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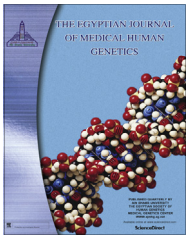

EDITORIAL

Subclinical hypothyroidism in children with Down syndrome: To treat or not to treat???

Congenital hypothyroidism is 30 times more frequent in newborns with Down syndrome (DS) than in the population of healthy children [1]. Mild isolated plasma thyrotropin (TSH) elevation with normal thyroxine (T4) levels is the most commonly seen pattern of thyroid dysfunction in these children [2,3]. Other terminology used for this pattern of abnormality includes isolated hyperthyrotropinemia, compensated hypothyroidism, and subclinical hypothyroidism [4,5]. The prevalence of mild TSH elevation (4–10 mIU/l) is estimated at 80–90% in early infancy and 30–50% thereafter [3].

The cause of neonatal hypothyroidism in this particular syndrome remains unclear; most patients have normal thyroid scans excluding thyroid agenesis or ectopic thyroid tissue. The absence of goiter suggests that it is not caused by dyshormonogenesis [6,7]. Some authors suggested that it could be due to a delay in the maturation of the hypothalamic-pituitary-thyroid axis [8]. Others postulated that infants with transient TSH elevation have a higher incidence of congenital malformations than infants with permanent congenital hypothyroidism [9]. So, it may be hypothesized that newborns with congenital malformations similar to DS suffer perinatal stress, which may lead to TSH elevation [10].

Other possible explanations include an inappropriate release of TSH related to a central disorder, the production of a less active form of TSH, or some form of TSH insensitivity in the thyroid gland [11].

The issue whether treatment of this mild form of subclinical hypothyroidism is beneficial to children with DS is still controversial especially that this particular type of thyroid dysfunction is self-limiting and high TSH tends to normalize spontaneously in most of the DS patients [11]. Keeping in mind that elevated TSH levels in early life cannot predict the development of manifest thyroid disease later in childhood [12].

It is known that mild thyroid insufficiency may diminish tissue sensitivity to growth hormone in normal children [13]. The same occurs in children with DS. Sharav et al. reported that growth in DS children with a TSH value >5.7 mIU/l was particularly retarded in comparison to the general population of children [14].

On the other hand, Selikowitz annually assessed the health condition of 101 children with DS. No significant differences in growth and development between those with subclinical hypothyroidism and those with normal thyroid function were revealed [15]. Also, Gruneiro de Papendieck et al. did not notice a significant difference in height SDS between groups of children with TSH levels below and above 5 mIU/l [16].

Later, a randomized double-blind 24-month trial comprising 196 DS neonates with subclinical or overt hypothyroidism was found to have a statistically significant difference in length and weight gains between treated and placebo groups [17]. This was further supported by Kowalczyk et al. [18] work which showed that early administration of L-thyroxin DS children with subclinical or overt hypothyroidism results in a significant improvement in the growth of these children [18]. Not only their physical growth but they also noticed a significant improvement in their psychomotor development [18].

Moreover, subclinical hypothyroidism may also significantly increase hypotonia and anemia in these children [19].

Subclinical hypothyroidism has also been associated with hypercholesterolemia atherosclerosis and eventually coronary heart disease particularly in those with a TSH concentration of 10 mIU/L or greater [20,21]. Moreover, subclinical hypothyroidism increases arterial stiffness and diastolic dysfunction [22].

It has long been known that DS patients have higher cholesterol levels [23] and recently they were found to have a significantly higher left ventricular diastolic dysfunction than that observed in the controls [24]. So not giving L-thyroxin to subclinical hypothyroidism in DS children would further increase their cholesterol level, diastolic dysfunction and their risk of coronary heart disease.

In conclusion, subclinical hypothyroidism is the most common thyroid dysfunction in DS. Although it is a self-limiting condition, L-thyroxin administration will improve growth, hypotonia and psychomotor functions. It may also decrease the risk of hypercholesterolemia, hypertension and eventually coronary heart disease in these children.

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