Opinion

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Challenges of Growth Hormone Therapy in PWS during Transition

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Patients with PWS present with a host of disorders (i.e., multiple hormone deficiencies, hyperphagia, obesity, sleep apnea, intellectual disabilities, and behavioral and psychiatric issues), many of which appear, or worsen, during adolescence. Optimal healthcare

Table 1. Growth hormone for Prader–Willi syndrome: challenges for future research (adapted from ref 8)

Pediatric age
Optimal dosage of GH therapy from early infancy to adolescence
Effects of GH treatment in PWS children born SGA (compared to AGA)
Clinical impact of GHD on GH therapeutical response
Transition age
Evaluation of GH secretory pattern with respect to the clinical response of subsequent GH therapy?
• Who and when do we retest?
• How do we retest?
• How is growth hormone deficiency defined?
• Who do we consider treating?
• What are the end points of growth hormone treatment?
• At what age does transition start?
• How transition process should be improved?
Clinical impact of GH therapy early after completion of linear growth and influence of GH secretory status
• Cognitive function and behavior
• Body composition
• Bone mineralization
• Muscle strength
• Others
Adult age (>25 years)
Evaluation of GH secretory pattern with respect to the clinical response of subsequent GH therapy
Influence of GH therapy in non-GH-deficient patients
Cardiovascular and respiratory effects of GH treatment
All ages
Long-term surveillance of benefits and risks of GH replacement, including risk of neoplasia
Genotype–phenotype correlation and GH therapy
Role of GH therapy on bone health
Role of concomitant therapies on GH therapeutic effects (sex steroids, diet, physical therapy, etc)

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management during this critical time requires a multidisciplinary transition team.

Several studies report an insufficient rise in GH upon stimulation (8–67%) and low IGF-I levels in the majority of adult patients (75–91%) with PWS indicating reduced activity of the GH/IGF-I axis[1-3]. There are conflicting results regarding GHD in young adult patients with PWS with more recent papers reporting fewer cases of GHD, perhaps due in part to the difficult diagnosis of GHD associated with obesity. While hormone replacement therapy does not change the intrinsic abnormalities of PWS, treatment with GH improves body composition, physical fitness, bone size and strength, and QoL[4]. Early diagnosis, combined with multidisciplinary care including GH replacement and use of other hormonal therapies, can ease PWS complications, ameliorate comorbidities, and improve QoL and transition to adult life in these patients[5]. Clinical experience suggests a positive response with replacement of sex steroids, confirmed in men with PWS in the only treatment trial conducted to date[6]. However, additional studies with hormone replacement, particularly during transition, are needed.

Current evidence supports the view that GH replacement for PWS exerts a beneficial effect on physical aspects, cognition, and behavioral phenotype in both pediatric and adult populations[7-9]. In particular, patients with a low cognitive function had more loss in IQ points during placebo versus GH treatment in a recent randomized, double-blind, placebo-controlled crossover study in young adults with PWS[9]. Thus, GH retesting after achievement of adult height should be taken into consideration in PWS patients with the intention to treat those with permanent GHD, and BMI-specific cutoff values of GH response to stimulation tests are warranted.

There is little literature on several topics related to the role of GH therapy in lifelong care of these patients and whether the genotype–phenotype correlations may be relevant to specific outcome measures related to GH therapy (Table 1). In this light, further research is required to improve our understanding of the physiopathology of GH/IGF-I axis during the entire lifespan of PWS subjects. A more detailed knowledge of the therapeutic targets of GH administration (Cognitive, body compostion, bone) is also needed, with the aim to optimize the clinical management of these individuals and their transition process[10]. At the same time, the role of concomitant therapies (sex steroids, dietary treatment, physical therapy) in the effects of GH administration should be better elucidated. Since most of the current studies are uncontrolled and of short duration, a long-term surveillance of benefits and risks (Diabetes ….) of GH therapy is strongly recommended for PWS population after the attainment of adult height.

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