Presentation of the International Network of Clinicians for Endocrinopathies in Thalassemia and Adolescence Medicine (ICET-A)

Today many subjects with thalassaemia major (β-thal) successfully survive into adult life, due to remarkable improvement of medical care and to a better understanding of pathogenesis, clinical manifestations and prevention of endocrine complications.

Despite the improvement of the treatment, the involvement of the endocrine system still burdens the life of these patients. In fact, several studies have reported that as many as 51% to 66% of patients may have pubertal failure, sexual dysfunction and infertility, due to hypogonadism.

The causes of endocrine complications in general population are multiple while in β-thal are classically considered to be mainly the result of iron deposition in the endocrine glands.
Iron overload may be the result of economic circumstances (expense of the chelation therapy), late onset of chelation therapy or poor compliance with treatment.

Other factors contributing to the variability of cellular iron overload are cell surface transferring receptors and the capacity of the cells to deploy defence mechanisms against inorganic iron. Liver disorders, chronic hypoxia and associated endocrine complications, such as diabetes may be additional factors.

Toxicity starts when the iron load in a particular tissue exceeds the tissue or blood-binding capacity of iron, and free non-transferrin iron appears. The 'free iron' is a catalyst of the production of oxygen species that damage cells and peroxidize membrane lipids, leading to cell destruction.

The anterior pituitary gland is particularly sensitive to the free radicals produced by oxidative stresses and exposure to these radicals injurious to the gland. Magnetic resonance imaging (MRI) shows that even a modest amount of iron deposition within the anterior pituitary can interfere with its function. Excess iron deposition in the anterior pituitary leads to degranulation of the adenohypophysis and decreased hormone storage with ensuing hypogonadism due to pituitary hyporesponsiveness to gonadotrophin releasing hormone .

Combined therapy (use of two chelators on the same day), may induce negative iron balance and may reverse hypogonadism and endocrine complications in severe iron overloaded β-thal subjects. Long-term studies have shown that deferiprone and deferoxamine (DFO) have shown to accelerate iron chelation by rapidly reducing liver iron, serum ferritin, and myocardial siderosis.Combination chelation therapy with deferasirox and DFO has also been shown beneficial.

Despite the fact that endocrine complications are very common in multi-transfused thalassaemia patients a recent survey conducted by the International Network of Clinicians for Endocrinopathies in Thalassemia and Adolescence Medicine (ICET-A) in 2014 in Acitrezza (Catania,Italy) showed that the major difficulties reported by hematologists or pediatricians experienced in thalassaemias or thalassaemia syndromes in following endocrine complications were:

1. Lack of familiarity with medical treatment of endocrine complications
2. Interpretation of endocrine tests
3. Lack of collaboration and on-time consultation between thalassaemic centers supervised by hematologists and endocrinologists

The practical objectives of ICET-A are to encourage and guide endocrinological follow up of multi-transfused patients in developing countries, to promote and support collaborative research in this field, to encourage and guide endocrinological follow up of multi-transfused patients, and to educate and train more endocrinologists and other paediatricians/physicians to prevent and improve management of the growth and endocrine complications in these patients. This is in agreement with a fundamental requirement of medical ethics, that any progress we make in research into growth disorders and endocrine complications in thalassaemia should be passed on to all those suffering from such disorders.

On the 8th of May, 2009 in Ferrara (Italy) the International Network on Endocrine Complications in Thalassaemia (I-CET) were founded. The team of doctors who have taken the initiative and have formed the initial core group include endocrinologists: Vincenzo de Sanctis (Italy), Ashraf Soliman (Qatar), Nicos Skordis (Cyprus), Mohamed El Kholy (Egypt), Heba El Sedfy (Egypt), Giuseppe Raiola (Italy), Ploutarchos Tzoulis (UK) and Piernicola Garofalo (Italy) . In addition doctors experienced in thalassaemia care are supporting the group. These include: Christos Kattamis (Greece), Mohamed Yassin (Qatar), Mehran Karimi (Iran), Praveen Sobti (India), Bernadette Fiscina (USA), Duran Canatan and Yurdanur Kilinç (Turkey), Michael Angastiniotis (Cyprus), Hala Rimawi (Jordan), Ludmila Papusha (Russia), Soad K Al Jaouni (Saudi Arabia), Shahina Daar (Oman), Su Han Lum (Malasya), Maria Concetta Galati, Saveria Campisi and Salvatore Anastasi (Italy).

From March 2014, the I-CET acronym has changed and extended to International Network of Clinicians for Endocrinopathies in Thalassemia and Adolescence Medicine (ICET-A).

We hope our effort will be useful for all those who are taking care of thalassaemic and adolescent patients with growth disorders and endocrine complications.

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