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ORIGINAL RESEARCH REPORT

Study of gonadal hormones in Egyptian female children with sickle cell anemia in correlation with iron overload: Single center study

Adel A. Hagag [a,*], Mohamed S. El-Farargy [a], Shaymaa Elrefaey [a], Amany M. Abo El-enein [b]

[a] Department of Pediatrics, Faculty of Medicine, Tanta University, Egypt
[b] Department of Clinical Pathology, Faculty of Medicine, Tanta University, Egypt

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KEYWORDS
Gonadal hormones;
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Abstract
Objective/Background: Sickle cell disease is a hereditary hemoglobinopathy characterized by abnormal hemoglobin production, hemolytic anemia, and intermittent occlusion of small blood vessels, leading to tissue ischemia, chronic organ damage, and organ dysfunction including endocrine organs. The aim of this work was to evaluate some gonadal hormones in female children with sickle cell anemia (SCA) in correlation with iron overload.
Methods: This study was conducted on 40 female children with SCA with a serum ferritin of > 1000 ng/mL, who were attendants at the Hematology Unit, Pediatric Department, Tanta University, Tanta, Egypt in the period from May 2012 to April 2014. Their ages ranged from 11 years to 15 years and the mean age value was 12.63 ± 1.36 years (Group I). Forty female children with SCA of matched age with no iron overload served as a control Group (Group II). For all patients in Groups I and II the following were performed/assessed: complete blood count, hemoglobin electrophoresis, serum iron status, serum estrogen, luteinizing hormone (LH), and follicle-stimulating hormone (FSH).
Results: There were significantly higher serum ferritin and serum iron levels and significantly lower total iron binding capacity, FSH, LH, and estrogen levels in Group I compared with Group II (mean serum ferritin was 2635.1 ± 918.9 in Group I vs. 292.55 ± 107.2 in Group II with a *p* value of .001; mean serum iron was 196.3 ± 55.6 in Group I vs. 120 ± 16.57 in Group II with a *p* value of .001 and mean serum total iron binding capacity was 247.3 ± 28.6 in Group I vs.

* Corresponding author at: 16 Elemam Moslem street branched from Elhelw Street, Tanta, Gharbia, Egypt.
E-mail address: adelhagag20@yahoo.com (A.A. Hagag).

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327.8.7 ± 21.96 in Group II with a *p* value of .001; mean FSH level was 1.36 ± 0.22 mIU/mL in Group I vs. 2.64 ± 0.81 mIU/mL in Group II with a *p* value of .021; mean LH level was 0.11 ± 0.006 mIU/mL in Group I vs. 1.78 ± 1.12 mIU/mL in Group II with a *p* value of .003; mean estrogen level was 21.45 ± 10.23 pg/mL in Group I vs. 42.36 ± 15.44 pg/mL in Group II with a *p* value of 0.001) with significant negative correlation between serum gonadal hormones and serum ferritin (r = − .835 and *p* value of .01 for FSH and serum ferritin; r = − .597 and a *p* value of .01 for LH and serum ferritin; and r = − 0.624 and *p* value of .01 for estrogen and serum ferritin.

Conclusion: Female patients with SCA with iron overload may have gonadal hormone deficiency with significant negative correlations between gonadal hormones including FSH, LH, estrogen, and serum ferritin. Recommendations include regular iron chelation for prevention of irreversible damage of the ovaries and attaining normal sexual maturation, and regular follow up for females with SCA with assessment of puberty as they are more vulnerable to develop hypogonadism and may require hormonal replacement therapy.

Introduction

Sickle cell disease (SCD) is a hereditary hemoglobinopathy characterized by abnormal sickle hemoglobin (HbS) production, hemolytic anemia, and intermittent occlusion of small blood vessels, leading to acute and chronic tissue ischemia, chronic organ damage, and organ dysfunction including endocrine organs [1]. HbS is common and clinically significant structural hemoglobin variant [2].

HbS is caused by a mutation in the *β-globin* gene in which the 17th nucleotide is changed from thymine to adenine and the sixth amino acid in *β-globin* chain is changed to valine instead of glutamic acid; this mutation produces hydrophobic motif in the deoxygenated HbS tetramer that results in binding between β1 and β2 chains of two hemoglobin molecules. This crystallization produces a polymer nucleus, which grows and fills the erythrocyte, disrupting its architecture and flexibility and promoting cellular dehydration, with physical and oxidative cellular stress [3].

Endocrine dysfunction is commonly encountered in hematological diseases like thalassemia and SCD. The physiopathology of endocrine organ pathology is not clear in patients with SCD; however, iron storage due to recurrent and frequent transfusions, or ischemia due to vaso-occlusive crises and inflammatory mediators during ischemia are proposed as the main reasons for endocrine dysfunctions [4].

The prevalence of endocrine complications among children with sickle-cell anemia (HbSS) varies in different populations depending on the literacy rate, socio-economic status, availability of regular chelation therapy, and transfusions [5].

Gonadal iron deposition and gonadal damage due to iron overload is an irreversible process even if the iron level is corrected at a later stage of the SCD [6]. This reflects the importance of early and regular use of iron chelators for prevention of irreversible damage of the ovaries and attaining normal sexual maturation and the necessity of regular follow up for gonadal hormones with assessment of puberty as females with thalassemia and SCA are more vulnerable to develop hypogonadism and may be in need of hormonal replacement therapy to be capable of achieving pregnancy [7]. The aim of this work was to evaluate some gonadal functions in females with HbSS.

Material and methods

This study was done after the approval from the Ethical Committee of the Research Center of Tanta University, Tanta, Egypt and parental consent was received for all children included in this study. The study was carried out on 40 females with HbSS who were attendants at the Hematology Unit, Pediatric Department, Tanta University in the period from May 2012 to April 2014, whose ages ranged from 11 years to 15 years and the mean age value was 12.63 ± 1.36 years (Group I), and 40 female children with HbSS with ages ranging from 11 years to 15 years and with a mean age value of 12.22 ± 1.13 years with no iron overload as a control group (Group II).

This study included females with HbSS with serum ferritin of >1000 ng/mL (with iron overload) that came to our Hematology Center within a 2-year period of the study (40 female patients).

Females with HbSS under hormonal therapy were excluded from this study.

All patient and control Groups were subjected to the following: (a) complete history taking; (b) thorough clinical examination with special attention to anthropometric measurements including weight and height, pallor, jaundice, splenomegaly, hepatomegaly, and Tanner staging for assessment of puberty [8]; and (c) laboratory investigations.

Specimen collection and handling

Five milliliters of venous blood were collected using sterile needles through gentle venipuncture after sterilization of the puncture site with alcohol, and collected samples were divided into: (a) 2 mL in 20 μL ethylenediaminetetraacetic acid solution for complete blood count including differential white blood cells count which was done on a Leishman stained peripheral blood smear with evaluation using an ERMA PCE-210 N cell counter (fully automated blood cells