Study of Growth Hormone Levels in Thalassemia Major Patients in Children

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Abstract
Introduction: Thalassemia is an inherited disorder of hemoglobin synthesis. Regular blood transfusions and chelation therapy have noticeably prolonged survival in thalassemic patients.[1] Despite a significant increase in the life span of these patients, they suffer from multiple abnormalities probably due to iron overload, including endocrinological abnormalities such as hypogonadism, diabetes mellitus, hypothyroidism and hyperparathyroidism.[2] The pattern of levels of growth hormone levels among the patients with thalassemia major undergoing repeated blood transfusions remain unexplored. Very few studies have been undertaken among Indian population.
Methodology: It is a prospective study and was conducted at St George hospital, Mumbai, on diagnosed patients of thalassemia major admitted to the paediatric wards. Duration of the study was 3 months and 20 patients were included.
Inclusion Criteria
1. All admitted patients of thalassemia major aged 18 years and below.
Exclusion Criteria
1. Chronic haemolytic anemia apart from thalassemia major
2. Those that was very sick
3. Those suffering from malnutrition
4. Those who were on supplementation of growth hormone.
Patients who were willing to participate and sign the inform consent were enrolled in the study. Growth hormone levels were done using CLIA.
Results: The mean age of the studied thalassemia patients was 9.65 ± 4.23 years with no gender preponderance. Mean (SD) Growth hormone levels was 0.769 ng/dl ± 0.540 ng/dl and was not found to be statistically significant (p>0.001).
Conclusion: It is evident from the present study that the levels of Growth Hormone are normal among β-thalassemia major patients on repeated blood transfusion. But GH supplementation can help these patients. Frequent monitoring and supplementation in deficient states is recommended.
Keywords: Beta Thalassemia major, Growth Hormone levels.
Introduction

Thalassemias are a group of autosomally recessive inherited conditions characterised by the absence or reduced synthesis of The one of the two polypeptide chains (alpha ($\alpha$) or beta ($\beta$)) that form the normal adult human haemoglobin molecule (haemoglobin A, $\alpha_2\beta_2$) leading to reduced haemoglobin in red cells and anaemia. The thalassaemia syndromes are named according to the globin chain affected or the abnormal haemoglobin involved; mutations of the $\alpha$ globin gene cause $\alpha$ thalassaemia, while the $\beta$ globin gene defects give rise to $\beta$ thalassaemia. It has been estimated that about 1.5% of the global population (80 to 90 million people) are carriers of $\beta$ thalassaemia, with approximately 60,000 symptomatic individuals born annually.\[1\]

Similarly, $\alpha$ thalassaemia occurs at high frequencies throughout tropical and subtropical regions of the world. The thalassaemias can be classified according to phenotype (clinical severity) or genotype (type of mutation) in which clinical presentation can be highly variable ranging from asymptomatic carriers to transfusion-dependent thalassaemia. The more clinically severe forms of thalassaemia affect multiple systems, where the manifestations are either caused by the condition itself or by the complications from various treatments such as frequent blood transfusions. These individuals usually present within the first two years of life with severe anaemia and if untreated or poorly transfused, they suffer from growth retardation, poor musculature, hepatosplenomegaly, leg ulcers, development of masses from extramedullary hematopoiesis and skeletal changes due to bone marrow expansion. Regular blood transfusions will improve growth and development, reduce hepatosplenomegaly as well as bone deformities, but can lead to complications of iron overload such as cardiomyopathy, liver cirrhosis and endocrinopathies.\[1\]

Growth hormone deficiency (GHD) has been recognised as one of the endocrine complications amongst people with thalassaemia, especially in children with defective growth hormone production. This usually involves an injection of growth hormone under the skin (subcutaneously) several days a week over a period of time. However, it is unclear whether the use of synthetic growth hormone provides any consistent or clear benefits to people with thalassaemia.\[2\]

Growth issues in people with thalassaemia should be addressed with measures such as ensuring optimal transfusion and chelation therapies, treating nutritional deficiencies and prompt diagnosis and treatment of endocrinopathies such

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as hypothyroidism, abnormal glucose homeostasis, pubertal delay and GHD). As many of these aspects (such as proper transfusion regimens and chelation therapies) have been addressed, attempts to improve linear growth has increasingly included the used of GH replacement therapy.[1]

Materials and Methods
A prospective study was conducted in the department of pediatrics, St George hospital Mumbai. The study was conducted on diagnosed patients of thalassemia major admitted to the pediatric wards. Duration of the study was 3 months. Taking into consideration of availability of patients within data collection period, a total of 20 children, diagnosed with \( \beta \) thalassemia major were enrolled in the study. All the necessary information regarding the study was explained to the parents and informed written consent was taken from the parents who were willing to participate in the study. After obtaining written informed consent in local vernacular language, the patients who were fulfilling the inclusion criteria were included in the study.

Inclusion Criteria
1. All admitted patients of thalassemia major aged 18 years and below.

Exclusion Criteria
1. Chronic haemolytic anemia apart from thalassemia major
2. Those that was very sick
3. Those suffering from malnutrition

Statistical Analysis
All the data collected were entered in to a spreadsheet on Microsoft office Excel Sheet and then transferred to SPSS IBM version 21.0 for analysis. Significance of p value was taken as \( p<0.001 \).

Results and Observation
The mean age of the studied thalassemia patients was 9.65 ±4.23 years with no gender predilection. Mean (SD) Growth Hormone levels was 0.769 ± 0.540 ng/dl. Only 2 out of 20 samples were found to be low normal levels of growth hormone. As per Indian pediatric population, Growth Hormone concentrations of >0.09 ng/mL (4.06 pmol/L) are considered as sufficient, and <0.09 ng/mL (<4.06 pmol/L) as deficient \([\text{Figure 1and table 1.}]\) as shown in figure 1 and table 1.

Discussion
Mean (SD) Growth Hormone levels was 0.769 ± 0.540 ng/dl. The cut off GH deficiency is 0.09 ng/ml. Similar lower GH deficiency was found in other studies as well. In our study, it is found that only 10 % patients had growth hormone levels lower than required. This was not found to be significant with p value >0.001. Several studies have reports low growth hormone levels in thalassemia patients.\([10-14]\) These
were attributed to hepatic dysfunction and dysfunctions of endocrine tissues.\(^{[12]}\) This shows that thalassemics are at a little risk for growth hormone deficiency and hence may require a need for growth hormone supplementation.

**Conclusion and Recommendations**

We can conclude that the levels of growth hormone are not deficient among β-thalassemia major patients on repeated blood transfusion. There is no need to give growth hormone supplement considering the untoward side effects of growth hormone supplementation. But, it is important to emphasize that treatment of thalassemia patients with aggressive nutritional support which include fortified cereals, fortified milk are highly recommended. Supplementation with GH in these children would also help in normalisation of various other growth markers such as calcium, phosphorous and ALP.

We should try to screen all B-thalassemic children for growth hormone abnormalities, other hormone, vitamin D levels, calcium, and phosphorus levels as well.

**References**