Growth hormone therapy for Prader-Willi syndrome: challenges and solutions

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Prader-Willi syndrome (PWS) is characterized by a dysregulation of growth hormone (GH)/insulin-like growth factor I axis, as the consequence of a complex hypothalamic involvement. PWS' clinical picture seems to resemble the classic non-PWS GH deficiency (GHD), including short stature. excessive body fat, decreased muscle mass, and impaired quality of life. GH therapy is able to ameliorate the phenotypic appearance of the syndrome, as well as to improve body composition, physical strength, and cognitive level. In this regard, however, some pathophysiologic and clinical questions still remain, representing a challenge to give the most appropriate care to PWS patients. Data about the prevalence of GHD in PWS children are not unequivocal, ranging from 40% to 100%. In this context, to establish whether the presence (or not) of GHD may have a different effect on clinical course during GH therapy may be helpful. In addition, the comparison of GH effects in PWS children diagnosed as small for gestational age with those obtained in subjects born appropriate for gestational age is of potential interest for future trials. Emerging information seems to demonstrate the maintenance of beneficial effects of GH therapy in PWS subjects after adolescent years. Thus, GH retesting after achievement of final height should be taken into consideration for all PWS patients. However, it is noteworthy that GH administration exerts positive effects both in PWS adults with and without GHD. Another critical issue is to clarify whether the genotype-phenotype correlations may be relevant to specific outcome measures related to GH therapy. Moreover, progress of our understanding of the role of GH replacement and concomitant therapies on bone characteristics of PWS is required. Finally, a long-term surveillance of benefits and risks of GH therapy is strongly recommended for PWS population, since most of the current studies are uncontrolled and of short duration.