990;vol. 72, no. 1, pp. 13–22.
- [17] S. Carreau, “Human Sertoli cells produce inhibin in vitro: an additional marker to assess the seminiferous epithelium development,” *Hum. Reprod.*, 1995;vol. 10, no. 8, pp. 1947–1949.
- [18] S. Bhasin *et al.*, “Stage dependent expression of inhibin α and β -B subunits during the cycle of the rat seminiferous epithelium,” *Endocrinology*, 1989;vol. 124, no. 2, pp. 987–991.
- [19] V. C. Canale, P. Steinherz, M. New, and M. Erlandson, “Endocrine function in thalassemia major,” *Ann. N. Y. Acad. Sci.*, 1974;vol. 232, no. 1, pp. 333–345.
- [20] Papadimas J, Mandala E, Pados G, Kokkas B, Georgiadis G, Tarlatzis B. Pituitary–testicular axis in men with β -thalassaemia major. *Hum Reprod.* 1996; 11:1900-4.
- [21] Bronsiegel-Weintrob N, Olivieri NF, Tyler B, Andrews DF, Freedman MH, Holland FJ. Effect of age at the start of iron chelation therapy on gonadal function in β -thalassemia major. *N Engl J Med.* 1990; 323:713-9.
- [22] Jensen CE, Tuck SM, Old J, Morris RW, Yardumian A, De Sanctis V, *et al.* Incidence of endocrine complications and clinical disease severity related to genotype analysis and iron overload in patients with beta-thalassaemia. *Eur J Haematol.* 1997; 59:76-81.
- [23] Kew, M.C. “Hepatic iron overload and hepatocellular carcinoma,” *Cancer Letters*, 2009;vol. 286, no. 1, pp. 38–43,
- [25] Al-Gubory, K.H., Garrel, C., Faure, P. and Sugino, N. Roles of antioxidant enzymes in corpus luteum rescue from reactive oxygen species-induced oxidative stress, *Reproductive Biomedicine Online*, 2012; vol. 25, no. 6, pp. 551–560,
- [26] Appasamy, M., Jauniaux, E., Serhal, P., Al-Qahtani, A., Groome, N.P. and Muttukrishna, S. Evaluation of the relationship between follicular fluid oxidative stress, ovarian hormones, and response to gonadotropin stimulation,” *Fertility and Sterility*, 2008;vol. 89, no. 4, pp. 912– 921.