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CONSENSUS DOCUMENT

Consensus document of the Neuroendocrinology area of the Spanish Society of Endocrinology and Nutrition on management of hypopituitarism during transition☆

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Hormone replacement

Abstract The transition period from child to adult represents a crucial phase in the growth process where multiple physical and psychosocial changes occur. It has been arbitrarily defined as the period extending from late puberty to full adult maturity (i.e., from mid to late teenage years until 6–7 years after achievement of final height).

The aim of this guideline is to emphasize the importance of adequate hormone replacement during this period and to review reassessment of pituitary function. In patients with GH deficiency diagnosed in childhood, an attempt is made to answer when to retest GH secretion, when to treat and how they should be monitored. Thyroxine, glucocorticoid, and sex steroid replacement is also reviewed.

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PALABRAS CLAVE
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Documento de consenso del área de conocimiento de Neuroendocrinología de la Sociedad Española de Endocrinología y Nutrición para el abordaje del hipopituitarismo durante la transición

Resumen Se entiende por periodo de transición del niño al adulto a una etapa de cambios físicos y psicológicos que, de forma arbitraria, se extiende desde el final de la pubertad hasta que la maduración adulta se completa. Comprende, habitualmente, los 6 a 7 años posteriores al momento en que el niño adquiere la talla adulta.

Con esta documento pretendemos poner de manifiesto la importancia de la adecuada sustitución de los diferentes déficits hipotálamo-hipofisarios durante este período. Para ello revisamos la reevaluación del status hipofisario en los pacientes deficitarios durante la infancia. Tratamos de dar respuesta a las preguntas que pueden surgir y ofrecemos unas recomendaciones claras de cómo abordar la deficiencia de GH en este período. Posteriormente abordamos también la evaluación y la sustitución del eje adrenal, tiroideo y gonadal.

Introduction. Definition of transition

The transition period from child to adult is defined as a stage of physical and psychological changes arbitrarily considered to extend from late puberty to complete adult maturity. It usually comprises the six or seven years subsequent to the attaining of adult height by the child.[1]

The transition of patients with growth hormone deficiency from the pediatric to the adult endocrinology teams

Although the use of growth hormone (GH) during the transition period continues to be controversial, there is increasing interest in determining: (a) tissue maturation over time in GH-deficient and healthy adolescents; (b) the potential consequences of treatment discontinuation or ''holidays''; and (c) the effect, if any, of GH replacement on fracture morbidity and cardiovascular disease. Only long-term follow-up in prospective studies can clarify these issues.

Growth vs body maturity. Current problems in the transition period

Longitudinal growth is considered to be completed when growth velocity is less than 1.5–2.5 cm/year and/or bone maturation is 97–98%. These goals are usually achieved at a bone age of 14–15 years in girls and 16–17 years in boys. In this situation, only a small residual capacity of longitudinal growth is left. However, body maturity—lean mass, fat, and bone mineral density (BMD)—is not complete yet, and may not occur in some cases until up to almost 30 years of age. It is generally accepted that:

- Peak bone mass is achieved between 20 and 25 years.
- Muscle mass increases even beyond 20 years of age in males and 14 years in females.
- Fat mass increases even beyond 20 years of age in females and until the end of puberty in males.
- That is, females gain fat mass and males gain muscle mass after the end of puberty.

A comparison of equivalent groups of patients with adult-onset (AO), previously untreated GH deficiency and patients with child-onset (CO) GH deficiency adequately treated to the end of longitudinal growth shows that the latter have: a shorter height (−1 standard deviation [SD]), lower body mass index (BMI), 80% of the lean mass, fat, and BMD values in the AO group, and levels of insulin-like growth factor type 1 (IGF-1) and insulin-like growth factor binding protein 3 (IGFBP3) 3 or 4 SD lower as compared to the AO group.

That is, for a similar GH deficiency, significant differences are seen between the CO and AO groups, which may be due to a restriction of adult body maturity due to untreated GH deficiency during the transition period. Thus, the discontinuation of treatment with GH in boys with GH deficiency at the end of longitudinal growth is associated with: (a) decreased muscle strength and mass; (b) increased body fat, mainly in the abdomen; (c) the arrest or reversal of muscle mass and BMD gain, with decreased bone formation markers; and (d) lipid profile impairment and, predictably, the occurrence of the typical features of adult-onset GH deficiency, which may lead to increased cardiovascular risk.[2–4]

Body development is not complete at the end of growth, and the available studies show evidence suggesting that GH action is required in the post-pubertal transition phase to achieve normal adult status. CO patients are not and should not be considered as adults at the time of the final dose of GH at the end of growth. We recommend that they receive specific care and continue to receive treatment to complete body development.

The transition phase is not usually clearly included in published consensuses and guidelines on GH treatment in children and adults, and we therefore face:

a) Clinical problems: the literature on transition is characterized by a lack of information about:
   - What the objectives of treatment with GH in this stage should be, and how previously deficient subjects should be re-evaluated (different clinical criteria).
   - GH dosage.