International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Impact Factor (2012): 3.358

Do Patients With Thalassaemia Major Manifest Endocrine Complications? Can We Solve Them?

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Abstract: ***It is estimated that endocrine abnormalities are present in thalasaemic patients. Despite the early diagnosis and the optimal iron chelation therapy, there are still important in many clinical situations like: delayed sexual maturation and impaired fertility. The aim of the study was to assess the correlation of ferritin level and growth and sexual hormones of organism in inidividuals with thalassaemia. A statistically negative correlation was found between ferritin level at the end of third year of treatment with Deferasirox and testosterone, (r=-0.6 p<0.01). High levels of Ferritin are associatted with low levels of estradiol (E2) (r=-0,68; p<0.001) and low levels of luteal hormone (r=-0.47 p<0.01). Patients with haemoglobinopathies and particularly with thalassaemia major, suffer form iron overload in their organism, due to transfusions, but at the same time as a result of increased intestinal absorption.***

Keywords: thalassaemia, iron, deferasirox, delayed puberty, hypogonadism

1. Introduction

Thalassaemia and other hameoglobinopathies are very often associatted with endocrine disorders. Despite the early diagnosis and the optimal iron chelation therapy, there are still important in many clinical situations like: delayed sexual maturation and impaired fertility (1,2). It is not so easy to estimate the prevalence of endocrine complications, due to the differencies in the age of starting iron chelation and at the same time continuous improvement of life expectancy at the patients compliant to iron chelation (3,4). *Delayed puberty and hypogonadism.* Delayed puberty and hypogonadism are the most frequent clinical consequences of iron overload. Delayed puberty is estimated as a complete absence of puberal development in girls at age 13 and in boys at age 14 years. Hypogonadism is estimated at boys as abscence of a complete development of testicules enlargement (less than 4 ml) and at girls as absence of breast development at age 16 (5). Delayed puberty is a common complication seen at patients with moderate to severe iron overload and is characterized by the lack of puberal progression for one year or more. In these cases the capacity of testicules remain 6-8ml, and breast dimension at stage B3. In such cases the annual velocity of growth is stopped (6,7). The majority of girls with Thalassaemia Major have primary amenorrhea, with secondary amenorrhea developed later, especially in patients with no optimal iron chelation. The ovarial function in such cases is generally normal, but the gonadotropinic response towards releasing factor of Gonadotropins is lower as compared to normal menstrual cycles (8). The treatment of delayed or stopped puberty and hypogonadotrophic hypogonadism depends on several factors like age, the severity of iron overload, dysfunction of hypothalamic –pituitary axis, chronic hepatic diseases, and at the same time it is connected to psychologic problems which result from hypogonadism. The aim of the study was to assess the correlation of ferritin level and growth and sexual hormones of organism in inidividuals with thalassaemia.

2. Material and Methods

This is a descriptive including 46 young boys and girls with thalassemia admitted to the pediatric hospital of a tertiary hospital during the year 2013. Allchidren underwent detailed hematological, biochemical and hormonological examination. Pearson correlation and simple linear regression ws used to assess the relationship of ferritin levels with sexual hormones. A p-value ≤0.05 was considered statistically significant.

3. Results and Discussion

Patients with thalassaemia major were in regular transfuzional treatment and iron chelation therapy (oral therapy). Ferritin level is the main biochemical marker, through which iron overload in organism is evaluated. We didn't notice any significant difference at females and males above18 years of age, between ferritin level at the end of the firts year compared to the end of third year of treatment (table 1). A significant negative correlation was found between ferritin level at the end of third year of treatment and testosteron level in boys (r=-0.6 p<0.01) and also estradiol level in girls (r=-0.68 p<0.001). For an increase of ferritin level with 1 unit, estradiol level decreases with 0.1 unit (fig. 1). The same argument applies for the evaluation of folicular stimulant hormone which was measured in girls. A significant negative correlation was found between ferritin level and folicular-stimulating hormone (FSH) (r=-0.65 p<0.001) and lutein hormon (r=-0.47 p<0.01) at the third year of treatment, (fig. 2 and 3). Patients with haemoglobinopathies and particularly thalassaemia major, can develop iron overload in their organism, due to regular transfusions and increased intestinal iron absorption. This

situation can cause organ damages, increased morbidity such as cardiac disfunction, hepatic dysfunction, endocrine dysfunction and death in absence of treatment) and mortality. Oral iron chelation with Deferasirox (like Deferrioxamina used at initation) has the goal to minimize the morbidity and mortality form iron overload, preventing iron accumulation in the organs. Hormonal changes are very important and play a crucial role in politransfused patients with heamoglobinopathies. Iron overload in organism cause endocrine dysfunction and as a consequence we can observe alteration of hormonal values in organism. A recent review in a group of thalassaemic patients showed that 41% of patients manifested at least one endocrine complication connected to the underlying disease (9). The same endocrine complications have been shown in patients with sickle cell disease (10). Many endocrine complications are caused as a result of pituitary dysfunction. For example, hypogonadotrophic hypogonadism (decreased secretion of luteinizing hormone and folicular-stimulating hormone) is a common complication of iron overload at young thalassaemic patients and it is thought that this can be cause low fertility in this group of patients. High values of ferritin level during childhood can be accompanied with hypogonadism. From the data obtained, it seems that males do not show very problematic endocrine problems. This can be seen in the table, where we can depict the mean testosteron level in the group of patients studied. From the diagrame of linear regression it is seen the increase of testosteron level towards normal values, paralelly to the decrease of ferritin level as a cosequence of treatment. Studying the trend of estradiol measured at females above 18 years of age, we can see that mean values tend to the lowest normal limit. High values of ferritin can be accompanied with low levels of estradiol (11). Using the linear regression, we can see that as ferritin level increaseswith 1 unit, estradiol levels decrease with 0.1 unit. We had the same result with folicular-stimulating hormone. luteinizing hormone (12).

4. Conclusion

As a result we can say that correlations found in our study, can support fully the importance of chelation therapy, in order to have a proper function of the organism of thalassaemic patients.

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Table 1: Ferritin level in males and females

	Ferritin Level (ng/ml)		P value
	First year	Third year	
Female >18yrs	1903.353	1783.5294	p= 0.28
Male >18 yrs	1901.941	1786.7647	p= 0.39

Table 2: Data of hormon levels

Variable	Testosteron	E2	FSH	LH
Number	20	26	26	26
Min. value	67.0	14.0	0.2	0.2
Max. value	987.0	45.0	4.6	12.0
Arithmetic mean	432.6	22.6	1.2	1.8
95% CI	299.5 - 565.6	19.4 - 25.8	0.87 - 1.64	0.66 - 3.10
SD	284.2	7.71	0.9	3.0

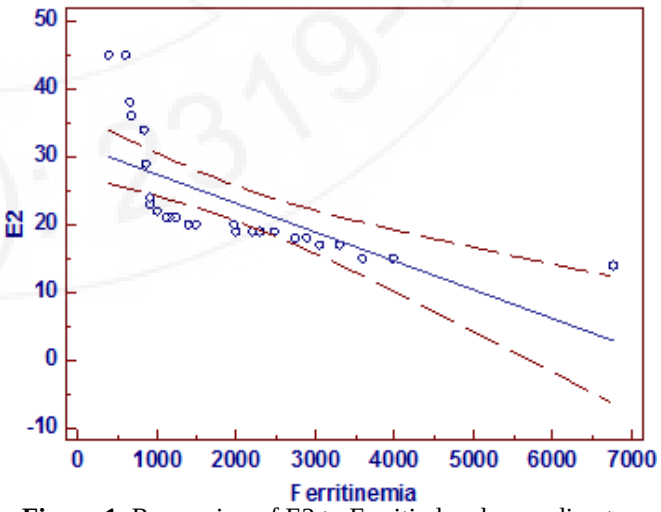

Figure 1: Regression of E2 to Ferritin level according to linear trend model (95%CI)

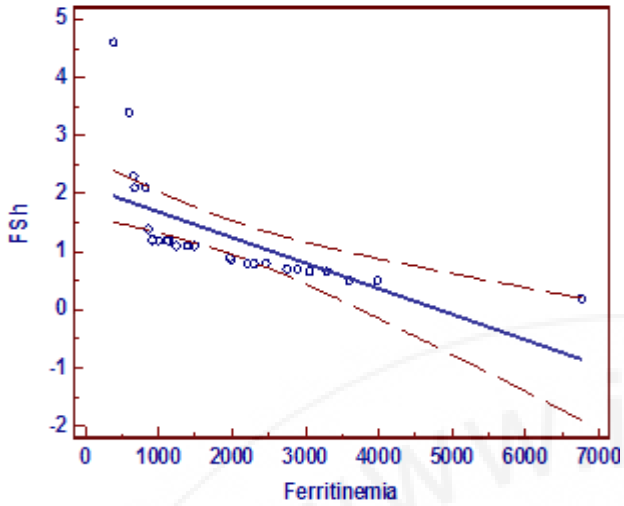

Figure 2: Regression of FSH to ferritin level according to linear trend model (95%CI)

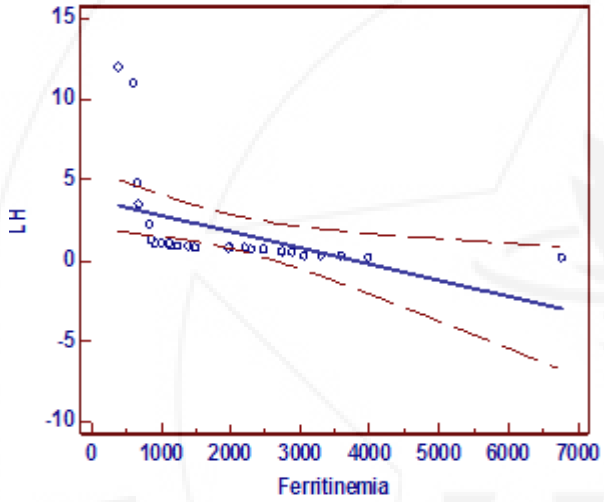

Figure 3: Regression of LH to ferritin level according to linear trend model (95%CI)

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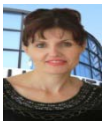

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