The recommendation of the International Network of Clinicians for Endocrinopathies in Thalassemia and Adolescent Medicine for the assessment of growth hormone secretion in thalassemia

Dear Sir,

In a previous paper published in your journal, we reported the Position Statement and Guidelines on Growth and Endocrine Disorders in Thalassemia.[1] The diagnosis of growth hormone deficiency (GHD) is generally straightforward in children as growth retardation is present. However, in adults the diagnosis of GHD is often challenging. GHD in adults is a clinical syndrome associated with lack of positive well-being, depressed mood, feelings of social isolation, decreased energy, alterations in body composition with reduced bone and muscle mass, diminished exercise performance and cardiac capacity and altered lipid metabolism with increase in adiposity.[2]

In patients with chronic diseases, the clinical evaluation of GHD is difficult because signs and symptoms may be subtle and nonspecific, and universal provocative testing in

all patients is difficult because the approach is cumbersome and expensive.[1,2] Therefore, other markers are needed to identify adults who may have GHD and could potentially benefit from GH replacement therapy. Recent studies suggest that insulin-like growth factor-1 (IGF-1) may be used for primary screening, to avoid performing GH stimulation tests in the majority of healthy or diseased subjects, when appropriate normative sex and age-correlated ranges are available.[3] Therefore, the International Network of Clinicians for Endocrinopathies in Thalassemia and Adolescence Medicine (ICET-A) promoted a study to collect more information on IGF-1 values in young adult Italian thalassemia major (TM) patients.

Plasma total IGF-1 was determined on ethylenediaminetetraacetic acid by chemiluminescent immunometric assay method (Nichols Institute Diagnostics, San Juan, CA). The assay was performed after separation of IGF-1 from binding proteins by Liaison® autoanalyzer (DiaSorin SpA, Saluggia, Italy). The sensitivity of the test was 6 ng/ml, whereas the intra- and inter-assay coefficients of variations of our in-house pooled serum control sample were 4.8% and 7.1%, respectively. Of the 120 patients, 58 (48%) were males and 62 (52%) females, with an age range of 26.0–53.2 years for females and 20.8–51.2 years for males. 64.4% of the patients were above 35 years of age. The mean body mass index was 22.48 ± 3.34 kg/m^2.

The results, expressed in percentiles, are reported in Figure 1. No significant differences were observed between IGF-1 values in men and women with TM (Student's *t*-test: 1.18; $P = 0.249$).

Based on the present results and data from the literature, ICET-A concluded their survey with the following recommendations: A GH stimulation test should be indicated in presence of the following clinical and laboratory parameters: Short stature (Height standard deviation scores <−2.5), severe and/or prolonged iron overload, presence of severe osteoporosis and/or serum IGF-I level <−2 standard deviations. Very low IGF-1 levels, especially in those patients with childhood-onset GHD, in the presence of pituitary iron deposition and/or atrophy are highly suggestive of GHD.[4] In adult TM patients, with normal liver function, an IGF-I level <50th percentile [Figure 1] should be taken in consideration as a cut-off level for the GH assessment.[3]

With kindest regards and thanks from the ICET-A network.

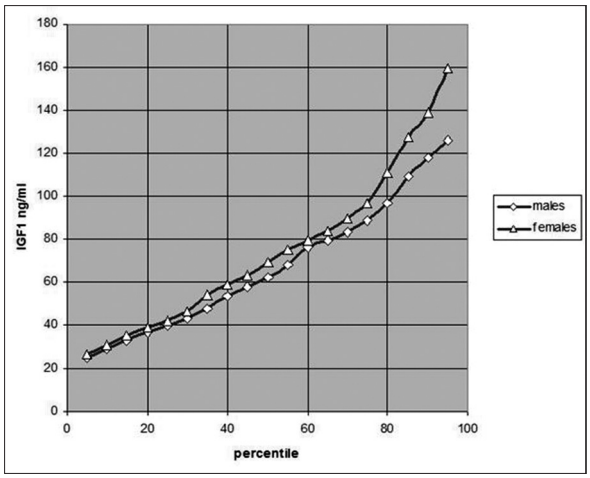

Figure 1: Percentile of insulin-like growth factor-1 level in females and males with β thalassemia major

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