Hormone related problems (Endocrinopathies and osteoporosis)

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The majority of cases of hemoglobinopathy -associated endocrine dysfunction have been reported in subjects with thalassemia major (TM) rather than thalassemia intermedia or with sickle cell disease (SCD). However, patients with SCD often require blood transfusion starting in early childhood.

Iron accumulates in tissues with high levels of transferrin-receptor such as liver, heart and endocrine glands.Delayed puberty and hypogonadism are the most obvious clinical consequences of iron overload. Other endocrine organs plagued by iron deposition secondary to multiple transfusions include the pancreas, thyroid, and parathyroid glands leading to diabetes mellitus (DM), acquired hypothyroidism and hypoparathyroidism, respectively. Apart from iron overload, other factors responsible for organ damage have been previously pointed out, including chronic hypoxia due to anemia that may potentiate the toxicity of iron deposition in endocrine glands. Also, chronic liver disease, zinc deficiency, under nutrition and psychosocial stress have been implicated in causing endocrine dysfunction.

Zinc deficiency due to urinary losses is common in subjects with SCD and studies by Prasad and Cossack suggested that zinc deficiency in adolescent patients with SCD was associated with growth retardation and hypogonadism in males. Although zinc supplementation in this population improved testosterone levels and longitudinal growth, the underlying mechanism has not been fully elucidated.

Osteopenia and osteoporosis are the most common bone complications of TM, despite regular transfusions and iron chelation therapy. The etiology of TM-induced bone mineral loss is multi-factorial. Medullary expansion due to anemia, patient age, duration of the disease, chronic liver disease, vitamin D deficiency, hypogonadism, concurrent hypothyroidism, and other endocrine-associated complications are significant contributory factors.

Blood exchange transfusion in SCD and the use of iron chelation therapy in subjects with iron overload (TM and SCD) may prevent, delay or improve the endocrine complications.To achieve this aim in dealing with amulti-organ pathology as encountered in these patients, a coordinated multidisciplinary team of specialists is required. Such a team must include an endocrinologist, preferably experienced in the management of hormonal deficiencies caused early in life by transfusion-induced iron overload.

Treatment of endocrine dysfunction includes replacement of particular hormone deficiency and improvement of nutritional status; the goals of hormone replacement therapy for patients with iron overload are to achieve normal levels of circulating hormones, restore normal physiology and to avoid symptoms of deficiency with minimal side effects. Endocrine referral is recommended for hormone replacement (estrogen for females, testosterone for males), adrenal insufficiency, vitamin D and calcium supplementation, and consideration of bisphosphonates.